STATISTICAL ANALYSIS PLAN

SEP361-304

A RANDOMIZED, DOUBLE-BLIND, ACTIVE COMPARATOR-CONTROLLED STUDY TO EVALUATE THE LONG-TERM SAFETY AND TOLERABILITY OF SEP-363856 IN SUBJECTS WITH SCHIZOPHRENIA

PHASE: PHASE III

AUTHOR: PPD

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STATISTICAL ANALYSIS PLAN SIGNATURE PAGE

Statistical Analysis Plan V0.6 (Dated 30JAN2023) for Protocol SEP361-304.

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Upon review of this document, the undersigned approves this version of the Statistical Analysis Plan, authorizing that the content is acceptable for the reporting of this study.

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1. INTRODUCTION

This document describes the rules and conventions to be used in the presentation and analysis of safety, efficacy and pharmacokinetic (PK) data for Protocol SEP361-304. It describes the data to be summarized and analyzed, including specifics of the statistical analyses to be performed.

This statistical analysis plan (SAP) is based on protocol version 3.00, dated 14JAN2021.

The Data and Safety Monitoring Board (DSMB) analysis plan will be described in a separate document. An Important Protocol Deviation (IPD) Review Plan and a Blinded Data Review (BDR) Plan will be written to describe the process and the outputs to be delivered during the IPD/BDR meetings.

2. STUDY OBJECTIVES AND ENDPOINTS

2.1. STUDY OBJECTIVES

2.1.1. STUDY OBJECTIVES

The primary objective is to evaluate the long-term safety and tolerability of flexibly-dosed SEP-363856 (50, 75, and 100 mg/day) in clinically stable adult subjects with chronic schizophrenia based on safety parameters, including the incidence of overall adverse events (AEs), serious AEs (SAEs) and AEs leading to discontinuation.

2.1.2. OTHER SAFETY OBJECTIVES

The other safety objectives are:

- To evaluate the long-term safety and tolerability of SEP-363856 by assessing:

  - Physical examinations (PE)

  - 12-lead electrocardiograms (ECG)

  - Vital sign measurements

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- Clinical laboratory tests

- Suicidality using the Columbia – Suicide Severity Rating Scale (C-SSRS)

- Movement disorder abnormalities using the modified Simpson-Angus Scale (SAS), the Barnes Akathisia Rating Scale (BARS) and the Abnormal Involuntary Movement Scale (AIMS)

- To evaluate the effects of SEP-363856 (50 to 100 mg/day) on prolactin, HbA1c, lipids, and glucose concentrations, body weight, and body mass index (BMI) compared to Quetiapine XR (400 to 800 mg/day)

- To evaluate the impact of SEP-363856 on healthcare resource utilization

2.1.3. OTHER EFFICACY OBJECTIVES

The other efficacy objectives are:

- To evaluate the long-term effectiveness of SEP-363856 and Quetiapine XR using the

  - Positive and Negative Syndrome Scale (PANNS)

  - Clinical Global Impression-Severity (CGI-S) scale

  - Brief Negative Symptom Scale (BNSS)

  - Montgomery-Asberg Depression Rating Scale (MADRS)

- To evaluate the maintenance efficacy of SEP-363856 and Quetiapine XR (including time to relapse, rate of relapse and frequency of hospitalization due to relapse)

- To evaluate adherence to study treatment based on time to all cause discontinuation

- To evaluate the effects of SEP-363856 and Quetiapine XR on daytime sleepiness as measured by the Epworth Sleepiness Scale (ESS)

- To assess the effects of SEP-363856 and Quetiapine XR on cognition as measured by the Brief Assessment of Cognition in Schizophrenia (BACS)

- To explore the effects of SEP-363856 and Quetiapine XR on functional capacity as measured by the University of California San Diego (UCSD) Performance-Based Skills Assessment – Brief Version

(UPSA-B)

- To evaluate the effects of SEP-363856 and Quetiapine XR on function as measured by the modified Specific Level of Functioning Scale (SLOF)

- To evaluate the effects of SEP-363856 and Quetiapine XR on health-related quality of life as measured by the EuroQol-5D-5L (EQ-5D-5L)

- To evaluate medication satisfaction as measured by the Medication Satisfaction Questionnaire (MSQ)

- To explore the impact of SEP-363856 on nicotine use

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2.2. STUDY ENDPOINTS

2.2.1. PRIMARY ENDPOINT

The primary endpoint is the incidence of overall AEs, SAEs, and AEs leading to discontinuation.

2.2.2. OTHER SAFETY ENDPOINTS

The other safety endpoints are:

- Observed values and changes from Baseline in clinical laboratory tests (hematology, chemistry and urinalysis)

- 12-lead ECG (including heart rate, RR, PR, QRS, QT, QTc-F, and QTc-B)

- Observed values and changes from Baseline in vital signs (including body weight, BMI, waist circumference, temperature, blood pressure [supine and standing], heart rate [supine and standing] and respiratory rate)

- Frequency and severity of suicidal ideation and suicidal behavior based on the C-SSRS

- Changes from Baseline in BARS, AIMS and SAS scores

- Healthcare resource utilization (HRU) (including numbers of physical office visits, emergency room (ER) visits and hospitalizations, length of hospital stays, employment status and average number of hours caregiver spends helping subjects per week).

2.2.3. OTHER EFFICACY ENDPOINTS

The other efficacy endpoints are:

- Changes from Baseline in:

    - PANSS total score and subscale scores (positive, negative, and general psychopathology)

    - CGI-S score

    - BNSS total score

    - MADRS total score

    - ESS total score

    - BACS composite score

    - UPSA-B total score

    - SLOF total and subscale scores

    - EQ-5D-5L visual analog scale (VAS), index score and dimension score

    - MSQ score

- Time to relapse, rate of relapse, and frequency of hospitalization due to relapse. Relapse will be defined as the earliest occurrence of any of the following:

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- Worsening of >30% PANSS total score from Baseline and CGI-S >3

- Hospitalization for worsening of psychosis

- Emergence of suicidal ideation, homicidal ideation and/or risk of harm to self or others

- Discontinuation from the study due to exacerbation of the underlying illness of schizophrenia

- Time to all cause discontinuation from the study

- Change from Baseline in tobacco use

- Plasma cotinine concentrations

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3. STUDY DESIGN

3.1. GENERAL DESCRIPTION

This is a 52-week, multicenter, randomized, double-blind, parallel-group, flexible-dose study designed to evaluate the long-term safety and tolerability of SEP-363856 (50 to 100 mg/day) in clinically stable adults with schizophrenia. This study is projected to randomize approximately 300 subjects to two treatment groups (SEP-363856 50 to 100 mg/day or Quetiapine XR 400 to 800 mg/day) in a 2:1 ratio.

Study drug will be taken at the same time each evening at bedtime and should be taken without food or with a light meal.

The study will consist of three periods: Screening/Washout (up to 21 days), Treatment (52 weeks) and a Follow-up Visit (7 days after the last study drug dose).

A study schematic is presented in Figure 1.

Figure 1: Study schematic
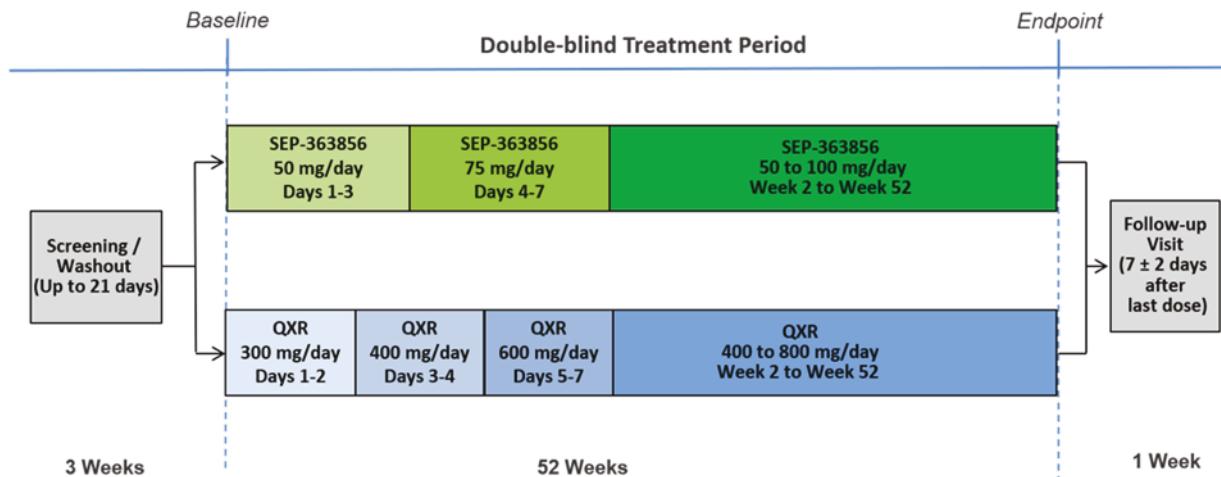
3.2. METHOD OF ASSIGNING SUBJECTS TO TREATMENT GROUPS

The randomization schedule is generated by a non-study biostatistician.

The randomization is stratified by country and the randomization schedule is based on permuted blocks.

Once a subject is deemed eligible to be randomized at Day 1, an interactive web response system (IWRS) will perform treatment assignment. Subjects will be randomized to one of the following treatment groups in a 2:1 ratio:

- Flexibly dosed SEP-363856 (50, 75, or 100 mg/day) for 52 weeks

- Flexibly dosed Quetiapine XR (400, 600, or 800 mg/day) for 52 weeks

Once a randomization number has been assigned, it cannot be reused.

3.3. BLINDING

Subjects, Investigators, clinical site staff, persons performing the assessments, clinical operations

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personnel, data analysts, and personnel at central laboratories will remain blinded to the identity of the treatment from the time of randomization until database lock and unblinding, using the following methods:

- Randomization data are kept strictly confidential until the time of unblinding in the IWRS and will not be accessible by anyone else involved in the study with the following exceptions: bioanalytical laboratory personnel involved in the analysis of PK samples, DSMB members involved in regular review of safety data, external statistical staff involved in preparing materials for DSMB reviews, pharmacovigilance department for evaluation and reporting of SAEs, and the Sponsor's clinical trial materials management.

- Prolactin levels will be blinded except for results from Visit 1 (Screening).

- The identity of the treatments will be concealed by the use of study drugs that are all identical in packaging, labelling, schedule of administration, and appearance.

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In the case of a medical emergency, where knowledge of study drug by the Investigator or an authorized delegate is essential for immediate medical management, a 24-hour code-break service will be available via the IWRS. The date and reason for unblinding are to be documented in the source documents. Any subject for whom the treatment assignment was unblinded is to be discontinued from further study participation. The subject should return for a final study assessment. The identity of those individuals at the study site who gain access to the unblinded treatment assignment must be documented. It is mandatory that all personnel who are involved in the unblinding and who have access to the unblind treatment assignment, maintain the confidentiality of the information and do not divulge the treatment assignment.

3.4. DETERMINATION OF SAMPLE SIZE

A total of 300 subjects are expected to be enrolled from approximately 50 global sites, including the US and Europe. Subjects will be assigned randomly to receive SEP-363856 or active comparator in an allocation ratio of 2:1. The determination of sample size was based upon clinical considerations. The sample size of 300 subjects will provide approximately 80 subjects who are expected to complete 1 year

of treatment with SEP-363856 to support sufficient long-term safety data on SEP-363856.

3.5. CHANGES IN THE CONDUCT OF THE STUDY

The first subject entered the study under protocol version 1.00 dated 28JUN2019. The protocol versions and amendments listed below were implemented after the screening and randomization of the first subject.

- Protocol version 2.00 (16-Sep-2020); Amendment 1.00 (16-SEP-2020)

- Protocol version 3.00 (14-Jan-2021); Amendment 2.00 (14-JAN-2021)

3.6. SCHEDULE OF EVENTS

Schedule of events can be found in Section 1, Table 2 of the Clinical Study Protocol (CSP). This table is also included in APPENDIX 9 of the SAP.

3.7. CHANGES TO ANALYSIS FROM PROTOCOL

The second criterion in the per protocol population definition is updated to only exclude subjects who had important protocol deviations that can potentially impact the integrity of the efficacy endpoints analysis. IPDs that do not affect efficacy endpoints analysis will not cause a subject to be excluded from the per protocol population.

The efficacy population definition is updated to clarify that at least one post-Baseline efficacy measurement is administered within 9 days after the last dose of study drug.

The first criterion in the per protocol population definition is removed.

4. PLANNED ANALYSES

The following analyses will be performed for this study:

- Analyses for Independent DSMB meetings

- Final Analysis

4.1. DATA SAFETY MONITORING BOARD

A DSMB SAP and charter, describing the methodology, meeting schedule, and presentation of results as well as access to results will be maintained by another CRO and Sunovion as separate documents. All DSMB analyses will be performed independently by the CRO approximately every 4 months after enough subjects are randomized.

4.2. INTERIM ANALYSIS

There is no interim analysis of efficacy data planned for this study.

4.3. FINAL ANALYSIS

All final planned analyses specified in this SAP will be performed by IQVIA following Sunovion authorization of this SAP, Sunovion authorization of analysis populations, database lock, and unblinding of treatment.

Some minor modifications may be necessary to the planned design of tables, figures, and listings to accommodate data collection during the actual study conduct.

5. ANALYSIS POPULATIONS

Agreement and authorization of subjects included/ excluded from each analysis population will be conducted prior to database lock and the unblinding of the study treatment.

No analysis population definition was updated due to COVID-19 impact or the Russia-Ukraine geopolitical conflict.

5.1. SAFETY (SAF) POPULATION

The safety (SAF) population will consist of all subjects who were enrolled and received at least one dose

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of study drug during the 52-week treatment period. The SAF population will be used for the long-term safety and tolerability analyses. Subjects will be analyzed according to the actual treatment received. The actual treatment group will be determined as follows:

- For subjects randomized to the SEP-363856 50 to 100 mg/day group:

  - If a subject took at least one dose of SEP-363856 treatment during the entire double-blind treatment period, then the actual treatment group = SEP-363856 50 to 100 mg/day.

  - If a subject took only Quetiapine XR treatment during the entire double-blind treatment period, then the actual treatment group = Quetiapine XR 400 to 800 mg/day.

- For subjects randomized to the Quetiapine XR 400 to 800 mg/day group:

  - If a subject took at least one dose of Quetiapine XR treatment during the entire double-blind treatment period, then the actual treatment group = Quetiapine XR 400 to 800 mg/day.

  - If a subject took only SEP-363856 treatment during the entire double-blind treatment period, then the actual treatment group = SEP-363856 50 to 100 mg/day.

5.2. EFFICACY (EFF) POPULATION

The efficacy population will consist of all subjects who are randomized, have received at least one dose of study drug, and have a Baseline and at least one post-Baseline efficacy measurement in PANSS or CGI-S administered within 9 days after the last dose of study drug. Subjects will be included in the EFF population regardless of any protocol deviation. The EFF population will be the primary population for the efficacy analyses. Subjects will be analyzed according to the treatment to which they are randomized.

5.3. PER PROTOCOL (PP) POPULATION

The per protocol (PP) population will consist of all EFF population subjects who satisfy the following conditions:

- Have no important protocol deviations that can potentially impact the integrity of the efficacy endpoints analysis, as determined by blinded data reviews prior to database lock

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Selected efficacy endpoints will be analyzed using the PP population. Subjects will be analyzed according to the treatment to which they are randomized.

6. GENERAL CONSIDERATIONS

6.1. REFERENCE START DATE AND STUDY DAY

Study Day will be calculated from the reference start date and will be used to show start/stop day of assessments and events.

Reference start date is defined as the day of the first dose of study medication, (Day 1 is the Study Day of the first dose of study medication).

- If the date of assessment or event is prior to the reference start date, then:

Study Day = (date of assessment or event – reference start date).

- If the date of assessment or event is on or after the reference start date, then:

Study Day = (date of assessment or event – reference date) + 1.

In the situation where the event date is partial or missing, Study Day and any corresponding durations will appear partial or missing in the listings. Partial assessment or event dates will, however, be presented as is in the listings.

6.2. BASELINE

Unless otherwise specified, Baseline is defined as the last non-missing measurement taken prior to the reference start date (including unscheduled assessments).

Whenever available, the time information should be accounted for in the derivation of Baseline values. In the case where time is not available and the date of the last non-missing measurement and the date of the first dose of study medication coincide, that measurement will be considered the Baseline.

Baseline will be derived for the following outcome measures:

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- PANSS: total score, subscale scores, Marder factor scores, UPSM factor scores and total factor score, and individual item scores. For a given subject, the Baseline values for all PANSS summary and individual item scores should come from the same assessment (i.e. have the same visit number and assessment start date/time) and it should be the last assessment prior to first dose where PANSS total score is available (i.e. not set to missing). In the rare event where no PANSS total score is available before first dose due to partially completed assessments, the assessment prior to first dose with the most PANSS item scores available should be taken as the Baseline assessment for all raw and derived scores as applicable.

- CGI-S score.

- BNSS: total score, subscale scores, and individual item scores. For a given subject, the Baseline values for all BNSS summary and individual item scores should come from the same assessment and it should be the last assessment prior to first dose where BNSS total score is available. In the rare event where no BNSS total score is available before first dose due to partially completed assessments, the assessment prior to first dose with most BNSS item scores available should be taken as the Baseline assessment for all raw and derived scores as applicable.

- MADRS: total score and individual item scores. For a given subject, the Baseline values for all MADRS summary and individual item scores should come from the same assessment and it should be the last assessment prior to first dose where MADRS total score is available. In the rare event where no MADRS total score is available before first dose due to partially completed assessments, the assessment prior to first dose with most MADRS item scores available should be taken as the Baseline assessment for all raw and derived scores as applicable.

- BACS: composite T score, component test T scores, and component test raw scores. For a given subject, the Baseline values for all BACS derived and raw scores should come from the same assessment and it should be the last assessment prior to first dose where BACS composite T score is available. In the rare event where no BACS composite T score is available before first dose due to partially completed assessments, the assessment prior to first dose with most BACS component test T scores available should be taken as the Baseline assessment for all raw and derived scores as applicable.

- ESS: total score and individual item scores. For a given subject, the Baseline values for all ESS summary and individual item scores should come from the same assessment and it should be the last assessment prior to first dose where ESS total score is available. In the rare event where no ESS

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total score is available before first dose due to partially completed assessments, the assessment prior to first dose with most ESS item scores available should be taken as the Baseline assessment for all raw and derived scores as applicable.

- SLOF: total score, subscale scores, and individual item scores. For a given subject, the Baseline values for all SLOF summary and individual item scores should come from the same assessment and it should be the last assessment prior to first dose where SLOF total score is available. In the rare event where no SLOF total score is available before first dose due to partially completed assessments, the assessment prior to first dose with most SLOF item scores available should be taken as the Baseline assessment for all raw and derived scores as applicable.

- EQ-5D-5L: visual analog scale (VAS), index value, and dimension scores. For a given subject, the Baseline value for EQ-5D-5L VAS should come from the last assessment prior to first dose where the VAS value is available; the Baseline values for the index value and dimension scores should come from the same assessment and it should be the last assessment prior to first dose where the index value is available. In the rare event where no index value is available before first dose due to partially completed assessments, the assessment prior to first dose with most dimension scores available should be taken as the Baseline assessment for the dimension scores.

- UPSA-B: total score, subscale scores and individual item scores. For a given subject, the Baseline values for all UPSA-B summary and individual item scores should come from the same assessment and it should be the last assessment prior to first dose where UPSA-B total score is available. In the rare event where no UPSA-B total score is available before first dose due to partially completed assessments, the assessment prior to first dose with most UPSA-B item scores available should be taken as the Baseline assessment for all raw and derived scores as applicable.

- MSQ score.

- C-SSRS: Suicidal ideation categories 1 to 5 (yes/no) and suicidal behavior categories 6-10 (yes/no); C-SSRS composite endpoints: any suicidal ideation (yes/no), any suicidal behavior (yes/no), any suicidality (yes/no); the suicidal ideation score (0-5). See Section 17.6.1 for the definition of a C-SSRS Baseline.

- SAS: mean score and individual item scores. For a given subject, the Baseline values for all SAS summary and individual item scores should come from the same assessment and it should be the last assessment prior to first dose where SAS mean score is available. In the rare event where no SAS

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mean score is available before first dose due to partially completed assessments, the assessment prior to first dose with most SAS item scores available should be taken as the Baseline assessment for all raw and derived scores as applicable.

- BARS: total score and individual item scores. For a given subject, the Baseline values for all BARS summary and individual item scores should come from the same assessment and it should be the last assessment prior to first dose where BARS total score is available. In the rare event where no BARS total score is available before first dose due to partially completed assessments, the assessment prior to first dose with most BARS item scores available should be taken as the Baseline assessment for all raw and derived scores as applicable.

- AIMS: total score and individual item scores. For a given subject, the Baseline values for all AIMS summary and individual item scores should come from the same assessment and it should be the last assessment prior to first dose where AIMS total score is available. In the rare event where no AIMS total score is available before first dose due to partially completed assessments, the assessment prior to first dose with most AIMS item scores available should be taken as the Baseline assessment for all raw and derived scores as applicable.

- Clinical laboratory parameters (blood chemistry, hematology, urinalysis, HOMA-IR). For a given subject, the Baseline values for the clinical laboratory parameters do not have to all come from the same assessment; the only exception is: the Baseline flag for the counts of leukocytes and its differential should be applied to records from the same assessment and it should be the last assessment prior to first dose where counts of leukocytes and its differential are reported. Baseline flag does not need to be derived for RBC morphology findings, WBC morphology findings, and urinalysis microscopic examination findings (excluding urine erythrocytes and leukocytes). Where results are available for both central laboratory and local laboratory for a given assessment, the central laboratory result will be considered baseline.

- Urine drug screening: For a given subject, the Baseline values for all urine drug screening parameters should come from the same assessment and it should be the last assessment prior to first dose where a urine drug screening test was administered.

- Vital sign parameters (supine and standing systolic blood pressure (SBP), supine and standing diastolic blood pressure (DBP), supine and standing pulse rate, respiratory rate, oral temperature), height, weight, BMI, and waist circumference. For a given subject, the Baseline values for all vital sign parameters, height, weight, BMI, and waist circumference do not have to come from the same

assessment; the only exceptions are: (1) the Baseline flag for weight and BMI should be applied to records from the same assessment and it should be the last assessment prior to first dose where weight is available, (2) the Baseline flag for supine systolic and diastolic blood pressure, standing systolic and diastolic blood pressure, and the derived corresponding orthostatic endpoints (i.e. standing SBP – supine SBP; standing DBP – supine DBP) should be applied to records from the same assessment and it should be the last assessment prior to first dose where all four BP measures are available, and (3) the Baseline flag for supine and standing pulse rate and the derived corresponding orthostatic endpoint (i.e. standing pulse rate – supine pulse rate) should be applied to records from the same assessment and it should be the last assessment prior to first dose where both pulse rate measures are available.

- ECG parameters: For a given subject, the Baseline values for all ECG parameters do not have to come from the same assessment Baseline flag does not need to be derived for ECG parameters in the category of "FINDING".

- Tobacco use data: Baseline of this outcome measure should come from the same assessment and it should be taken strictly from the assessment given at Visit 2 without regard to its temporal relationship to the first dose of study medication.

- Plasma cotinine concentrations.

- Healthcare resource utilization data: Baseline of this outcome measure should come from the same assessment and it should be taken strictly from the assessment given at Visit 2 without regard to its temporal relationship to the first dose of study medication.

The Baseline flag may be derived for additional outcome measures based on the needs during analyses.

6.3. DERIVED TIMEPOINTS

The last non-missing post-Baseline (i.e., post-first dose) measurement collected up to and including the Visit 17 (EOT/ET) measurement and within 9 days post the last dose will be carried forward and defined as the last observation carried forward (LOCF) endpoint. Both scheduled and unscheduled assessments as well as the early termination assessments that are collected during this period will contribute to the derivation of the LOCF endpoint. However, scheduled and unscheduled measurements taken after the Visit 17 (EOT/ET) measurement or beyond 9 days post the last dose will not be used in the derivation.

The LOCF endpoint will be derived for the following outcome measures:

- PANSS: total score, subscale scores, Marder factor scores, UPSM factor scores and total factor score, individual item scores, and derived binary variables for PANSS response. For a given subject, the LOCF values for all PANSS summary and individual item scores and derived binary variables should come from the same assessment and it should be the last post-Baseline assessment up to and including Visit 17 (EOT/ET) measurement and within 9 days post the last dose where PANSS total score is available. In the rare event where no PANSS total score is available after first dose due to partially completed assessments, the last post-Baseline assessment up to and including Visit 17 (EOT/ET) measurement and within 9 days post the last dose should be taken as the LOCF assessment for all raw and derived scores as applicable.

- CGI-S score.

- BNSS: total score, subscale scores, and individual item scores. For a given subject, the LOCF values for all BNSS summary and individual item scores should come from the same assessment and it should be the last post-Baseline assessment up to and including Visit 17 (EOT/ET) measurement and within 9 days post the last dose where BNSS total score is available. In the rare event where no BNSS total score is available after first dose due to partially completed assessments, the last post-Baseline assessment up to and including Visit 17 (EOT/ET) measurement and within 9 days post the last dose should be taken as the LOCF assessment for all raw and derived scores as applicable.

- MADRS: total score and individual item scores. For a given subject, the LOCF values for all MADRS summary and individual item scores should come from the same assessment and it should be the last post-Baseline assessment up to and including Visit 17 (EOT/ET) measurement and within 9 days post the last dose where MADRS total score is available. In the rare event where no MADRS total score is available after first dose due to partially completed assessments, the last post-Baseline assessment up to and including Visit 17 (EOT/ET) measurement and within 9 days post the last dose should be taken as the LOCF assessment for all raw and derived scores as applicable.

- BACS: composite T score, component test T scores, and component test raw scores. For a given subject, the LOCF values for all BACS derived and raw scores should come from the same assessment and it should be the last post-Baseline assessment up to and including Visit 17 (EOT/ET) measurement and within 9 days post the last dose where BACS composite T score is available. In the rare event where no BACS composite T score is available after first dose due to partially completed assessments, the last post-Baseline assessment up to and including Visit 17

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(EOT/ET) measurement and within 9 days post the last dose should be taken as the LOCF assessment for all raw and derived scores as applicable.

- ESS: total score and individual item scores. For a given subject, the LOCF values for all ESS summary and individual item scores should come from the same assessment and it should be the last post-Baseline assessment up to and including Visit 17 (EOT/ET) measurement and within 9 days post the last dose where ESS total score is available. In the rare event where no ESS total score is available after first dose due to partially completed assessments, the last post-Baseline assessment up to and including Visit 17 (EOT/ET) measurement and within 9 days post the last dose should be taken as the LOCF assessment for all raw and derived scores as applicable.

- SLOF: total score, subscale scores, and individual item scores. For a given subject, the LOCF values for all SLOF summary and individual item scores should come from the same assessment and it should be the last post-Baseline assessment up to and including Visit 17 (EOT/ET) measurement and within 9 days post the last dose where SLOF total score is available. In the rare event where no SLOF total score is available after first dose due to partially completed assessments, the last post-Baseline assessment up to and including Visit 17 (EOT/ET) measurement and within 9 days post the last dose should be taken as the LOCF assessment for all raw and derived scores as applicable.

- EQ-5D-5L: visual analog scale (VAS), index value, and dimension scores. For a given subject, the LOCF value for EQ-5D-5L VAS should come from the last post-Baseline assessment up to and including Visit 17 (EOT/ET) measurement and within 9 days post the last dose where the VAS value is available; the LOCF values for the index value and dimension scores should come from the same assessment and it should be the last post-Baseline assessment up to and including Visit 17 (EOS/ET) measurement and within 9 days post the last dose where the index value is available. In the rare event where no index value is available after first dose due to partially completed assessments, the last post-Baseline assessment up to and including Visit 17 (EOT/ET) measurement and within 9 days post the last dose should be taken as the LOCF assessment for the dimension scores.

- UPSA-B: total score, subscale scores, and individual item scores. For a given subject, the LOCF values for all UPSA-B summary and individual item scores should come from the same assessment and it should be the last post-Baseline assessment up to and including Visit 17 (EOT/ET) measurement and within 9 days post the last dose where UPSA-B total score is available. In the rare event where no UPSA-B total score is available after first dose due to partially completed assessments, the last post-Baseline assessment up to and including Visit 17 (EOT/ET) measurement

and within 9 days post the last dose should be taken as the LOCF assessment for all raw and derived scores as applicable.

- MSQ score.

- C-SSRS suicidal ideation score (0-5).

- SAS: mean score and individual item scores. For a given subject, the LOCF values for all SAS summary and individual item scores should come from the same assessment and it should be the last post-Baseline assessment up to and including Visit 17 (EOT/ET) measurement and within 9 days post the last dose where SAS mean score is available. In the rare event where no SAS mean score is available after first dose due to partially completed assessments, the last post-Baseline assessment up to and including Visit 17 (EOT/ET) measurement and within 9 days post the last dose should be taken as the LOCF assessment for all raw and derived scores as applicable.

- BARS: total score and individual item scores. For a given subject, the LOCF values for all BARS summary and individual item scores should come from the same assessment and it should be the last post-Baseline assessment up to and including Visit 17 (EOT/ET) measurement and within 9 days post the last dose where BARS total score is available. In the rare event where no BARS total score is available after first dose due to partially completed assessments, the last post-Baseline assessment up to and including Visit 17 (EOT/ET) measurement and within 9 days post the last dose should be taken as the LOCF assessment for all raw and derived scores as applicable.

- AIMS: total score and individual item scores. For a given subject, the LOCF values for all AIMS summary and individual item scores should come from the same assessment and it should be the last post-Baseline assessment up to and including Visit 17 (EOT/ET) measurement and within 9 days post the last dose where AIMS total score is available. In the rare event where no AIMS total score is available after first dose due to partially completed assessments, the last post-Baseline assessment up to and including Visit 17 (EOT/ET) measurement and within 9 days post the last dose should be taken as the LOCF assessment for all raw and derived scores as applicable.

- Clinical laboratory parameters (blood chemistry, hematology, urinalysis, HOMA-IR). For a given subject, the LOCF values for the clinical laboratory parameters do not have to all come from the same assessment; the only exception is: the LOCF flag for the counts of leukocytes and its differential should be applied to records from the same assessment and it should be the last post-Baseline assessment up to and including Visit 17 (EOT/ET) measurement and within 9 days post the last dose

where counts of leukocytes and its differential are reported. LOCF endpoint does not need to be derived for RBC morphology findings, WBC morphology findings, and urinalysis microscopic examination findings (excluding urine erythrocytes and leukocytes). Where results are available for both central laboratory and local laboratory for a given assessment, the central laboratory result will be considered LOCF endpoint.

- Urine drug screening (adolescent subjects only): For a given subject, the LOCF values for all urine drug screening parameters should come from the same assessment and it should be the last post-Baseline assessment up to and including Visit 17 (EOT/ET) measurement and within 9 days post the last dose where a urine drug screening test was administered.

- Vital sign parameters (supine and standing SBP, supine and standing DBP, supine and standing pulse rate, respiratory rate, oral temperature), height, weight, BMI, and waist circumference. For a given subject, the LOCF values for all vital sign parameters, height, weight, BMI, and waist circumference do not have to come from the same assessment; the only exceptions are: (1) the LOCF flag for weight and BMI should be applied to records from the same assessment and it should be the last post-Baseline assessment up to and including Visit 17 (EOT/ET) measurement and within 9 days post the last dose where weight is available, (2) the LOCF flag for supine systolic and diastolic blood pressure, standing systolic and diastolic blood pressure, and the derived corresponding orthostatic endpoints (i.e. standing SBP – supine SBP; standing DBP – supine DBP) should be applied to records from the same assessment and it should be the last post-Baseline assessment up to and including Visit 17 (EOT/ET) measurement and within 9 days post the last dose where all four BP measures are available, and (3) the LOCF flag for supine and standing pulse rate and the derived corresponding orthostatic endpoint (i.e. standing pulse rate – supine pulse rate) should be applied to records from the same assessment and it should be the last post-Baseline assessment up to and including Visit 17 (EOT/ET) measurement and within 9 days post the last dose where both pulse rate measures are available.

- ECG parameters: For a given subject, the LOCF values for all ECG parameters do not have to come from the same assessment. LOCF endpoint does not need to be derived for ECG parameters in the category of "FINDING".

- Tobacco use data: LOCF of this outcome measure should come from the same assessment and it should be the last assessment post first dose up to and including Visit 17 (EOS/ET) measurement and within 9 days post the last dose where any data are reported.

- Plasma cotinine concentrations.

- Healthcare resource utilization data: LOCF of this outcome measure should come from the same assessment and it should be the last assessment post first dose up to and including Visit 17 (EOS/ET) measurement and within 9 days post the last dose where any data are reported.

The study visits will be mapped to analysis visits for table summaries and statistical analyses where applicable (Table 1). No follow-up visit (i.e. Visit 18) data will be included in any MMRM/ANCOVA analyses.

Table 1: Mapping of study visits to analysis visits.

Study Visit	Analysis Visit Number	Analysis Visit
Visit 1	1	Screening/Visit 1
Visit 2	2	Randomization/Visit 2
NA	2.5	Baseline
Visit 3	3	Week 1/Visit 3
Visit 4	4	Week 2/Visit 4
Visit 5	5	Week 4/Visit 5
Visit 6	6	Week 8/Visit 6
Visit 7	7	Week 12/Visit 7
Visit 8	8	Week 16/Visit 8
Visit 9	9	Week 20/Visit 9
Visit 10	10	Week 24/Visit 10
Visit 11	11	Week 28/Visit 11

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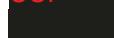
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Visit 12	12	Week 32/Visit 12
Visit 13	13	Week 36/Visit 13
Visit 14	14	Week 40/Visit 14
Visit 15	15	Week 44/Visit 15
Visit 16	16	Week 48/Visit 16
Visit 17 (if representing true EOT visit). For ET visit mapping, see Section 6.4.	17	Week 52/Visit 17
Visit 18	18	Follow-up/Visit 18

Original study visit collected on the case report forms (CRFs) will be displayed in the listings.

6.4. RETESTS, UNSCHEDULED VISITS, AND EARLY TERMINATION DATA

In general, for by-visit summaries, data recorded at the planned visits where assessment is intended to be given and collected within 9 days post last dose will be presented, as well as the derived Baseline value and the LOCF value.

Unscheduled measurements will not be included in by-visit summaries as a separate time point. Unscheduled measurements collected prior to the first dose of study medication will contribute to the derivation of the Baseline value. Unscheduled measurements collected post Baseline up to and including 9 days after the last dose of study drug will contribute to the derivation of the LOCF value, the potentially clinically significant (PCS) value, and the best/worst case value where required (e.g. shift table).

In the case of a retest, the assessment recorded under the planned visit will be used for by-visit summaries, and the assessment(s) recorded under unscheduled visit(s) will be presented in listings only.

As per protocol, study Visit 17 can be a Week 52/End of Treatment (EOT) visit or an Early Termination (ET) visit. If a subject terminates early, his/her measurements taken at the ET visit and within 9 days post the last dose will be mapped to the next planned visit (after the last scheduled visit the subject attended)

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during which that assessment was expected to be performed as specified by the Schedule of Assessments table in the protocol. This applies to both efficacy and safety data. ET measurements taken beyond 9 days post the last dose will not be mapped.

Listings will include scheduled, unscheduled, retest, and early discontinuation data without regard to the 9-day window, with original dates and visits displayed.

6.5. WINDOWING CONVENTIONS

No visit windowing will be performed during the analysis for this study. Data will be analyzed according to the schedule outlined in the CSP. However unless otherwise specified, any data collected beyond 9 days post the last dose will be excluded from efficacy and safety analyses; these data will be presented in data listings only.

6.6. STATISTICAL TESTS

The default significance level will be 5%; confidence intervals (CIs) will be 95%; and all p-values will be two-sided, unless otherwise specified in the description of the analyses or the outputs.

6.7. COMMON CALCULATIONS

For quantitative measurements, change from Baseline will be calculated as:

- Test Value at Visit X – Baseline Value

For PANSS Total score, percentage change from Baseline will be calculated as:

- (Test Value at Visit X – Baseline Value) × 100 / (Baseline Value – 30)

For other quantitative measurements, percentage change from Baseline will be calculated as:

- (Test Value at Visit X – Baseline Value) × 100 / Baseline Value

6.8. SOFTWARE VERSION

All analyses will be conducted using SAS version 9.4 or higher.

7. STATISTICAL CONSIDERATIONS

7.1. ADJUSTMENTS FOR COVARIATES AND FACTORS TO BE INCLUDED IN ANALYSES

The following covariates and factors are used in the analyses. For details of their inclusion in the models, see the specific analysis section.

- Baseline value of the variable to be analyzed

- Country

  - United States

  - Russia

  - Romania

  - Ukraine

- Geographic region:

  - US

  - Non-US

7.2. MULTICENTER STUDIES

This study will be conducted by multiple Investigators at multiple centers in the US and non-US countries, including Russia, Romania, and Ukraine. Randomization is stratified by country.

When specified, statistical analysis will be adjusted for country.

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A term for treatment-by-country interaction at Week 52/Visit 17 will be explored as part of the subgroup analysis (see Section 16.1.1.4). A significant interaction effect is defined as having a nominal p- value ≤0.10. Additionally, graphical methods (i.e. Forest plots) will be used to present the analysis results separately for each country and to assess whether the interaction, if there is one, is quantitative (i.e. the treatment effect is consistent in direction but not in size) or qualitative (i.e. the treatment is beneficial for some but not for other countries).

Center pooling will not be implemented in the analyses for this study.

7.3. MISSING DATA

For the MMRM models on observed data, missing observations are treated as missing at random (MAR) and no imputation for missing data will be applied.

Individual missing items in any scale will not be imputed in any analysis. If one or more items are missing at a visit when calculating a total score, subscale score, or any summary scores based on more than one item, then an associated summary score will be set to missing. For additional details, see the individual scale description sections.

- Handling of missing efficacy data, if any, is described in Section 16.2.10.

- Handling of missing safety data, if any, is described in Sections 17.1, and 17.6.

- See APPENDIX 2 for details of handling incomplete/missing dates.

7.4. MULTIPLE COMPARISONS/ MULTIPLICITY

No multiplicity adjustment is defined for analysis. Nominal p-values (i.e. without multiplicity adjustment) will be reported for statistical tests.

7.5. EXAMINATION OF SUBGROUPS

Subgroup analysis will be conducted for subjects as stated in Section 16.1.1.4 for PANSS, Section 16.2.1 for CGI-S and Section 17.1.10 for Adverse Events.

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The following subgroups will be assessed:

- Geographic region:

  - US

  - Non-US

- Country:

  - United States

  - Russia

  - Romania

  - Ukraine

- Sex:

  - Female

  - Male

- Age group:

  - ≤40 years

  - >40 years

- Race (in 3 categories):

  - White (White)

  - Black (Black or African American)

  - Other (All other races combined)

- Number of prior hospitalizations for treatment of schizophrenia:

  - 0

  - 1

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- 2

- 3

- 4 or more

- Duration of schizophrenia (years):

  - <5

  - ≥5

- BMI (kg/m²) categories:

  - Underweight: <18.5 kg/m²

  - Normal: ≥18.5 to <25.0 kg/m²

  - Overweight: ≥25.0 to <30.0 kg/m²

  - Obese: ≥30.0 kg/m²

- Baseline patient type based on UPSM factor scores at Baseline (only used in the subgroup analysis of PANSS total score) (Hopkins et al. 2020):

  - Type 1: Prominently Disorganized

  - Type 2: Prominently Negative

  - Type 3: Prominently Hostile

  - Type 4: Prominently Positive

  - Type 5: Prominently Affective

  Subjects will be classified into one of 5 patient types based on their PANSS UPSM factor scores at Baseline. See APPENDIX 12 for details of how the classification will be made.

8. OUTPUT PRESENTATIONS

APPENDIX 1 shows conventions for presentation of data in outputs.

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The templates provided with this SAP describe the presentations for this study and therefore the format and content of the summary tables, figures, and listings to be provided by IQVIA.

9. DISPOSITION AND WITHDRAWALS

Unless otherwise specified, the disposition summary tables will include the following columns: SEP-363856 50 to 100 mg/day, Quetiapine XR 400 to 800 mg/day, and Total.

All subjects who provide informed consent will be accounted for in this study.

Subject disposition will be presented by the actual treatment group (where applicable). The number and percentage of subjects who were screened, screen failed, randomized, received study drug, randomized but did not receive study drug, and completed or discontinued from the double-blind treatment period (including reasons for discontinuation) will be presented. Disposition will be presented separately for each country as well.

With respect to the above, the following definitions apply:

- Screened Subjects: Any subject who signed the study specific informed consent.

- Screen Failures: Any subject who signed the study specific informed consent but either failed to meet study requirements during screening or met study requirements at screening and was not randomized.

- Randomized Subjects: Any subject who was randomized into treatment period of the study and was assigned a randomization number.

Subjects who were screened more than once will be counted only once in the disposition summary based on the outcome of the last screening. If a subject failed multiple screenings, they will only be counted once as a screen failure. If a subject is randomized after multiple screenings, they will only be counted once as a randomized subject.

Discontinuation by visit will be summarized for the SAF population by the actual treatment group.

Time to discontinuation of the double-blind treatment since first dose of study drug will be plotted using Kaplan-Meier curves for the SAF population by the actual treatment group. The log rank testing method will be used to test for differences among the treatment groups for time to discontinuation.

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The number and percentage of subjects will also be summarized by Region, Country, and Site, by the actual treatment group for the SAF population.

Lastly, the number and percentage of randomized subjects included in and excluded from each analysis population will be summarized by the actual treatment group, along with the reason for exclusion.

COVID-19 related analysis updates:

The number of subjects who failed screening due to COVID-19 related reasons and who discontinued early due to COVID-19 related reasons will be summarized in the disposition table.

Subjects affected by COVID-19 related study disruptions will be provided in data listings. These subjects will be identified by:

- Subjects who failed screening due to COVID-19 related reasons.

- Subjects who were randomized but discontinued from the treatment period due to COVID-19 related reasons.

- Subjects who experienced a pre-treatment event / adverse event related to COVID-19.

- Subjects who had any protocol deviations related to COVID-19.

- Subjects who had any investigator comments related to COVID-19.

A subject may be identified in one or more categories listed above.

Russia-Ukraine geopolitical conflict related analysis:

The number of subjects who discontinued early due to geopolitical conflict related reasons will be summarized in the disposition table.

Subjects affected by geopolitical conflict related study disruptions will be provided in data listings. These subjects will be identified as:

- *Subjects who discontinued from the treatment period due to geopolitical conflict.*

- *Subjects who experienced an adverse event related to geopolitical conflict.*

- *Subjects who had any protocol deviations related to geopolitical conflict.*

- *Subjects who had any investigator comments related to geopolitical conflict.*

A subject may be identified in one or more categories listed above.

9.1. DERIVATIONS

- Time to discontinuation of the double-blind treatment in days

  For the purpose of this analysis, a subject's last dose date will be derived as follows:

  - If a subject's observed last dose date is before or on the date of Study Day 364, the derived last dose date will be set to the observed last dose date.
  - If a subject's observed last dose date is after the date of Study Day 364, the derived last dose date will be set to the date of Study Day 364.

  Time to discontinuation (days) = Derived last dose date – First dose date + 1.

  Subjects who complete the double-blind treatment will be censored on the derived last dose date.

10. IMPORTANT PROTOCOL DEVIATIONS

Important protocol deviations (IPDs) will be identified and documented based on blinded reviews of data listings and the protocol deviations log.

Unless otherwise specified, the IPD summary tables will include the following columns: SEP-363856 50 to 100 mg/day, Quetiapine XR 400 to 800 mg/day, and Total.

The IPD categories may include, but may not be limited to:

- Did not satisfy inclusion and/or exclusion criteria

- Received prohibited medication

- Overall double-blind compliance rate <75% or >125%

The IPDs will be identified for all randomized subjects and presented in a data listing. The number and percentage of subjects within each IPD category will be summarized by the actual treatment group for the SAF population.

A dedicated listing will present protocol deviations related to COVID-19 in randomized subjects. A separate dedicated listing will present protocol deviations related to the Russia-Ukraine geopolitical conflict in all enrolled subjects.

Two sets of clinical trial management system (CTMS) deviation categories are used in the study: former

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categories used for deviations reported up to 15MAY2022 and new categories for deviations reported as of 16MAY2022. These categories will be presented as is in the listings.

11. DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

Unless otherwise specified, the demographic and Baseline characteristics summary tables will include the following columns: SEP-363856 50 to 100 mg/day, Quetiapine XR 400 to 800 mg/day, and Total.

Demographic data and other Baseline characteristics will be presented for the SAF population, EFF population, and PP population. For the EFF and PP populations, the data will be presented by the randomized treatment group. For the SAF population, the data will be presented by the actual treatment group. Basic demographic data (age, sex, race, ethnicity, country, and region) will also be summarized for all screened subjects by randomization status (i.e. randomized vs. not randomized).

No statistical testing will be carried out for demographic or other Baseline characteristics.

The following demographic and other Baseline characteristics will be reported for this study:

- Age (years) - calculated relative to date of informed consent as a continuous variable

- Age (years) categories:

  - <18 years

  - ≥18 to ≤40 years

  - >40 to ≤65 years

  - >65 years

- Age (years) categories for ClinicalTrials.gov (CTR.GOV):

  - ≤18 years

  - >18 to <65 years

  - ≥65 years

- Age (years) categories for European Union Drug Regulating Authorities Clinical Trials Database

(EudraCT):

- <12 years

- ≥12 to <18 years

- ≥18 to <65 years

- ≥65 years

● Sex

- Female

- Male

● Race

- American Indian or Alaska Native

- Asian

- Black or African American

- Native Hawaiian or Other Pacific Islander

- White

- Multiracial

- Other

● Ethnicity

- Hispanic or Latino

- Not Hispanic or Latino

● Country

- United States

- Russia

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- - Romania

  - Ukraine

- Geographic Region

  - US

  - Non-US

- Baseline Height (cm), as a continuous variable

- Baseline Weight (kg), as a continuous variable

- Baseline BMI (kg/m^2), as a continuous variable

- Baseline BMI (kg/m^2) category

  - Underweight: <18.5 kg/m^2

  - Normal: ≥18.5 to <25.0 kg/m^2

  - Overweight: ≥25.0 to <30.0 kg/m^2

  - Obese: ≥30.0 kg/m^2

- Baseline Waist Circumference (cm), as a continuous variable

- Baseline PANSS Total Score, as a continuous variable

- Baseline PANSS Total Score categories:

  - <Overall median Baseline value

  - ≥Overall median Baseline value

- Baseline PANSS Subscale Scores, as continuous variables

- Baseline PANSS Subscale Score categories:

  - <Overall median Baseline value

  - ≥Overall median Baseline value

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- Baseline PANSS Positive vs Negative Subscale Score categories:

    - Positive Subscale Score <Negative Subscale Score

    - Positive Subscale Score ≥Negative Subscale Score

- Patient type based on Baseline UPSM factor scores

    o Type 1: Prominently Disorganized

    o Type 2: Prominently Negative

    o Type 3: Prominently Hostile

    o Type 4: Prominently Positive

    o Type 5: Prominently Affective

- Baseline CGI-S Score, as a continuous variable

- Baseline CGI-S Score categories:

    - <4

    - =4

    - >4

The following psychiatric history data will be summarized for the SAF population, EFF population, and PP population in separate tables. For the EFF and PP populations, the data will be presented by the randomized treatment group. For the SAF population, the data will be presented by the actual treatment group.

- Time since initial onset of schizophrenia (years) – calculated relative to date of informed consent.

- Time since initial onset of schizophrenia (years) categories:

    - <5 years

    - ≥5 to <10 years

    - ≥10 to <20 years

- ≥20 years

- Age at initial onset of schizophrenia (years)

- Time since schizophrenia diagnosis (years) – calculated relative to date of informed consent

- Time since last acute exacerbation of schizophrenia (days) – calculated relative to date of informed consent

- DSM-5 schizophrenia subtype diagnosis

  - 295.90 Schizophrenia

  - 293.89 Schizophrenia with Catatonia

- Number of prior hospitalizations for treatment of schizophrenia

  - 0

  - 1

  - 2

  - 3

  - 4 or more

- Time since first hospitalization for treatment of schizophrenia (years) – calculated relative to date of informed consent

- Age at first hospitalization for treatment of schizophrenia (years)

- Time since first anti-psychotic drug therapy of at least 2 weeks duration intended for treatment of schizophrenia (years) – calculated relative to date of informed consent

- Age at first anti-psychotic drug therapy of at least 2 weeks duration intended for treatment of schizophrenia (years)

- Any other psychiatric disorders

  - Yes

- No

Diagnosis and DSM-5 code for any current psychiatric disorders will be summarized in a separate table. These other current psychiatric disorders will be coded using Medical Dictionary for Regulatory Activities (MedDRA) central coding dictionary, Version 22.0, and presented by System Organ Class (SOC), and Preferred Term (PT).

11.1. DERIVATIONS

- BMI expressed in kg/m^2:

Weight (kg)/ height (m)^2.

- Time since initial onset of schizophrenia, expressed in years:

(Date of Informed Consent - Date of initial onset of schizophrenia <observed or imputed [see APPENDIX 2]>) / 365.25

Note: Round to one decimal place for each subject's calculated duration.

- Age at initial onset of schizophrenia, expressed in years:

(Date of initial onset of schizophrenia <observed or imputed [see APPENDIX 2]> - Date of birth + 1)/365.25

Note: Round to one decimal place for each subject's calculated age.

- Time since schizophrenia diagnosis, expressed in years:

(Date of Informed Consent - Date of schizophrenia diagnosis <observed or imputed [see APPENDIX 2]>)/365.25

Note: Round to one decimal place for each subject's calculated duration.

- Time since last acute exacerbation of schizophrenia, expressed in days:

Date of Informed Consent - Date of last acute exacerbation of schizophrenia <observed or imputed [see APPENDIX 2]>

Note: Round to one decimal place for each subject's calculated duration.

- Time since first hospitalization for treatment of schizophrenia, expressed in years:

(Date of Informed Consent – Date of first hospitalization for treatment of schizophrenia <observed or imputed [see APPENDIX 2]>)/365.25

Note: Round to one decimal place for each subject's calculated duration.

- Age at first hospitalization for treatment of schizophrenia, expressed in years:

(Date of first hospitalization for treatment of schizophrenia <observed or imputed [see APPENDIX 2]> - Date of birth + 1)/365.25

Note: Round to one decimal place for each subject's calculated age.

- Time since first anti-psychotic drug therapy of at least 2 weeks duration intended for treatment of schizophrenia, expressed in years:

(Date of Informed Consent - Start date of first anti-psychotic drug therapy of at least 2 weeks duration <observed or imputed [see APPENDIX 2]>)/365.25

Note: Round to one decimal place for each subject's calculated duration.

- Age at first anti-psychotic drug therapy of at least 2 weeks duration intended for treatment of schizophrenia, expressed in years:

(Start date of first anti-psychotic drug therapy of at least 2 weeks duration <observed or imputed [see APPENDIX 2]> - Date of birth + 1)/365.25

Note: Round to one decimal place for each subject's calculated age.

12. MEDICAL HISTORY

Unless otherwise specified, the medical and surgical history summary tables will include the following columns: SEP-363856 50 to 100 mg/day, Quetiapine XR 400 to 800 mg/day, and Total.

Medical and surgical history information, including both past and concomitant medical conditions and major surgical history, as collected on the *"Medical History"* CRF form, will be coded using MedDRA

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Version 22.0, and presented by SOC and PT for the SAF population by the actual treatment group. Data will be sorted by SOC based on the internationally agreed order (see APPENDIX 10) and by PT in decreasing frequency in the "SEP-363856 50 to 100 mg/day" column.

13. MEDICATIONS

Unless otherwise specified, the medications summary tables will include the following columns: SEP-363856 50 to 100 mg/day, Quetiapine XR 400 to 800 mg/day, and Total.

Medications will be coded to Anatomical Therapeutic Chemical (ATC) Levels and Preferred Names according to World Health Organization Drug (WHODRUG) dictionary, Version 01MAR2019.

Whenever available, the time information should be accounted for in the derivation of prior, concomitant, and post-treatment medications. See APPENDIX 2 for the handling of partial dates for medications. In the case where it is not possible to define a medication as prior, concomitant, or post treatment, the medication will be classified by the worst case, i.e. concomitant.

- Prior medications are medications which stopped prior to the first dose of study medication.

- Concomitant medications are medications which started at the same time of or after the first dose of study medication and at the same time of or before the last dose of study medication; or started prior to and ended at the same time of or after the first dose of study medication; or started at the same time of or prior to the last dose of study medication and marked as ongoing.

- Post-treatment medications are medications which started after the last dose of study medication.

Prior and concomitant medication use will be summarized by ATC Level 3 and Preferred Base Name for the SAF population by the actual treatment group. Medications will be sorted by ATC Level 3 alphabetically and by Preferred Base Name in decreasing frequency in the "SEP-363856 50 to 100 mg/day" column.

Prior, concomitant, and post-treatment medications will be provided in data listings.

Psychotropic and/or Sedating Medications taken by subjects prior to each visit as collected on the "*Timing of last dose of Psychotropic and/or Sedating Medications*" CRF form will be summarized by ATC Level 3 and Preferred Base Name for the SAF population by the actual treatment group and visit.

14. STUDY MEDICATION EXPOSURE

Unless otherwise specified, the study medication exposure summary tables will include the following columns: SEP-363856 50 to 100 mg/day, Quetiapine XR 400 to 800 mg/day, and Total.

Exposure to study medication data will be summarized for the SAF population by the actual treatment group.

If a subject takes treatment that is not their planned treatment for a period of time, that period of other drug exposure will not be included in the various exposure and compliance summaries. However, this information will be presented with the subject specific listings.

The date/time of first dose of study drug and date/time of last dose of study drug will be respectively derived as the earliest ("Date Dosing Started" & "Time Dosing Started") pair and the latest ("Date Dosing Ended" & "Time Dosing Ended") pair as collected on the "*Study Drug Administration / Drug Accountability*" CRF form. The start and end dates/times from blister cards with the number of tablets dispensed equal to the (number of tablets returned + number of tablets reported lost) are excluded from the derivation.

Duration of exposure (in days) will be summarized both as a continuous variable for the double-blind treatment period and categorically:

- Number and percentage of subjects with exposure ≥1, ≥14, ≥28, ≥42, ≥90, ≥120, ≥150, ≥180, ≥270, and ≥360 days;

- Number and percentage of subjects with exposure for 1 to 13, 14 to 27, 28 to 41, 42 to 89, 90 to 119, 120 to 149, 150 to 179, 180 to 269, 270 to 359 and ≥360 days

Total person-years of exposure will be calculated for each treatment group and overall for all subjects.

Mean daily dose and modal daily dose will be calculated for the entire double-blind treatment period and summarized.

The dose adjustment decision at each visit will be summarized in a shift table.

Lastly, the number of days that a subject received SEP-363856 50, 75, 100 mg/day, Quetiapine XR 300, 400, 600 and 800 mg/day dose level will be summarized for the SAF population both as a continuous variable and categorically:

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- Number and percentage of subjects with exposure to a particular dose level for 1 to 13, 14 to 27, 28 to 41, 42 to 89, 90 to 119, 120 to 149, 150 to 179, 180 to 269, 270 to 359 and ≥360 days

14.1. DERIVATIONS

- For subjects randomized to the SEP-363856 group, a titration card is dispensed at Visit 2 which contains:

  - 3 capsules of 50 mg dose level and 3 capsules of placebo for 3 days

  - 6 capsules of 75 mg dose level and 6 capsules of placebo for 6 days

  Drug accountability data is not separately collected for these dose levels at Visit 2. For subjects who were dispensed the titration card at Visit 2, the following assumptions will be made during analysis:

  - The first six out of the total number of capsules a subject receives during the Visit 2 treatment period are assumed to be 3 of 50 mg and 3 capsules of placebo. The other capsules are assumed to be half 75 mg and half placebo.

  Examples are:

  - If a subject randomized to the SEP-363856 group took 6 capsules during the Visit 2, the cumulative dose is 150 mg (= 50 mg * 3 + 0 mg * 3).

  - If a subject randomized to the SEP-363856 group took 8 capsules during the Visit 2, the cumulative dose is 225 mg (= 50 mg * 3 + 0 mg * 3 + 75 mg * 1 + 0 mg * 1).

- For subjects randomized to the Quetiapine XR group, a titration card is dispensed at Visit 2 which contains:

  - 2 capsules of 300 mg dose level and 2 capsules of placebo for 2 days

  - 2 capsules of 400 mg dose level and 2 capsules of placebo for 2 days

  - 5 capsules of 300 mg dose level and 5 capsules of 300 mg for 5 days

  Drug accountability data is not separately collected for these dose levels at Visit 2. For subjects who were dispensed the titration card at Visit 2, the following assumptions will be made during analysis:

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- The first four out of the total number of capsules a subject receives during the Visit 2 treatment period are assumed to be 2 capsules of 300 mg and 2 capsules of placebo. The next four out of the total number of capsules a subject receives during the Visit 2 treatment period are assumed to be 2 capsules of 400 mg and 2 capsules of placebo. The other capsules are assumed to be 300 mg.

Examples are:

- If a subject randomized to the Quetiapine XR group took 4 capsules during the Visit 2, the cumulative dose is 600 mg (= 300 mg * 2 + 0 mg * 2).

- If a subject randomized to the Quetiapine XR group took 8 capsules during the Visit 2, the cumulative dose is 1400 mg (= 300 mg * 2 + 0 mg * 2 + 400 mg * 2 + 0 mg * 2).

- If a subject randomized to the Quetiapine XR group took 10 capsules during the Visit 2, the cumulative dose is 2000 mg (= 300 mg * 2 + 0 mg * 2 + 400 mg * 2 + 0 mg * 2 + 300 mg * 2).

- Study drug will be provided in one-week blister cards containing 18 capsules arranged in 9 columns and 2 rows. In addition to the above assumptions, it is also established that capsules are taken starting from left (day 1) to right (extra day) and from top (row 1) to bottom (row 2).

An example is:

Weeks 2 to 52: Blinded Middle Dose (from protocol Section 9.2.1)

Day	1	2	3	4	5	6	7	Extra day	Extra day
Row 1	SEP-363856 75 mg or QXR 300 mg	SEP-363856 75 mg or QXR 300 mg	SEP-363856 75 mg or QXR 300 mg	SEP-363856 75 mg or QXR 300 mg	SEP-363856 75 mg or QXR 300 mg	SEP-363856 75 mg or QXR 300 mg	SEP-363856 75 mg or QXR 300 mg	SEP-363856 75 mg or QXR 300 mg	SEP-363856 75 mg or QXR 300 mg
Row 2	Placebo Or QXR 300 mg	Placebo Or QXR 300 mg	Placebo Or QXR 300 mg	Placebo Or QXR 300 mg	Placebo Or QXR 300 mg	Placebo Or QXR 300 mg	Placebo Or QXR 300 mg	Placebo Or QXR 300 mg	Placebo Or QXR 300 mg

- If the above blister card of SEP-36385 was dispensed and a subject took 5 capsules, the cumulative dose is 225 mg (= 75 mg * 3 + 0 mg * 2).

- Duration of exposure (days) = date of last study medication administration – date of first study

medication administration + 1. Interruptions in exposure (i.e. missed doses) and dose changes (if any) are not considered in the calculation of overall exposure.

- Total person-years of exposure is the sum of all durations of exposure in days / 365.25.

- Mean daily dose (mg/day):

$$\frac{\sum \text{Dose per capsule for Visit } j * (\#\text{ Capsules Dispensed for Visit } j - \#\text{ Capsules Returned for Visit } j - \#\text{ Capsules Lost for Visit } j)}{\text{Duration of Exposure}}$$

At Visit 2, for subjects who were dispensed the titration card with mixed dose levels, please refer to the first and the second bullet in this current section for assumptions to be used in dose calculation. At all visits, please refer to the third bullet in this current section for an assumption to be used in dose calculation.

If the number of capsules dispensed, returned, and/or lost as collected on the "*Study Drug Administration / Drug Accountability*" CRF form is missing for one or more visits, the mean daily dose will be calculated based on visits with complete drug accountability data available. That is, the numerator of the formula above will only include visits with the number of tablets dispensed, returned, and lost available, and the denominator should be adjusted to exclude dosing periods covered by visits excluded from the calculation (i.e., Duration of Exposure – dosing periods [sum of [EXENDTC – EXXTDTC+1]] covered by visits with missing or incomplete accountability data). If the dose level of a visit is unknown, that visit should be excluded from the calculation as well in both the numerator and the denominator.

- Modal daily dose will be determined as the daily dose that is taken for the most time (in terms of number of days) among all doses taken. A subject's modal daily dose may fall in one of the categories below:

  - SEP-363856 50 mg/day

  - SEP-363856 75 mg/day

  - SEP-363856 100 mg/day

  - Quetiapine XR 300 mg/day

  - Quetiapine XR 400 mg/day

  - Quetiapine XR 600 mg/day

- Quetiapine XR 800 mg/day

- Tie between xx and yy (i.e. the subject was on xx mg/day and yy mg/day for the same amount of time) (if needed)

15. STUDY MEDICATION COMPLIANCE

Unless otherwise specified, the study medication compliance summary tables will include the following columns: SEP-363856 50 to 100 mg/day, Quetiapine XR 400 to 800 mg/day, and Total.

Compliance to study medication will be presented for the SAF population, by the actual treatment group.

Percent compliance will be calculated overall for the double-blind treatment period. Non-compliance is defined as less than 75% or more than 125% non-missing compliance for the double-blind treatment period. Subjects with missing compliance will not be classified as non-compliant. Compliance will be summarized both as a continuous variable and categorically (i.e. number and percentage of subjects with compliance <75%, 75% - 125%, >125%, and missing).

15.1. DERIVATIONS

Overall Compliance (%) to study medication in percentage will be calculated as follows:

$$\frac{\sum(\text{\# Capsules Dispensed for Visit } j - \text{\# Capsules Returned for Visit } j - \text{\# Capsules Lost for Visit } j)}{\text{\# Capsules should be taken per day} \times \text{Duration of Exposure}} \times 100\%$$

If the number of capsules dispensed, returned, and/or lost as collected on the "*Study Drug Administration / Drug Accountability*" CRF form is missing for one or more visits, the overall compliance will be calculated based on visits with complete drug accountability data available. That is, the numerator of the formula above will only include visits with the number of tablets dispensed, returned, and lost available, and the denominator should be adjusted to exclude dosing periods covered by visits excluded from the calculation (i.e., change "Duration of Exposure" to be Duration of Exposure – dosing periods [sum of (EXENDTC – EXSTDTC+1)] covered by visits with missing or incomplete accountability data).

16. EFFICACY OUTCOMES

Unless otherwise specified, the efficacy analysis and summary tables will include the following columns:

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SEP-363856 50 to 100 mg/day, Quetiapine XR 400 to 800 mg/day.

All analyses of the efficacy variables will be based on the EFF population and, for selected variables/analyses, the PP population by the randomized treatment group.

Efficacy data collected after an emergency treatment unblinding (see protocol Section 7.2.3) will not be used in any statistical analysis. These data will be listed in data listings only.

16.1. PANSS

The PANSS (Positive and Negative Syndrome Scale) is an interview-based measure of the severity of psychopathology in adults with psychotic disorders and comprises 30 items and 3 subscales. The positive subscale assesses hallucinations, delusions, and related symptoms (7 items); the negative subscale assesses emotional withdrawal, lack of motivation, and related symptoms (7 items); and the general psychopathology subscale assesses other symptoms such as anxiety, somatic concern, and disorientation (16 items). An anchored Likert scale from 1 to 7 (1 = absent, 7 = extreme, with values of 2 and above indicating the presence of progressively more severe symptoms) is used to score each item.

Individual items are summed to derive the following scores:

- Total score = sum of all 30 items. Total score ranges from 30 to 210.

- Subscale scores = sum of items within each of the following subscales:

  - Positive subscale: delusions, conceptual disorganization, hallucinatory behavior, excitement, grandiosity, suspiciousness/persecution, hostility. The subscale score ranges from 7 to 49.

  - Negative subscale: blunted affect, emotional withdrawal, poor rapport, passive/apathetic social withdrawal, difficulty in abstract thinking, lack of spontaneity and flow of conversation, stereotyped thinking. This subscale score ranges from 7 to 49.

  - General psychopathology subscale: somatic concern, anxiety, guilt feelings, tensions, mannerisms and posturing, depression, motor retardation, uncooperativeness, unusual thought content, disorientation, poor attention, lack of judgment and insight, disturbance of volition, poor impulse control, preoccupation, active social avoidance. This subscale score ranges from 16 to 112.

- Marder factor scores = sum of items within each of the following factors (Marder, Davis, Chouinard. 1997):

  - Negative symptoms: blunted affect, emotional withdrawal, poor rapport, passive/apathetic social withdrawal, lack of spontaneity and flow of conversation, motor retardation, active social avoidance. This Marder factor score ranges from 7 to 49.

  - Positive symptoms: delusions, hallucinatory behavior, grandiosity, suspiciousness/persecution, stereotyped thinking, somatic concern, unusual thought content, lack of judgment and insight. This Marder factor score ranges from 8 to 56.

  - Disorganized thought: conceptual disorganization, difficulty in abstract thinking, mannerisms and posturing, poor attention, disturbance of volition, preoccupation, disorientation. This Marder factor score ranges from 7 to 49.

  - Uncontrolled hostility/excitement: excitement, hostility, uncooperativeness, poor impulse control. This Marder factor score ranges from 4 to 28.

  - Anxiety/depression: anxiety, guilt feelings, tension, depression. This Marder factor score ranges from 4 to 28.

- UPSM (Uncorrelated PANSS Score Matrix) factor scores = PANSS item scores of each subject at each visit transformed using the UPSM to obtain scores of 7 transformed PANSS factors (Hopkins et al. 2018):

  - POS: Positive

  - DIS: Disorganized

  - NAA: Negative apathy/avolition

  - NDE: Negative deficit of expression

  - HOS: Hostility

  - ANX: Anxiety

  - DEP: Depression

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- The transformation will be done as follows:

$$[\text{Transformed PANSS Factor Data}]_{(N \times 7)} = [\text{PANSS Data}]_{(N \times 30)} * [\text{UPSM}]_{(30 \times 7)}$$

where

- o [Transformed PANSS Factor Data]$_{(N \times 7)}$ is the transformed matrix with N sets of scores for the 7 transformed PANSS factors.

- o [PANSS Data]$_{(N \times 30)}$ is a matrix with N PANSS assessments and 30 columns containing the scores of 30 PANSS items ordered in the same way as shown in UPSM.

- o [UPSM]$_{(30 \times 7)}$ is a matrix with 30 rows (one for each PANSS item) and 7 columns (one for each of the 7 transformed PANSS factors). This matrix is presented in APPENDIX 5.

- UPSM total factor score = sum of the 7 UPSM factor scores.

PANSS is assessed at these study visits: Visit 1, Visit 2, Visit 3, Visit 5, Visit 6, Visit 8, Visit 10, Visit 12, Visit 14, Visit 16, and Visit 17.

16.1.1. OBSERVED VALUES AND CHANGE FROM BASELINE IN PANSS TOTAL SCORE

16.1.1.1. Exploratory Analysis of PANSS Total Score

Data will be analyzed using a mixed model for repeated measures (MMRM) under the MAR assumption. Under this assumption, the efficacy outcome of subjects in each treatment group after early discontinuation will exhibit the same future evolution as subjects in the same group remaining in the study. The MMRM model will include fixed factors for treatment, visit (Weeks 1, 4, 8, 16, 24, 32, 40, 48, 52; as a categorical variable), country, and treatment-by-visit interaction and include Baseline PANSS total score as a covariate. An unstructured covariance matrix will be used to model the within-subject correlation. Kenward-Roger approximation will be used to calculate the denominator degrees of freedom.

The least squares (LS) mean difference in PANSS total score change from Baseline at Week 52 (SEP-363856 group vs. Quetiapine), their standard errors, the two-sided 95% CIs, and the associated nominal p-values will be calculated from the MMRM model.

In addition, the following statistics will be reported in the MMRM table:

- The LS mean difference in PANSS total score change from Baseline at Weeks 1, 4, 8, 16, 24, 32, 40, 48; their standard errors; the two-sided 95% CIs; and the associated nominal p-values.

- The LS mean of PANSS total score change from Baseline at each time point for each treatment group, their standard errors, and the two-sided 95% CIs.

- Within group effect size at each time point, calculated as the LS mean of each treatment group at each time point divided by the model estimate of standard deviation, obtained as the square root of the corresponding diagonal element of the residual covariance matrix (R matrix from PROC MIXED).

- Between group effect size vs. Quetiapine at each time point, calculated as the LS mean difference of each SEP-363856 group vs. Quetiapine at each time point divided by the model estimate of standard deviation, obtained as the square root of the corresponding diagonal element of the residual covariance matrix (R matrix from PROC MIXED).

In case the model above fails to converge, a spatial exponential covariance structure and a spatial power covariance structure along with an empirical sandwich estimator for the standard errors of the fixed effect parameters will be assumed sequentially. The first covariance structure to yield convergence will be used in the analysis. If the model fails to converge with all three structures specified above, the compound symmetry covariance structure will be assumed.

The normality and homoscedasticity assumptions underlying the primary MMRM model will be assessed graphically and included in the SAS outputs. Marginal studentized and Pearson-type residuals will be plotted against the predicted marginal mean values, respectively; the quantile-quantile (Q-Q) plots of these residuals versus the expected quantiles of the standard normal distribution will also be included in the SAS outputs to provide a graphical view of similarity and difference in the 2 distributions.

16.1.1.2. Sensitivity Analyses of PANSS Total Score

Patterns of the observed data in the exploratory endpoint will be examined through graphical tools based on the reason and the timing of study treatment withdrawal.

Mean change from Baseline in PANSS total score at each time point will be plotted by the reason of early discontinuation (adverse event [separately by COVID-19 relatedness], lack of efficacy, lost to follow-up, withdrawal by subject, non-compliance with study drug, protocol deviation, death [separately by COVID-19 relatedness], pregnancy, other [separately by COVID-19 relatedness]) and for completers, separately for each treatment group. Similar reasons may be combined, depending on the number of subjects who

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discontinued under each reason. Reason pooling will be determined at the Blinded Data Review meeting prior to database lock and treatment unblinding.

Mean change from baseline in PANSS total score at each time point will also be plotted by the timing of early discontinuation (Week 1 terminators, Week 4 terminators, Week 8 terminators, Week 16 terminators, Week 24 terminators, Week 32 terminators, Week 40 terminators, Week 48 terminators, Week 52 terminators) and for completers, separately for each treatment group.

- Week 1 terminators: subjects who discontinue after Visit 2 but before or on Visit 3;

- Week 4 terminators: subjects who discontinue after Visit 3 but before or on Visit 5;

- Week 8 terminators: subjects who discontinue after Visit 5 but before or on Visit 6;

- Week 16 terminators: subjects who discontinue after Visit 6 but before or on Visit 8;

- Week 24 terminators: subjects who discontinue after Visit 8 but before or on Visit 10;

- Week 32 terminators: subjects who discontinue after Visit 10 but before or on Visit 12;

- Week 40 terminators: subjects who discontinue after Visit 12 but before or on Visit 14;

- Week 48 terminators: subjects who discontinue after Visit 14 but before or on Visit 16;

- Week 52 terminators: subjects who discontinue after Visit 16 but before Visit 17 (the EOT visit).

16.1.1.3. Supplementary Analyses of PANSS Total Score

- Analysis of covariance

Change from Baseline in PANSS total score at each scheduled visit and at the LOCF endpoint will be analyzed using an analysis of covariance (ANCOVA) model. The model will include factors for treatment and country, and include Baseline PANSS total score as a covariate. The LS mean of each treatment group, LS mean differences (SEP-383656 vs. Quetiapine), their standard errors and two-sided 95% CIs, and the nominal p-values for treatment differences will be obtained from the model.

Based on the ANCOVA analysis, within group effect size at a given time point will be calculated as the LS mean of the treatment group divided by the standard deviation, obtained as the standard error of the LS mean multiplied by the square root of the treatment group sample size at that time point. Between group

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effect size at a given time point will be calculated as the LS mean difference of SEP-363856 vs. Quetiapine divided by the pooled standard deviation, obtained as the standard error of the LS mean difference divided by the square root of the sum of inverse treatment group sample sizes at that time point.

Baseline PANSS total score will also be analyzed by an ANCOVA model including factors for treatment and country. The nominal p-values for treatment differences will be obtained from the model.

- Complete case analysis

The complete case analysis will be performed on the subset of subjects in the efficacy population who completed the double-blind treatment period and have Week 52/Visit 17 PANSS total score data available within 9 days post the last dose. The MMRM analysis as described in Section 16.1.1.1 will be performed on these subjects.

- Analysis on the PP population

The MMRM analysis as described in Section 16.1.1.1 will be performed on the PP population to evaluate the efficacy of the treatment for these subjects.

- Analysis with missing PANSS item(s) imputed

Due to the use of electronic clinical outcome assessment (eCOA) technology and extensive data quality monitoring during the study, no partially completed PANSS assessments are expected. However, in the rare event of a partially completed PANSS assessment, missing PANSS item scores will be imputed as described below.

In contrast to all other analyses of the efficacy variable where missing PANSS item scores are not imputed and the corresponding PANSS total score is set to missing, in this supplementary analysis, if a PANSS assessment is partially available at a visit (i.e. one or more PANSS items are missing), the missing PANSS item(s) will be imputed. It should be noted that entirely missing PANSS assessments will not be filled in using imputation in this analysis.

The Markov Chain Monte Carlo (MCMC) method is used to obtain full datasets. Under the assumption that each PANSS item X score and dichotomized countries have a multivariate normal distribution, the MCMC method is used to impute missing values assuming MAR (using the SAS MI procedure with the MCMC statement and the IMPUTE=FULL option), by using a data augmentation algorithm, with each

iteration n consisting of an imputation step and a posterior step. The imputation step uses a random draw of $\theta^{(n)}$, parameter of the joint imputation model, to sample missing values from a conditional distribution $P(Y_{mis}|x, y_{obs}, \theta^{(n)})$, obtaining $y_{mis}^{(n)}$, the subset of missing values that need to be filled in to obtain full datasets. The posterior step simulates a new draw of the parameter $\theta^{(n+1)}$ from the posterior distribution given the current full data $P(\theta|x, y_{obs}, y_{mis}^{(n)})$ with a non-informative Jeffreys prior. Treatment group will be taken into account for this imputation (i.e., missing data will be imputed for each treatment group separately). These steps are repeated to obtain 1000 full datasets. The random seed number is specified in the sample SAS code (APPENDIX 3).

For each PANSS item X that needs such imputation, MCMC imputation will be performed based on a multivariate normal distribution including variables for dichotomized countries, Baseline PANSS item X score, and all post-Baseline PANSS item X scores (Week 1/Visit 3, Week 4/Visit 5, Week 8/Visit 6, Week 16/Visit 8, Week 24/Visit 10, Week 32/Visit 12, Week 40/Visit 14, Week 48/Visit 16, Week 52/Visit 17). The imputation will be done by treatment group. By using this method, those visits where entire PANSS assessments are missing will have item X filled in as well. When calculating PANSS total scores on the imputed datasets, the imputed values for those visits should be ignored.

A total of 1000 imputed datasets will be generated for each PANSS item to be imputed this way. Upon completion of the imputation for all individual PANSS items, the datasets for each PANSS item will be combined by the imputation number. PANSS total scores will be calculated for the visits where PANSS assessments are completely or partially available in the original data, using observed/imputed PANSS item scores. As stated earlier, for visits where PANSS assessments are entirely missing in the original data, the PANSS total score should be left as missing.

Each of the 1000 imputed datasets with PANSS total score calculated will be analyzed using the MMRM analysis as described in Section 16.1.1.1. Results from the analysis of each imputed dataset, i.e., the LS means of each treatment group, the LS mean treatment differences (vs. Quetiapine XR), and their standard errors, will be combined using Rubin's imputation rules to produce pooled LS mean and LS mean difference estimates, their standard errors and 95% CIs, and pooled p-values.

16.1.1.4. Subgroup Analyses of PANSS Total Score

For each of the subgroup factors listed in Section 7.5, change from Baseline in PANSS total score at Week 52 will be analyzed using the MMRM method. For the subgroup factors other than country, the MMRM model will include fixed effects for treatment, subgroup, visit, country, Baseline PANSS total

score, and treatment-by-subgroup, treatment-by-visit, subgroup-by-visit, and treatment-by-subgroup-by-visit interactions. For the subgroup factor of country, the MMRM model will include fixed effects for treatment, country, visit, Baseline PANSS total score, and treatment-by-country, treatment-by-visit, country-by-visit, and treatment-by-country-by-visit interactions.

Subgroups that do not have at least 2 EFF population subjects with change from Baseline in PANSS total score data available at Week 52/Visit 17 in each of the two treatment groups will be excluded from the analysis.

Estimates obtained from the MMRM model will be presented separately for each subgroup. The nominal p-value for the treatment-by-subgroup interaction at Week 52/Visit 17 will be presented. The presence of a significant interaction effect will be assessed at the 0.10 level for homogeneity of the treatment effect across the different categories of a subgroup factor. In case of a significant interaction effect, estimates by subgroup will be examined to determine the nature of the interaction (qualitative or quantitative). The MMRM results of all subgroup analyses will also be presented using forest plots.

The observed PANSS total score and the change from Baseline values will also be summarized descriptively by treatment group and visit for each subgroup.

16.1.1.5. Other Analyses of PANSS Total Score

LS Means (+/- Standard Error) of PANSS total score change from Baseline over time based on MMRM estimates will be plotted as described in the figure shell.

The observed values of PANSS total score at Baseline and each scheduled post-Baseline visit will be summarized descriptively. The Baseline PANSS total score will be derived as described in Section 6.2.

The change from Baseline in PANSS total score will be summarized for each scheduled post-Baseline visit. The change from Baseline in PANSS total score will be derived as described in Section 6.7.

PANNS total score will also be summarized by subgroups as listed in Section 7.5.

16.1.2. Observed Values and Change from Baseline in PANSS Subscale Scores

For PANSS subscale scores, the change from baseline at each scheduled post-Baseline will be analyzed as described in Sections 16.1.1.1 and 16.1.1.3 (Analysis of covariance (including LOCF)).

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The observed values of PANSS subscale scores at Baseline and each scheduled post-Baseline visit will be summarized descriptively. The Baseline PANSS subscale scores will be derived as described in Section 6.2.

The change from Baseline in PANSS subscale scores will be summarized for each scheduled post-Baseline visit. The change from Baseline in PANSS subscale scores will be derived as described in Section 6.7.

16.1.3. OBSERVED VALUES AND CHANGE FROM BASELINE IN PANSS MARDER FACTOR SCORES

For PANSS Marder factor scores, the change from baseline at each scheduled post-Baseline will be analyzed as described in Sections 16.1.1.1 and 16.1.1.3 (Analysis of covariance (including LOCF)).

The observed values of PANSS Marder factor scores at Baseline and each scheduled post-Baseline visit will be summarized descriptively. The Baseline PANSS Marder factor scores will be derived as described in Section 6.2.

The change from Baseline in PANSS Marder factor scores will be summarized for each scheduled post-Baseline visit. The change from Baseline in PANSS Marder factor scores will be derived as described in Section 6.7.

16.1.4. OBSERVED VALUES AND CHANGE FROM BASELINE IN PANSS UPSM FACTOR SCORES

For PANSS UPSM factor scores, the change from baseline at each scheduled post-Baseline will be analyzed as described in Sections 16.1.1.1 and 16.1.1.3 (Analysis of covariance (including LOCF)).

The observed values of PANSS UPSM factor scores at Baseline and each scheduled post-Baseline visit will be summarized descriptively. The Baseline PANSS UPSM factor scores will be derived as described in Section 6.2.

The change from Baseline in PANSS UPSM factor scores will be summarized for each scheduled post-Baseline visit. The change from Baseline in PANSS UPSM factor scores will be derived as described in Section 6.7.

16.1.5. Observed Values and Change from Baseline in PANSS UPSM Total Factor Score

For PANSS UPSM total factor scores, the change from baseline at each scheduled post-Baseline will be analyzed as described in Sections 16.1.1.1 and 16.1.1.3 (Analysis of covariance (including LOCF)).

The observed values of PANSS UPSM total factor score at Baseline and each scheduled post-Baseline visit will be summarized descriptively. The Baseline PANSS UPSM total factor score will be derived as described in Section 6.2.

The change from Baseline in PANSS UPSM total factor score will be summarized for each scheduled post-Baseline visit. The change from Baseline in PANSS UPSM total factor score will be derived as described in Section 6.7.

16.1.6. Proportion of Subjects Who Achieve a Response

PANSS response is defined as a 20% or greater improvement (i.e. decrease) in PANSS total score from Baseline.

The percent change in PANSS total score from Baseline will be calculated by:

$$\frac{\text{PANSS total score at a visit or the Week 52 LOCF endpoint - PANSS total score at Baseline}}{\text{PANSS total score at Baseline - 30}} \times 100\%$$

For each subject, the responder indicator will be set to Y if the percent change is negative and the magnitude is equal to or greater than 20%. The indicator will be set to N if the percentage is negative but the magnitude is less than 20% or the percentage is non-negative. The indicator will be set to missing if the percentage is missing.

In addition, PANSS response defined by two more stringent thresholds will be assessed; that is, having a 30% or greater and 50% or greater improvement in PANSS total score from Baseline.

PANSS response at all three thresholds will be derived for all post-Baseline time points.

PANSS response at each scheduled visit and at the LOCF endpoint will be analyzed using a logistic regression model with responder indicator as the dependent variable and include factors for treatment and geographic region, and include Baseline PANSS total score as a covariate. The Number Needed to Treat (NNT) will be provided:

- The NNT for each SEP-363856 group will be derived as:

- $\text{NNT} = \dfrac{1}{\text{Risk Reduction (RR)}} = \dfrac{1}{\text{PANSS Response Rate}_{\text{SEP-363856}} - \text{PANSS Response Rate}_{\text{Quetiapine XR}}}$

- Only positive NNT results will be presented. The NNT results will be provided in whole numbers with any fractional values rounded up to the nearest whole number. The 95% CI of NNT will also be presented and are computed by taking the reciprocal of the 95% CI lower and upper bounds of the RR when both bounds are positive. The lower confidence limit will be rounded down to the largest whole number that is less than the computed estimate, and the upper confidence limit will be rounded up to the smallest whole number that is greater than the computed estimate.

The number and percentage of subjects who achieve a PANSS response will also be summarized descriptively by treatment group and visit.

Lastly, the proportion of subjects achieving a given percentage change threshold in PANSS total score from Baseline at the LOCF endpoint will be calculated for each treatment group. This calculation will be performed at multiple thresholds, starting from -100% and increases at 5% increments or until all subjects are accounted for in all treatment groups, with 5% increments.

16.2. OTHER EFFICACY VARIABLES

16.2.1. OBSERVED VALUES AND CHANGE FROM BASELINE IN CGI-S SCORE

The CGI-S (Clinical Global Impression-Severity) is a clinician-related assessment of the subject's current illness state on a 7-point scale, where a higher score is associated with greater illness severity. The CGI-S score takes one of the following values: 1 (normal, not at all ill), 2 (borderline mentally ill), 3 (mildly ill), 4 (moderately ill), 5 (markedly ill), 6 (severely ill), 7 (among the most extremely ill patients).

CGI-S is assessed at these study visits: Visit 1, Visit 2, Visit 3, Visit 5, Visit 6, Visit 8, Visit 10, Visit 12, Visit 14, Visit 16 and Visit 17.

The change from baseline in CGI-S score at each scheduled post-Baseline will be analyzed as described in Sections 16.1.1.1, 16.1.1.2, 16.1.1.3 (Analysis of covariance (including LOCF), Complete case analysis and Analysis on the PP population) and 16.1.1.4.

LS Means (+/- Standard Error) of CGI-S score change from Baseline over time based on MMRM estimates will be plotted as described in the figure shell.

The observed values of CGI-S score at Baseline and each scheduled post-Baseline visit will be summarized descriptively. The Baseline CGI-S score will be derived as described in Section 6.2.

The change from Baseline in CGI-S score will be summarized for each scheduled post-Baseline visit. The change from Baseline in CGI-S score will be derived as described in Section 6.7.

CGI-S score will also be summarized by subgroups as listed in Section 7.5.

16.2.2. OBSERVED VALUES AND CHANGE FROM BASELINE IN BNSS TOTAL SCORE AND SUBSCALE SCORES

The BNSS (Brief Negative Symptom Scale) is a rating scale that measures the current level of severity of negative symptoms in schizophrenia and schizoaffective disorder. The measure is comprised of 13 individual items organized into 6 subscales: blunted affect (items 9, 10, 11), alogia (items 12, 13), avolition (items 7, 8), anhedonia (items 1, 2, 3), asociality (items 5, 6), and distress (item 4). Each of the items are scored on a Likert-type 7-point scale from 0-6, where values of 0 indicates the symptom is absent and a value of 6 means the symptom is a severe form. The subscale scores are calculated by summing the individual items within each scale. The 13 items are also summed to provide a total score which ranges from 0 to 78.

BNSS is assessed at these study visits: Visit 2, Visit 3, Visit 5, Visit 6, Visit 8, Visit 10, Visit 12, Visit 14, Visit 16, and Visit 17.

For BNSS total score, the change from baseline at each scheduled post-Baseline will be analyzed as described in Sections 16.1.1.1 and 16.1.1.3 (Analysis of covariance (including LOCF) and Analysis with missing PANSS item(s) imputed).

LS Means (+/- Standard Error of BNSS total score change from Baseline over time based on MMRM estimates will be plotted as described in the figure shell.

For BNSS subscale scores, the change from baseline at each scheduled post-Baseline will be analyzed as described in Sections 16.1.1.1 and 16.1.1.3 (Analysis of covariance (including LOCF)).

The observed values of BNSS total score and BNSS subscale scores at Baseline and each scheduled post-Baseline visit will be summarized descriptively. The Baseline BNSS total score and BNSS subscale scores will be derived as described in Section 6.2.

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The change from Baseline in BNSS total score and BNSS subscale scores will be summarized for each scheduled post-Baseline visit. The change from Baseline in BNSS total score and BNSS subscale scores will be derived as described in Section 6.7.

16.2.3. OBSERVED VALUES AND CHANGE FROM BASELINE IN MADRS TOTAL SCORE

The MADRS (Montgomery-Asberg Depression Rating Scale) is a clinician-rated assessment of the subject's level of depression. The measure contains 10 items that measure apparent and reported sadness, inner tension, reduced sleep and appetite, difficulty concentrating, lassitude, inability to feel, and pessimistic and suicidal thoughts. Each item is scored in a range of 0 to 6 points, with higher scores indicating increased depressive symptoms. Total score will be equal to the sum of the 10 items (range between 0 and 60).

MADRS is assessed at these study visits: Visit 2, Visit 3, Visit 5, Visit 6, Visit 8, Visit 10, Visit 12, Visit 14, Visit 16, and Visit 17.

For MADRS total score, the change from baseline at each scheduled post-Baseline will be analyzed as described in Sections 16.1.1.1 and 16.1.1.3 (Analysis of covariance (including LOCF) and Analysis with missing PANSS item(s) imputed).

LS Means (+/- Standard Error) of MADRS total score change from Baseline over time based on MMRM estimates will be plotted as described in the figure shell.

The observed values of MADRS total score at Baseline and each scheduled post-Baseline visit will be summarized descriptively. The Baseline MADRS total score will be derived as described in Section 6.2.

The change from Baseline in MADRS total score will be summarized for each scheduled post-Baseline visit. The change from Baseline in MADRS total score will be derived as described in Section 6.7.

16.2.4. OBSERVED VALUES AND CHANGE FROM BASELINE IN BACS COMPOSITE T SCORE AND COMPONENT TEST T SCORES

The BACS (Brief Assessment of Cognition in Schizophrenia) assesses 6 domains of cognition: verbal memory/learning, working memory, motor function, verbal fluency, speed of processing, and executive function. An electronic tablet-based version of the traditional BACS, called the BAC App, is used in this study. The BAC App was developed to allow standardized presentation of task instructions and stimuli,

audio-recording of responses, and automatized scoring and data management.

The six domains of cognition assessed by BACS are listed below:

- Verbal Memory/Learning is assessed with the Verbal Memory task. Subjects are presented with a list of 15 words and asked to recall as many as possible. This procedure is repeated 5 times. The outcome measure is the number of words recalled.

- Working Memory is assessed with the Digit Sequencing task. Subjects are presented with auditory clusters of numbers (e.g. 936) of increasing length and asked to tell the rater the numbers in order from lowest to highest. The outcome measure is the number of correct responses.

- Motor Function is assessed with the Token Motor task. Subjects are presented with tokens and asked to drag them to a center container as quickly as possible for 60 seconds. The outcome measure is the number of tokens correctly dragged into the container.

- Verbal Fluency is assessed with the Semantic Fluency and Letter Fluency tasks. Subjects are given 60 seconds to generate as many words as possible in a given category (semantic) or for a given letter of the alphabet (letter). The outcome measure for each fluency test is the number of words generated.

- Speed of Processing is assessed with the Symbol Coding task. Subjects are provided a key and asked to fill the corresponding number beneath a series of symbols as quickly as possible within 90 seconds. The outcome measure is the number of correct items.

- Executive Function is assessed with the Tower of London task. Subjects are asked to give the minimum number of times the balls in one picture would need to be moved in order to make the arrangement of balls identical to that in the opposing picture. The outcome measure is the number of correct responses.

The raw scores of the 6 domains of cognition are transformed into component test T scores and then a composite T score summarizing all six domains are derived as described in (Keefe, et al. 2008). The component test T scores and composite T score for each subject at each visit are provided by the BACS vendor for direct use in downstream statistical analyses.

BACS is assessed at these study visits: Visit 2, Visit 7, Visit 10, and Visit 17.

For BACS component test T scores and composite T score, the change from baseline at each scheduled

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post-Baseline will be analyzed as described in Sections 16.1.1.1 and 16.1.1.3 (Analysis of covariance (including LOCF)).

The observed values of BACS component test T scores and composite T score at Baseline and each scheduled post-Baseline visit will be summarized descriptively. The Baseline BACS component test T scores and composite T score will be derived as described in Section 6.2.

The change from Baseline in BACS component test T scores and composite T score will be summarized for each scheduled post-Baseline visit. The change from Baseline in BACS component test T scores and composite T score will be derived as described in Section 6.7.

16.2.5. OBSERVED VALUES AND CHANGE FROM BASELINE IN ESS TOTAL SCORE

The ESS (Epworth Sleepiness Scale) is a self-administered questionnaire with 8 questions. Respondents are asked to rate, on a 4-point scale (0-3), their usual chances of dozing off or falling asleep while engaged in eight different activities. The ESS scale (the sum of the 8 item scores) can range from 0 to 24.

The ESS is assessed at these study visits: Visit 2, Visit 10, and Visit 17.

For ESS total score, the change from baseline at each scheduled post-Baseline will be analyzed as described in Sections 16.1.1.1 and 16.1.1.3 (Analysis of covariance (including LOCF)).

The observed values of ESS total score at Baseline and each scheduled post-Baseline visit will be summarized descriptively. The Baseline ESS total score will be derived as described in Section 6.2.

The change from Baseline in ESS total score will be summarized for each scheduled post-Baseline visit. The change from Baseline in ESS total score will be derived as described in Section 6.7.

16.2.6. OBSERVED VALUES AND CHANGE FROM BASELINE IN SLOF TOTAL SCORE AND SUBSCALE SCORES

The SLOF (Modified Specific Level of Functioning Scale) is designed to measure directly observable behavioural functioning and daily living skills of patients with chronic mental illness (Schneider). The modified version of the SLOF consists of 24 items divided into 2 subscales (Social functioning [comprised of interpersonal relationships] and Community Living Skills [comprised of activities and work skills]). Each item is rated on a 5-point scale. Individual items are summed to determine scores for the total score and

the 2 subscales.

The SLOF is assessed at these study visits: Visit 2, Visit 7, Visit 10, and Visit 17.

For SLOF total score and SLOF subscale scores, the change from baseline at each scheduled post-Baseline will be analyzed as described in Sections 16.1.1.1 and 16.1.1.3 (Analysis of covariance (including LOCF)).

The observed values of SLOF total score and SLOF subscale scores at Baseline and each scheduled post-Baseline visit will be summarized descriptively. The Baseline SLOF total score and SLOF subscale scores will be derived as described in Section 6.2.

The change from Baseline in SLOF total score and SLOF subscale scores will be summarized for each scheduled post-Baseline visit. The change from Baseline in SLOF total score and SLOF subscale scores will be derived as described in Section 6.7.

16.2.7. OBSERVED VALUES AND CHANGE FROM BASELINE IN EQ-5D-5L VAS, INDEX VALUE, AND OBSERVED EQ-5D-5L DIMENSION SCORES

The EQ-5D-5L (EuroQol-5 Dimensions – 5 Levels) is a standardized instrument developed by the EuroQol Group as a measure of health-related quality of life that can be used in a wide range of health conditions and treatments. The EQ-5D-5L consists of two parts: a) the EQ-5D-5L descriptive system, and b) the EQ VAS.

The EQ-5D-5L descriptive system comprises five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has 5 levels: level 1 (no problems), level 2 (slight problems), level 3 (moderate problems), level 4 (severe problems), and level 5 (extreme problems/unable to do). The patient is asked to indicate his/her health state by ticking the box next to the most appropriate statement in each of the five dimensions. This decision results in a 1-digit number that expresses the level selected for that dimension (i.e. the dimension score).

The dimension scores for the five dimensions can be combined into a 5-digit code that describes the patient's health state. An index value (a weighted scoring of the 5 dimension scores with a possible range from less than 0 [where 0 is the value of a health state equivalent to dead; negative values representing values as worse than dead] to 1 [the value of full health]) will be assigned to each observed health state using the US standard value set as defined in APPENDIX 6.

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The EQ VAS records the patient's self-rated health on a vertical visual analogue scale from 0 to 100, where the endpoints are labelled 'The best health you can imagine' and 'The worst health you can imagine'. The VAS can be used as a quantitative measure of health outcome that reflect the patient's own judgment.

EQ-5D-5L is assessed at these study visits: Visit 2 and Visit 17.

For EQ-5D-5L VAS and index value, the change from baseline at each scheduled post-Baseline will be analyzed as described in Section 16.1.1.3 (Analysis of covariance (including LOCF)).

The observed values of EQ-5D-5L VAS, index value and dimension score at Baseline and each scheduled post-Baseline visit will be summarized descriptively. The Baseline EQ-5D-5L VAS, index value and dimension score will be derived as described in Section 6.2.

The change from Baseline in EQ-5D-5L VAS and index value will be summarized for each scheduled post-Baseline visit. The change from Baseline in EQ-5D-5L VAS and index value will be derived as described in Section 6.7.

The number and percentage of subjects reporting each level of problem under each of the 5 dimensions (i.e. the frequency distribution of the dimension scores) will be summarized descriptively by treatment group and visit. The treatment difference in the frequency distribution of each of the 5 dimensions at Week 52/ Visit 17 and the LOCF endpoint will be assessed by using a Chi-squared test.

The EQ-5D health state at a given post-Baseline time point relative to the health state at Baseline will be categorized into:

• Better: If the health state at the post-Baseline time point is better in at least one dimension and is no worse in any other dimension than the health state at Baseline.

• Worse: If the health state at the post-Baseline time point is worse in at least one dimension and is no better in any other dimension than the health state at Baseline.

• Same: If the health state is exactly the same between the post-Baseline time point and Baseline.

• Mixed: If the health state at the post-Baseline time point is better in one dimension but worse in another dimension than the health state at Baseline.

The frequency distribution of the post-Baseline categorized EQ-5D health state relative to the Baseline

will be summarized descriptively by treatment group and visit. The treatment difference in the frequency distribution at Week 52/Visit 17 and the LOCF endpoint will be assessed by using a Chi-squared test.

16.2.8. Observed Values and Change from Baseline in UPSA-B Total Score and Subscale Scores

The UPSA-B (University of California San Diego (UCSD) Performance-based Skills Assessment – Brief Version) assesses everyday functioning in persons with serious mental illness. The UPSA-B is a measure of functional capacity in which patients are asked to role-play tasks in 2 areas of functioning: communication and finances.

The raw score of the financial subscale is the sum of the 10 financial items and ranges from 0 to 11, and the raw score of the communication subscale is the sum of 9 communication items and ranges from 0 to 9. Each subscale score is calculated by dividing the raw score by the highest possible raw score of that subscale and then multiplying by 50, so both subscale scores range from 0 to 50. The UPSA-B total score, calculated as the sum of two subscale scores, ranges from 0 to 100. Higher scores reflect better performance.

UPSA-B is assessed at these study visits: Visit 2, Visit 7, Visit 10, and Visit 17.

For UPSA-B total score and UPSA-B subscale scores, the change from baseline at each scheduled post-Baseline will be analyzed as described in Sections 16.1.1.1 and 16.1.1.3 (Analysis of covariance (including LOCF)).

The observed values of UPSA-B total score and UPSA-B subscale scores at Baseline and each scheduled post-Baseline visit will be summarized descriptively. The Baseline UPSA-B total score and UPSA-B total scores will be derived as described in Section 6.2.

The change from Baseline in UPSA-B total score and UPSA-B subscale scores will be summarized for each scheduled post-Baseline visit. The change from Baseline in UPSA-B total score and UPSA-B subscale scores will be derived as described in Section 6.7.

16.2.9. Observed Values and Change from Baseline in MSQ Score

The MSQ (Medication Satisfaction Questionnaire) is a single-item, patient-rated, rater-administered questionnaire that requires the subject to use a 7-point, Likert-type scale to rate how satisfied they are

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with their current antipsychotic medication. The subject will be asked the following question: "Overall, how satisfied are you with your current antipsychotic medication".

Subjects will select 1 of 7 potential responses based on their level of satisfaction from extremely dissatisfied (1) to extremely satisfied (7) as follows:

(1) Extremely dissatisfied

(2) Very dissatisfied

(3) Somewhat dissatisfied

(4) Neither dissatisfied nor satisfied

(5) Somewhat satisfied

(6) Very satisfied

(7) Extremely satisfied

The MSQ is assessed at these study visits: Visit 1 and Visit 17.

For MSQ total score, the change from baseline at each scheduled visit post-Baseline will be analyzed as described in Section 16.1.1.3 (Analysis of covariance (including LOCF)).

The analysis of MSQ data will be limited to subjects who were being treated with an antipsychotic medication at the time of screening or had been treated with antipsychotic medications within 30 days prior to the Screening visit. These subjects will be identified at the Blinded Data Review meeting prior to database lock and treatment unblinding.

The observed values of MSQ total score at Baseline and each scheduled post-Baseline visit will be summarized descriptively. The Baseline MSQ total score will be derived as described in Section 6.2.

The change from Baseline in MSQ total score will be summarized for each scheduled post-Baseline visit. The change from Baseline in MSQ total score will be derived as described in Section 6.7. In addition, the frequency distribution of the MSQ score will be summarized descriptively by treatment group and visit.

16.2.10. TOBACCO USE

Tobacco use is assessed at these study visits: Visit 2, Visit 7, Visit 10 and Visit 17. Tobacco use data will be summarized descriptively by treatment group and visit.

For each tobacco type, the amount being used at Week 12/Visit 7, Week 24/Visit 10, Week 52/Visit 17 and LOCF in comparison with the amount being used at Baseline will be classified as "increased", "decreased", or "unchanged" for every subject, based on the reported amount used in a given period. If a subject quit using a particular type of tobacco since Baseline, the amount used for that tobacco type will be classified as "decreased". If a subject newly started or restarted using a particular type of tobacco since Baseline, the amount used for that tobacco type will be classified as "increased".

Then for subjects whose changes in amount for all tobacco types between Baseline and each scheduled post-Baseline visit (Week 12/Visit 7, Week 24/Visit 10, Week 52/Visit 17 and LOCF) are not in opposite directions, a subject's overall tobacco consumption at each scheduled post-Baseline visit in comparison with Baseline will be classified as "increased", "decreased", or "unchanged" based on the following:

- o If the change in amount for each tobacco type is either "increased" or "unchanged", the subject's overall consumption will be classified as "increased".

- o If the change in amount for each tobacco type is either "decreased" or "unchanged", the subject's overall consumption will be classified as "decreased".

- o If the change in amount for all tobacco types is "unchanged", the subject's overall consumption will be classified as "unchanged".

The number and percentage of subjects in each overall consumption amount change category will be summarized by treatment group.

In addition, for subjects who reported using "Cigarettes" at either Baseline or each scheduled post-Baseline visit (Week 12/Visit 7, Week 24/Visit 10, Week 52/Visit 17 and LOCF) or at both time points, the number of cigarettes used per day will be derived for both time points. The following conversion will be applied if necessary:

- o Amount: 1 Pack = 20 Cigarettes.

- o Time period: 1 Week = 7 Days; 1 Month = 30 Days.

The amount of cigarette used per day and the change from Baseline values will be summarized by treatment group and visit.

16.2.11. PLASMA COTININE CONCENTRATIONS

Plasma cotinine levels are assessed at these study visits: Visit 2, Visit 7, Visit 10 and Visit 17.

The observed plasma cotinine levels and change from Baseline values at each post-Baseline scheduled visit (Week 12/Visit 7, Week 24/Visit 10, Week 52/Visit 17) will be summarized descriptively by treatment group and visit.

16.2.12. RELAPSE

Relapse is defined as the earliest occurrence of any of the following:

- Worsening of >30% PANSS total score from Baseline (Day 1) and a CGI-S score >3

- Hospitalization for worsening of psychosis

- Emergence of suicidality, homicidality and/or risk of harm to self or others

- Discontinuation from the study due to exacerbation of the underlying illness of schizophrenia.

PANSS and CGI-S assessments taken at both scheduled and unscheduled visits will be considered when identifying the relapse event. The percent change in PANSS total score from Baseline will be calculated as described in Section 16.1.6. Occurrence of hospitalization for worsening of psychosis will be identified by medical review of the data collected on the "*Psychiatric Hospitalization*" CRF page as well as the SAEs prior to database lock. Emergence of suicidality, homicidality, and/or risk of harm to self or others will be identified as outlined in APPENDIX 11. Discontinuation from the study due to exacerbation of the underlying illness of schizophrenia will be identified as an AE included in the SMQ search listed in APPENDIX 13 that has action taken = "Drug Withdrawn".

The evaluation period for relapse will be from the day of the first dose of study medication to 2 days after the day of the last dose of study medication.

The date of relapse is defined as the earliest of: the start date of the assessment at which the qualifying PANSS and CGI-S data were collected, the date of hospital admission for worsening of psychosis, the

date of the assessment at which a qualifying C-SSRS event is identified, the start date of the qualifying adverse event for the second and third criteria, and the last dose date for the fourth criterion.

Time-to-relapse (in days) is defined as the date of relapse – the first dose date + 1. Subjects completing/discontinuing from the study without meeting the criteria for relapse will be censored on 2 days after the last dose of study medication.

If the event date is due to the fourth criterion and is beyond Study Day 364, it will be re-set to the date of Study Day 364. If the event date is due to one of the other three relapse criteria and is beyond Study Day 365, it will be re-set to the date of Study Day 365. A censoring date that is beyond Study Day 365 will be re-set to the date of Study Day 365.

Kaplan-Meier estimates of the median time-to-relapse and the 25th percentile and 75th percentile of time-to-relapse, along with the respective 95% confidence intervals, will be calculated. Kaplan-Meier estimate of the probability of relapse at the end of the treatment period, and its 95% confidence interval, will also be calculated. The time-to-relapse data will be presented in a Kaplan-Meier curve along with log rank test statistic. The log rank test will be used to compare the time-to-relapse (in days) between SEP-363856 50 to 100 mg/day and Quetiapine XR 400 to 800 mg/day treatment groups.

The rate of relapse will be calculated as the proportion of subjects demonstrating a relapse during the 52-week period treatment period out of the EFF population. The 95% confidence interval for the rate of relapse will also be calculated.

The frequency of hospitalizations due to relapse will be summarized by treatment group.

16.2.13. MISSING DATA METHODS FOR EFFICACY VARIABLE(S)

Other than one supplementary analysis for PANSS total score (see Section 16.1.1.3 (Analysis with missing PANSS item(s) imputed)), BNSS total score (see Section 16.2.2) and MADRS total score (see Section 16.2.3), Individual missing item in any scale will not be imputed.

For derived scores that depend on more than one individual item (e.g. PANSS total score, PANSS subscale scores, PANSS Marder factor scores, PANSS UPSM factor scores and UPSM total factor score, BNSS total score, BNSS subscale scores, MADRS total score, ESS total score, SLOF total score, SLOF subscale scores, EQ-5D-5L index value, and UPSA-B total score), if one or more items are missing at a visit, the derived score will be set to missing. The corresponding change from Baseline value at a given

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post-Baseline time point will be set to missing if the Baseline derived score is missing or if the derived score at that time point is missing.

For PANSS response, any subject with a missing PANSS total score at Baseline or at any post-Baseline time point will have their PANSS response set to missing for that time point.

17 SAFETY OUTCOMES

All outputs for the safety outcomes will be based on the SAF Population.

Unless otherwise specified, the safety summary tables will include the following columns: SEP-363856 50 to 100 mg/day and Quetiapine XR 400 to 800 mg/day.

Safety data will be used in analysis irrespective of emergency treatment unblinding (see protocol Section 7.2.3).

17.1 ADVERSE EVENTS AND PRE-TREATMENT EVENTS

Adverse events (AEs) and pre-treatment events will be coded using MedDRA central coding dictionary, Version 22.0.

Any COVID-19 related Adverse Events and pre-treatment events will be identified using a pre-defined search:

Table 2: Predefined search criteria for COVID-19 related adverse events or pre-treatment events.

Lower Level Term	Lower Level Term Code	**Preferred Term**	Preferred Term Code	Search Criteria for COVID-19 Related Adverse Events or Pre-treatment Events
Coronavirus test positive	1007025	Coronavirus test positive	10070255	Preferred Term Code = 10070255 or 10053983
Coronavirus infection	10051905	Corona virus infection	10053983	

Any adverse events related to the Russia-Ukraine geopolitical conflict will be identified by the reported term containing "BCP22".

AEs are defined as untoward medical occurrences that started at the same time of or after the first dose of study drug. Untoward medical occurrences that started prior to the first dose of study drug are pre-treatment events.

Whenever available, the time information should be accounted for in the derivation of AEs vs. pre-treatment events. In the case where time is not available, untoward medical occurrences that started on or after the day of the first dose of study drug will be considered AEs; those that started before the day of the first dose of study drug will be considered pre-treatment events.

See APPENDIX 2 for handling of partial dates for AEs. In the case where it is not possible to classify an untoward medical occurrence as an AE or a pre-treatment event, it will be classified by the worst case; i.e. AE.

Unless otherwise specified, for the purpose of statistical analysis, the AEs in the 361-304 database which started within 9 days after the last dose of 361-304 study drug, will be used in table summaries. All records in the 361-304 AE database, including those that started beyond 9 days after the last dose of study drug, will be listed in data listings.

Overall summary of the incidence of all AEs, AEs related to COVID-19, AEs related to geopolitical conflict, study medication-related AEs, severe AEs, serious AEs, AEs leading to discontinuation from study, AEs leading to study medication withdrawal, AEs leading to study medication interruption, AEs leading to dose reduction, AEs leading to dose increase and AEs leading to death will be provided by treatment group. This summary will also be repeated by the geographic region, sex, age group, number of prior hospitalizations for treatment of schizophrenia, duration of schizophrenia, and BMI category subgroups.

Listings will be provided for all AEs, severe AEs, serious AEs, AEs leading to discontinuation from the study, AEs leading to study medication withdrawal, AEs leading to study medication interruption, AEs leading to dose reduction, AEs leading to dose increase, AEs leading to death, AEs of potential drug abuse and dependence and extrapyramidal AEs, and psychiatric AEs leading to discontinuation from the study (PAEDCs), AEs related to geopolitical conflict, AEs related to COVID-19. A listing of pre-treatment events will also be presented. When complete event start date and complete event end date are available, duration of AEs/pre-treatment events will be calculated as: event end date – event start date +

1. Duration will be presented in data listings.

For all summaries, each subject will be counted only once within each category (e.g. an AE type, a severity level, a relationship category, a duration of exposure category, a SOC, a high level term (HLT), and a PT). If not otherwise specified, all summaries will present the number and percentage of subjects as well as the number of events. For summaries by SOC and PT, AEs will be sorted by SOC based on the internationally agreed order (see APPENDIX 10) and then by PT in decreasing frequency in the "SEP-363856 50 to 100 mg/day" column. For summaries by SOC, HLT, and PT, AEs will be sorted by SOC based on the internationally agreed order and then by HLT and PT in decreasing frequency in the "SEP-363856 50 to 100 mg/day" column.

COVID-19 related pre-treatment events and AEs and geopolitical conflict related pre-treatment events and AEs will be displayed similarly as any other pre-treatment events and AEs.

17.1.1 ALL AEs

All AEs will be summarized by SOC and PT, as well as by SOC, HLT, and PT. The summary by SOC and PT will also be presented for the following subgroups: geographic region, sex, age group, number of prior hospitalizations for treatment of schizophrenia, duration of schizophrenia, and BMI category.

In addition, summary tables (by SOC and PT) will be generated for those AEs starting after the last dose of study drug and those AEs starting more than 1 day after the last dose of study drug.

AEs reported by ≥2.0% (without rounding) of subjects in any treatment group will be summarized by SOC and PT.

Non-serious AEs reported by >5.0% (without rounding) of subjects in any treatment group will be summarized by SOC and PT.

The summary by SOC and PT will be broken down further by maximum severity, by strongest relationship to study medication and by duration of exposure to study medication at earliest onset. These summaries are described in the sections below.

17.1.1.1. Severity

Severity is classed as mild/ moderate/ severe (increasing severity). AEs with a missing severity will be classified as severe.

If a subject reported an AE more than once within that SOC/ PT with different severity levels, the subject will be assigned to a severity level for that SOC/ PT based on the worst case severity (i.e. maximum severity). Event counts will not be included in this summary.

In a separate table, severe AEs will be summarized by SOC and PT.

17.1.1.2. Relationship to Study Medication

Relationship to study medication, as indicated by the Investigator, is classified as "not related"/ "possible"/ "probable"/ "definite" (increasing strength of relationship). A "related" AE is defined as an AE with a relationship to study medication as "possible", "probable" or "definite". AEs with a missing relationship to study medication will be regarded as related to the study medication. For this summary, AEs will be presented in 2 categories, related and not related.

If a subject reported an AE more than once within the same SOC/ PT in different relationship categories, the subject will be assigned to a category for that SOC/ PT based on the worst case relationship (i.e. strongest relationship). Event counts will not be included in this summary.

In a separate table, study medication-related AEs will be summarized by SOC and PT.

17.1.1.3. Duration of Exposure

Duration of exposure to study medication at earliest onset is categorized below:

1 to 13, 14 to 27, 28 to 41, 42 to 89, 90 to 179, 180 to 269, 270 to 359 and ≥360 days.

If a subject reported an AE more than once within the same SOC/ PT in different exposure categories, the subject will be assigned to a category for that SOC/ PT based on the earliest onset. Event counts will not be included in this summary.

Denominators for exposure intervals will be based on the number of subjects who were exposed as of the first day of the interval. For cases where events start after the last dose, the exposure interval for the event will be considered the interval of the last day of exposure to study medication.

17.1.2 AEs Leading to Study Medication Withdrawal

AEs leading to permanent withdrawal from the study medication are those AEs with "Action Taken with

Study Treatment" = "Drug Withdrawn" on the "*Adverse Events*" CRF form.

AEs leading to study medication withdrawal will be summarized by SOC and PT.

17.1.3 AEs LEADING TO STUDY MEDICATION INTERRUPTION

AEs leading to study medication interruption are those AEs with "Action Taken with Study Treatment" = "Drug Interrupted" on the "*Adverse Events*" CRF form.

AEs leading to study medication interruption will be summarized by SOC and PT.

17.1.4 AEs LEADING TO DOSE REDUCTION

AEs leading to dose reduction are those AEs with "Action Taken with Study Treatment" = "Dose Reduced" on the "Adverse Events" CRF form.

AEs leading to dose reduction will be summarized by SOC and PT.

17.1.5 AEs LEADING TO DOSE INCREASE

AEs leading to dose increase are those AEs with "Action Taken with Study Treatment" = "Dose Increased" on the "Adverse Events" CRF form.

AEs leading to dose increase will be summarized by SOC and PT.

17.1.6 AEs LEADING TO DISCONTINUATION FROM STUDY

AEs leading to discontinuation from the study are those AEs with "Caused Study Discontinuation" = "Yes" or missing on the "*Adverse Events*" CRF form.

AEs leading to discontinuation from the study will be summarized by SOC and PT.

17.1.7 SERIOUS ADVERSE EVENTS

SAEs are those AEs recorded as "Serious" on the "*Adverse Events*" CRF form.

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SAEs will be summarized by SOC and PT. The summary will also be presented for the following subgroups: geographic region, sex, age group, number of prior hospitalizations for treatment of schizophrenia, duration of schizophrenia, and BMI category.

Another table will summarize SAEs for European Union Drug Regulating Authorities Clinical Trials Database (EudraCT), including the number of causally related events.

In a separate table, SAEs starting within 7 days after the last dose of study drug will be summarized by SOC and PT as well.

17.1.8 ADVERSE EVENTS LEADING TO DEATH

AEs leading to death are those AEs with "Outcome" = "Fatal" on the "*Adverse Events*" CRF form.

COVID-19 related AEs that led to death are those AEs related to COVID-19 with "Outcome" = "Fatal".

Geopolitical conflict related AEs that led to death are those AEs with reported term containing "due to Geopolitical conflict" and "Outcome" = "Fatal". AEs leading to death will be summarized by SOC and PT.

17.1.9 ADVERSE EVENTS OF POTENTIAL DRUG ABUSE AND DEPENDENCE

AEs associated with potential drug abuse and dependence will be identified as described in APPPENDIX 7.

These AEs will be summarized by PT only.

17.1.10 EXTRAPYRAMIDAL ADVERSE EVENTS

Extrapyramidal AEs will be identified by MedDRA SMQ 20000095 Extrapyramidal syndrome as described in APPENDIX 4.

These AEs will be summarized by PT only.

17.1.11 ADVERSE EVENTS EXPLORATORY ANALYSIS

Odds ratios (OR) with 95% CIs and p-values will be provided for all AEs, SAEs, AEs leading to

discontinuation, and AEs relating to extrapyramidal symptoms (EPS) between the two treatment groups using a logistic regression model with treatment and geographic region as categorical factors.

Each subject will be counted only once for each AE type. Categories for each treatment group will be AE vs no AE for each AE type listed above.

17.1.12 ADVERSE EVENTS BY SUBGROUPS

The subgroup factors of interest for AE summaries include: geographic region, sex, age group, number of prior hospitalizations for treatment of schizophrenia, duration of schizophrenia, and BMI category (see Section 7.5). AE by subgroup summaries are described in the individual sections above.

17.1.13 PSYCHIATRIC ADVERSE EVENTS LEADING TO DISCONTINUATION FROM STUDY (PAEDCs)

Additional information is collected for the non-serious psychiatric AEs that led to discontinuation from the study as well as for all serious psychiatric AEs within the study.

1. Could the psychiatric AE be accounted for by an exacerbation of the underlying mental illness? Describe how the symptoms or behaviors of the psychiatric AE are characteristic of or similar to those typically experienced by the patient and/or how they are atypical/different.

2. Describe any new psychosocial stressors that may have contributed to the event.

3. Describe any adverse reactions to other concomitant medications that may have accounted for / contributed to the event.

4. Describe any recreational drug use that may have accounted for / contributed to the event. Please provide results of any recent drug screens.

5. Describe any other medical conditions that could manifest with psychiatric symptoms that might have accounted for or contributed to the event.

6. Were there any new physical or neurological symptoms that emerged at the same time as worsening of psychiatric symptoms? Please provide any details of the medical review of body systems at the time of the event.

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The above information is recorded in separate trackers and not part of the CRF. This information will be presented in separate data listings only.

17.2 LABORATORY EVALUATIONS

Results from the central laboratory to be reported for this study include Hematology, Chemistry (including lipid panel and thyroid panel), Urinalysis, Urine drug screening, Serology panel, Serum pregnancy (β-HcG) (in female subjects only), Urine pregnancy (in female subjects only), Follicle stimulating hormone (FSH) (in female subjects with suspected menopause). Due to the Russia-Ukraine geopolitical conflict, some patients from these regions will not be able to utilize the central laboratory and instead report results from local laboratories. These local laboratory results will be evaluated along the central laboratory results however not normalized against the central laboratory results. If, for a given visit, both local and central laboratory results are available, preference will be given to the central lab result.

Serum and urine pregnancy results in female subjects, FSH level in female subjects, serology panel, and any unexpected lab parameters not specified in protocol Section 21 (APPENDIX II. CLINICAL LABORATORY TESTS) will only be listed. Laboratory parameters prespecified in protocol Section 21 under the categories of "HEMATOLOGY", "BLOOD CHEMISTRIES" (plus HOMA-IR), "URINALYSIS", and "URINE DRUG SCREENING" will be summarized in tables as well as presented in listings.

Listing presentations will use both standard international (SI) Units and conventional units. Table summaries will also be provided using both SI units and conventional units.

Quantitative laboratory measurements reported as "<X", i.e. below the lower limit of quantification (BLQ), or ">X", i.e. above the upper limit of quantification (ULQ), will be converted to X for the purpose of quantitative summaries, but they will be presented as recorded, i.e. as "<X" or ">X" in the listings.

The following summaries will be provided:

● By-visit summary of observed values and change from Baseline values for quantitative measurements in hematology, chemistry, and urinalysis. Serum prolactin results will be summarized overall and separately by sex. Glucose, insulin, HOMA-IR, and lipid panel results (total cholesterol, LDL cholesterol, HDL cholesterol and triglycerides) will be summarized by fasting status: fasting only and overall (fasting, non-fasting, or fasting status unknown combined). Change from Baseline for glucose, insulin, HOMA-IR, and lipid panel results will only be calculated if post-Baseline fasting

status is matching Baseline fasting status.

- By-visit summary of the number and percentage of subjects in each outcome category for qualitative measurements in urinalysis (as applicable) and for urine drug screening results. Urine drug screening results will be reported as "Positive"/ "Negative".

- Shift in laboratory results (chemistry, hematology, urinalysis) from Baseline to Week 1/Visit 3, Week 4/Visit 5, Week 12/Visit 7, Week 24/Visit 10, Week 36/Visit 13, Week 52/Visit 17, and LOCF Endpoint according to the reference range criteria. The existing reference range indicators provided by the central laboratory will be mapped as needed to categories of "Normal" (within the reference range) / "Abnormal" (outside the reference range) for urinalysis non-pH results, and to categories of "Low" (below the reference range) / "Normal" (within the reference range) / "High" (above the reference range) for chemistry and hematology results as well as urinalysis pH results.

- Number and percentage of subjects with at least one potentially clinically significant (PCS) laboratory value (see APPENDIX 8) post-Baseline. The period of evaluation includes both the double-blind treatment period and the follow-up period up to and including 9 days after the last dose of study drug, including unscheduled visits. Subjects will be counted in a particular PCS category if they met that PCS criteria at least once during the period of evaluation, regardless of their Baseline value.

- The change from Baseline values at Week 52/Visit 17 and LOCF Endpoint for selected laboratory parameters will be evaluated using a nonparametric rank ANCOVA analysis to compare SEP-363856 50 to 100 mg/day and Quetiapine XR 400 to 800 mg/day treatment groups. Baseline values and change from Baseline values will be ranked. A linear regression analysis will be performed on the change from Baseline value ranks with the Baseline value ranks as the independent variable, to produce regression residuals. Using the values of the residuals as scores, the Cochran-Mantel-Haenszel row mean scores test will be used to compare between the SEP-363856 and Quetiapine XR treatment groups. This analysis will be conducted for prolactin (overall and by sex), glucose (overall and fasting), insulin (overall and fasting), HOMA-IR (overall and fasting), lipid panel (overall and fasting), and HbA1c.

In order to assess the potential cardiometabolic effect of SEP-363856, select laboratory parameters will be summarized based on the subgroup of subjects who are identified to be metabolically impaired at Baseline (see Section 17.2.3) and on the subgroup of subjects who are non- metabolically impaired at Baseline. The following summaries will be provided on this subset of subjects:

- By-visit summary of observed values and change from Baseline values for LDL, HDL, total cholesterol, triglycerides, glucose, and HbA1c. LDL, HDL, total cholesterol, triglycerides, and glucose results will be summarized by fasting status: fasting only and overall (fasting, non-fasting, or fasting status unknown combined). Change from Baseline for LDL, HDL, triglycerides, and glucose results will only be calculated if post-Baseline fasting status is matching Baseline fasting status.

All laboratory data will be provided in data listings, with the values outside the reference ranges flagged. In addition, separate listings will be provided to present the laboratory data that met the PCS criteria.

A boxplot will be created to present Baseline, Week 1/Visit 3, Week 4/Visit 5, Week 12/Visit 7, Week 24/Visit 10, Week 36/Visit 13, and Week 52/Visit 17 values by treatment group for lipid parameters (total cholesterol, LDL, HDL, and triglycerides) and glucose by fasting status: fasting only and overall (fasting, non-fasting, or fasting status unknown combined). In addition, a boxplot will be created to present Baseline, Week 1/Visit 3, Week 4/Visit 5, Week 12/Visit 7, Week 24/Visit 10, Week 36/Visit 13, and Week 52/Visit 17 prolactin values by treatment group by sex: Overall, males, females. Lastly, the values of HbA1c will be presented by visit and treatment group in a boxplot as well. Results of LDL, HDL, triglycerides, glucose, and HbA1c will be plotted for all subjects, for the subset of subjects who are metabolically impaired at Baseline, and for the subset of subjects who are non-metabolically impaired at baseline. Each of these boxplots will be repeated to present the change from Baseline values.

17.2.1 LABORATORY SPECIFIC DERIVATIONS

- Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) will be calculated for each visit:

HOMA-IR = Glucose (mg/dL) × Insulin (mU/L) / 405

- The following conversion factors will be used if needed:

Glucose (mg/dL) = Glucose (mmol/L) × 18.015588;

Insulin (mU/L) = Insulin (pmol/L) × (1/6).

If both central and local lab results are available for a given assessment, preference should be given to the central lab result.

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17.2.2 LABORATORY REFERENCE RANGES

Laboratory reference range indicators will be provided by the laboratory vendor and used in statistical analyses. Only if a reference range indicator is missing in the data transfer will it be derived in the analysis step as described below.

- Quantitative laboratory measurements (that are not urinalysis erythrocytes or urinalysis leukocytes) will be compared with the relevant laboratory reference ranges in original units and categorized as:

  - Low: Below the lower limit of the laboratory reference range.

  - Normal: Within the laboratory reference range (upper and lower limit included).

  - High: Above the upper limit of the laboratory reference range.

- For laboratory parameters with categorical outcomes, as well as urinalysis erythrocytes and urinalysis leukocutes, if the result is within the reference range, the indicator is "NORMAL"; if the result is not within range, the indicator is "ABNORMAL".

17.2.3 DEFINITION OF METABOLIC IMPAIRMENT

Based on Alberti et al, metabolic impairment is defined as follows:

- If a male subject meets at least 3 out of 5 of the characteristics listed below, the subject is considered metabolically impaired at Baseline.

  - Baseline waist circumference ≥ 102 cm

  - Baseline fasting triglycerides ≥ 150 mg/dL (1.7 mmol/L) or use of drug treatment for elevated triglycerides at Baseline

  - Baseline fasting HDL < 40 mg/dL (1.0 mmol/L) or use of drug treatment for reduced HDL at Baseline

  - (Baseline supine systolic blood pressure ≥ 130 mmHg and/or Baseline supine diastolic blood pressure ≥ 85 mmHg) or use of anti-hypertensive medications at Baseline

  - Baseline fasting glucose ≥ 100 mg/dL or use of antidiabetic medications at Baseline

- If a female subject meets at least 3 out of 5 of the characteristics listed below, the subject is considered metabolically impaired at baseline.

    o Baseline waist circumference ≥ 88 cm

    o Baseline fasting triglycerides ≥ 150 mg/dL (1.7 mmol/L) or use of drug treatment for elevated triglycerides at Baseline

    o Baseline fasting HDL < 50 mg/dL (1.3 mmol/L) or use of drug treatment for reduced HDL at Baseline

    o (Baseline supine systolic blood pressure ≥ 130 mmHg and/or Baseline supine diastolic blood pressure ≥ 85 mmHg) or use of anti-hypertensive medications at Baseline

    o Baseline fasting glucose ≥ 100 mg/dL or use of antidiabetic medications at Baseline

The use of medications for elevated triglycerides or reduced HDL, anti-hypertensive medications, and antidiabetic medications at Baseline will be determined based on blinded data review prior to database lock. These medications must have started before study medication first dose and must have ended after study medication first dose or be ongoing to be considered as being used at Baseline.

17.3 ECG EVALUATIONS

Data from the centrally over-read ECG (Electrocardiogram) results will be included in the reporting of this study.

The following ECG parameters will be reported for this study:

- PR Interval (msec)

- RR Interval (msec)

- QRS Duration (msec)

- QRS Axis (deg)

- QT Interval (msec)

- QTcF Interval (msec) (Fridericia's Correction of QT interval)

- QTcB Interval (msec) (Bazett's Correction of QT interval)

- Heart Rate (bpm)

- Overall assessment of ECG as determined by the central over-read:

    o Normal

    o Abnormal, Insignificant

    o Abnormal, Potentially Significant

    o Abnormal, Significant

    o Not Evaluable

- ECG findings

    o ECG findings will only be listed. Other ECG data will be summarized in tables as well as presented in listings.

    o The following summaries will be provided:

- By-visit summary of observed values and change from Baseline values for quantitative measurements.

- By-visit summary of ECG overall assessment results as determined by the central over-read ("Normal", "Abnormal, Insignificant", "Abnormal, Potentially Significant", "Abnormal, Significant", "Not Evaluable").

- Shift in ECG overall assessment as determined by the central over-read from Baseline to Week 1/Visit 3, Week 4/Visit 5, Week 12/Visit 7, Week 24/Visit 10, Week 36/Visit 13, Week 52/Visit 17, and LOCF Endpoint.

- Number and percentage of subjects who met each of the QTc interval prolongation criteria (see Section 17.3.1). The period of evaluation includes both the double-blind treatment period and the follow-up period up to and including 9 days after the last dose of study drug, including unscheduled visits.

- Number and percentage of subjects with at least one PCS ECG value (see Section 17.3.2) post-

Baseline. The period of evaluation includes both the double-blind treatment period and the follow-up period up to and including 9 days after the last dose of study drug, including unscheduled visits. Subjects will be counted in a particular PCS category if they met that PCS criteria at least once during the period of evaluation, regardless of their Baseline value.

All ECG parameters, overall assessment as determined by the central over-read, and findings will be provided in a data listing. In addition, separate listings will be generated to present the QTc interval data of subjects who met at least one QTc prolongation criterion and the ECG data that met the PCS criteria.

17.3.1 QTc INTERVAL PROLONGATION CRITERIA

QTc interval prolongation will be identified in accordance with the following predefined criteria (same criteria apply to both QTcF and QTcB):

- >450 msec at any post-Baseline time point (including unscheduled visit) not present at Baseline

- >480 msec at any post-Baseline time point (including unscheduled visit) not present at Baseline

- >500 msec at any post-Baseline time point (including unscheduled visit) not present at Baseline

- ≥30 msec increase from Baseline for at least one post-Baseline measurement (including unscheduled visits) and <60 msec increase from Baseline for all post-Baseline measurements (including unscheduled visits)

- ≥60 msec increase from Baseline for at least one post-Baseline measurement (including unscheduled visits)

17.3.2 ECG POTENTIALLY CLINICALLY SIGNIFICANT CRITERIA

Potentially clinically significant ECG measurements will be identified in accordance with the following predefined PCS criteria:

Table 3: Predefined ECG PCS criteria.

ECG Parameter	PCS Low	PCS High

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Heart Rate (beats/min)	--	≥100
PR Interval (msec)	--	≥210
QRS Interval (msec)	--	≥120

17.4 VITAL SIGNS

The following Vital Signs measurements will be reported for this study:

- Supine and Standing SBP (mmHg)

- Supine and Standing DBP (mmHg)

- Supine and Standing Pulse Rate (bpm)

- Respiratory Rate (breaths/min)

- Temperature (ºC)

- Weight (kg)

- BMI (kg/m^2)

- Waist Circumference (cm)

The following summaries will be provided for vital signs data:

- By-visit summary of observed values and change from Baseline values for vital sign measurements, including Follow-up/Visit 18.

- Number and percentage of subjects with at least one PCS vital sign value (see Section 17.4.2) post-Baseline. The period of evaluation includes both the double-blind treatment period and the follow-up period up to and including 9 days after the last dose of study drug, including unscheduled visits. Subjects will be counted in a particular PCS category if they met that PCS criteria at least once during the period of evaluation, regardless of their Baseline value.

- Number and percentage of subjects with orthostatic hypotension and/or orthostatic tachycardia (see

Section 17.4.1). The data will be summarized for Baseline and the overall post-Baseline period (which covers both the double-blind treatment period and the follow-up period up to and including 9 days after the last dose of study drug, including unscheduled visits), as well as by visit, including Follow-up/Visit 18.

- By-visit summary of BMI category and shift in BMI category from Baseline to each post-Baseline time point. BMI categories are listed in Section 7.5.

- By-visit summary of observed values and change from Baseline values for vital signs measurements by BMI category.

- The change from Baseline values at Week 52/Visit 17 and LOCF Endpoint for weight and BMI will be analyzed using nonparametric rank ANCOVA similarly to the analysis described in Section 17.2.

- By-visit summary and PCS summary based on metabolically impaired subjects at baseline (see Section 17.2.3) and non-metabolically impaired subjects at baseline.

All vital signs data will be provided in a data listing. In addition, a separate listing will be generated to present the vital signs data that met the PCS criteria. All occurrences of orthostatic hypotension and orthostatic tachycardia will also be presented in a listing.

A boxplot will be created to present weight data by time point and treatment group for all subjects, for the subset of subjects who are metabolically impaired at Baseline, and for the subset of subjects who are non-metabolically impaired at baseline. The boxplots will be repeated to present the change from Baseline values.

17.4.1 VITAL SIGNS SPECIFIC DERIVATIONS

- BMI expressed in kg/m^2 = Weight (kg)/ height (m)^2.

The height collected at Visit 1 will be used to derive BMI where needed throughout the study.

- Orthostatic hypotension is defined as a decrease of ≥20 mmHg in SBP or ≥10 mmHg in DBP after a subject has been standing for at least 2 to 4 minutes, compared to the SBP and DBP in the supine position, respectively.

- Orthostatic tachycardia is defined as a heart rate increase of ≥20 bpm after a subject has been

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standing for at least 2 to 4 minutes compared to the heart rate measured in the supine position, and a heart rate of >100 bpm after the subject has been standing for at least 2 to 4 minutes.

17.4.2 VITAL SIGNS POTENTIALLY CLINICALLY SIGNIFICANT CRITERIA

Potentially clinically significant vital sign measurements will be identified in accordance with the following predefined PCS criteria:

Table 4: Predefined vital sign PCS criteria.

Vital Sign Parameter	PCS Low	PCS High
SBP (Supine, Standing) (mmHg)	Value ≤90 and ≥20 decrease from Baseline	Value ≥180 and ≥20 increase from Baseline
DBP (Supine, Standing) (mmHg)	Value ≤50 and ≥15 decrease from Baseline	Value ≥105 and ≥15 increase from Baseline
Pulse Rate (Supine, Standing) (beats/min)	Value ≤50 and ≥15 decrease from Baseline	Value ≥120 and ≥15 increase from Baseline
Weight (kg)	≥7% decrease from Baseline	≥7% increase from Baseline
Temperature (°C)	NA	Value ≥38.3°C and ≥0.8°C increase from Baseline

17.5 PHYSICAL EXAMINATION

As all physical and neurological findings will be recorded as medical history or AEs, no specific analysis of physical and neurological examination will be performed.

17.6 OTHER SAFETY ASSESSMENTS

17.6.1 COLUMBIA SUICIDE SEVERITY RATING SCALE (C-SSRS)

The C-SSRS is a tool designed to systematically assess and track suicidal behavior and suicidal ideation for life time, one month prior to the screening visit for suicidal ideation and 6 months prior to the screening visit for suicidal behavior, and throughout the study. The strength of this suicide classification system is in its ability to comprehensively identify suicidal events while limiting the over-identification of suicidal behavior. The C-SSRS Baseline/Screening Version is used at the screening visit and the C-SSRS Since Last Visit Version is used from Visit 2 and onward. Subjects with Type 4 (active suicidal ideation with some intent to act, without specific plan) or Type 5 (active suicidal ideation with specific plan and intent) suicidal ideation during the study will be discontinued from the study and referred to a mental health professional.

C-SSRS includes two main sections: Suicidal Ideation and Suicidal Behavior.

The following outcomes are C-SSRS categories and have binary responses (yes/no). The categories are re-ordered from the scale to facilitate the definitions of the C-SSRS endpoints, and to provide clarity in the presentation of the results.

- Suicidal ideation is measured by 5 categories, representing 5 subtypes of suicidal ideation with increasing severity:

    - Category 1: Wish to be Dead

    - Category 2: Non-specific Active Suicidal Thoughts

    - Category 3: Active Suicidal Ideation with Any Methods (Not Plan) without Intent to Act

    - Category 4: Active Suicidal Ideation with Some Intent to Act, without Specific Plan

    - Category 5: Active Suicidal Ideation with Specific Plan and Intent

- Suicidal behavior is measured by 5 categories, representing 5 subtypes of suicidal behavior:

    - Category 6: Preparatory Acts or Behavior

    - Category 7: Aborted Attempt

- Category 8: Interrupted Attempt

- Category 9: Actual Attempt (non-fatal)

- Category 10: Completed Suicide

The 10 categories above are not mutually exclusive. Subjects will be counted in each category for which they have an event.

Self-injurious behavior without suicidal intent is a non-suicide-related C-SSRS outcome, and also has a binary response (yes/no).

For the purpose of C-SSRS analysis, "Baseline" and the overall "post-Baseline" period are defined as follows.

Time point	Study Visit	C-SSRS Version	Derivation Rule
Baseline	Visit 1	Baseline/Screening – Past 1 Month for Suicidal Ideation / Past 6 Months for Suicidal Behavior	Most severe outcome
	Visit 2*	Since Last Visit	
Post-Baseline	All post-Baseline visits up to and including 9 days after the last dose of study drug, including unscheduled visits	Since Last Visit	Most severe outcome

* Note: The Visit 2 C-SSRS assessment must be administered prior to the first dose of study medication in order to be used in the C-SSRS Baseline derivation.

The following C-SSRS composite endpoints will be derived for each time point of interest (i.e. Baseline, overall post-Baseline, and each scheduled visit including Follow-up/Visit 18) as follows:

- Any suicidal ideation: A "yes" answer to any one of the 5 suicidal ideation questions on C-SSRS (Categories 1 to 5).

- Any suicidal behavior: A "yes" answer to any one of the 5 suicidal behavior questions on the C-SSRS (Categories 6 to 10).

- Any suicidality: A "yes" answer to any one of the 10 suicidal ideation and behavior questions on the C-SSRS (Categories 1-10).

For each subject, the suicidal ideation score at each time point of interest (i.e. Baseline, overall post-Baseline, the LOCF endpoint, and each scheduled visit including Follow-up/Visit 18) is defined as the maximum suicidal ideation category (1-5) present for the time point of interest. If no ideation is present a score of 0 is assigned.

The number and percentage of subjects with any suicidality, any suicidal ideation and subtypes of ideation, any suicidal behavior and subtype of behavior, and any non-suicidal self-injurious behavior will be presented for:

- Baseline (as defined above)

- The overall post-Baseline period (as defined above)

- Each scheduled visit: Screening/Visit 1 (lifetime; past 1 month for ideation/past 6 months for behavior), Randomization/Visit 2, Week 1/Visit 3, Week 2/Visit 4, Week 4/Visit 5, Week 8/Visit 6, Week 12/Visit 7, Week 16/Visit 8, Week 20/Visit 9, Week 24/Visit 10, Week 28/Visit 11, Week 32/Visit 12, Week 36/Visit 13, Week 40/Visit 14, Week 44/Visit 15, Week 48/Visit 16, Week 52/Visit 17, and Follow-up/Visit 18.

Difference between SEP-363856 50 to 100 mg/day treatment group against the Quetiapine XR 400 to 800 mg/day group for the proportion of subjects with any suicidality, any suicidal behavior, and any suicidal ideation at Baseline and during the overall post-Baseline period will be evaluated using Fisher's Exact test.

Shift in suicidal ideation score from Baseline to the overall post-Baseline period, to each of the scheduled visits (Week 1/Visit 3, Week 2/Visit 4, Week 4/Visit 5, Week 8/Visit 6, Week 12/Visit 7, Week 16/Visit 8, Week 20/Visit 9, Week 24/Visit 10, Week 28/Visit 11, Week 32/Visit 12, Week 36/Visit 13, Week 40/Visit 14, Week 44/Visit 15, Week 48/Visit 16, Week 52/Visit 17, and Follow-up/Visit 18), and to the LOCF endpoint will be presented.

Intensity of ideation for the most severe ideation subtype is measured in terms of frequency, duration, controllability, deterrents, and reasons for ideation. Each is measured with responses ranging from 1 to 5 for frequency and duration, and from 0 to 5 for controllability, deterrents, and reasons for ideation. The ideation intensity total score is the sum of responses to the five items and can range from 2 to 25 for

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subjects with endorsed suicidal ideation. For subjects with endorsed suicidal ideation, if one or more of these five items are missing at an assessment, the total score will be set to missing. If a subject did not endorse any suicidal ideation, a score of 0 for the ideation intensity total score will be given.

Actual lethality associated with actual attempts is rated on a 6-point scale from 0 = 'No physical damage or very minor physical damage' to 5 = 'Death'. Potential lethality of actual attempts (if actual lethality = 0) is rated on a 3-point scale from 0 = 'Behavior not likely to result in injury' to 2 = 'Behavior likely to result in death despite available medical care'.

Responses to each C-SSRS question will be listed. The ideation intensity total score and the actual lethality and potential lethality of actual attempts will only be presented in data listings.

17.6.2 ABNORMAL INVOLUNTARY MOVEMENT SCALE (AIMS)

The AIMS is a clinician-rated assessment of abnormal movements consisting of unobtrusive observation of the subject at rest (with shoes removed) and several questions or instructions directed toward the subject. It contains seven items related to: facial, lip, jaw, and tongue movements (items 1 -4), upper and lower extremity movements (items 5 - 6), and trunk movements (item 7). Three other items assess the subject at a global level (items 8 - 10), and two items assess dental status (items 11 - 12).

The (non-global) AIMS total score is the sum of items 1 through 7. (Items 8 through 12 are not used in AIMS total score calculation.) The possible range for AIMS total score is 0 to 28. Higher values of the AIMS total score indicate increased severity in abnormal movement. If one or more of the 7 items contributing to AIMS total score calculation are missing at a visit, the total score will be set to missing for that visit.

AIMS total score at each visit is classified as 'abnormal' if: either at least two items (out of items 1 - 7) have a response of 'Mild' or higher (i.e. item score ≥2); or at least one item (out of items 1 - 7) has a response of 'Moderate' or higher (i.e. item score ≥3). Otherwise, the non-missing AIMS total scores is classified as 'normal'.

Item 8 of AIMS represents the global severity score. Post-Baseline AIMS global severity scores will be classified as 'worsened', 'unchanged', or 'improved', relative to a subject's Baseline response to item 8. A higher score than that of the Baseline would be classified as 'worsened'. Conversely, a lower score would be classified as 'improved'. If the score is equal to that of Baseline, the score will be classified as 'unchanged'.
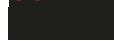
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AIMS is assessed at these study visits: Visit 2, Visit 3, Visit 5, Visit 10, and Visit 17.

Change from Baseline in AIMS total score at each scheduled visit (Week 1/Visit 3, Week 4/Visit 5, Week 24/Visit 10, Week 52/Visit 17) will be analyzed using an MMRM similar to the model described in Section 16.1.1.1, with Baseline AIMS total score as the covariate. In addition, the MMRM analysis will be performed for subgroups of subjects based on whether the subject took concomitant medications for treatment of movement disorders during the study, which is similar to the model described in Section 16.1.1.4. The list of medications will be determined by a review of the coded medication terms before database lock and study unblinding.

Change from Baseline in AIMS total score at each scheduled visit (Week 1/Visit 3, Week 4/Visit 5, Week 24/Visit 10, Week 52/Visit 17) will be analyzed using an ANCOVA model similar to the model described in Section 16.1.1.3 (Analysis of covariance (including LOCF)), with Baseline AIMS total score as the covariate.

The observed AIMS total score and the change from Baseline values will also be summarized descriptively by treatment group and visit. In addition, the observed AIMS total score and the change from Baseline values will be summarized descriptively by the subgroups of concomitant medication use for treatment of movement disorders.

Shift from Baseline in AIMS total score category (Normal/Abnormal) to each post-Baseline scheduled visit (Week 1/Visit 3, Week 4/Visit 5, Week 24/Visit 10, Week 52/Visit 17) and to the overall post-Baseline period (including both the double-blind treatment period and the follow-up period up to and including 9 days after the last dose of study drug) will be summarized descriptively by treatment group.

The observed AIMS global severity score and the change from Baseline values will be summarized descriptively by treatment group and visit. In addition, the frequency distribution of the AIMS global severity item will be summarized descriptively by treatment group and visit. Post-Baseline changes in AIMS global severity score (Worsened/Unchanged/Improved) will also be summarized descriptively by treatment group and visit.

17.6.3 BARNES AKATHISIA RATING SCALE (BARS)

The BARS is a rating scale geared toward assessment of neuroleptic-induced akathisia, though it can be used to measure akathisia associated with other drugs as well. The BARS consists of four items, including one item assessing objective restlessness (item 1), two items targeting subjective restlessness

(awareness and related distress; items 2 - 3), and one global clinical assessment of akathisia item (item 4). The objective and subjective items are anchored and utilize a 4-point scale. The global assessment item has a 6-point scale (from absence of akathisia through severe akathisia).

The BARS total score is the sum of items 1 through 3 and ranges from 0 to 9. Higher values of the BARS total score indicate higher severity of akathisia. If one or more of items 1 to 3 are missing at a visit, the BARS total score will be set to missing for that visit.

The post-Baseline BARS Global Clinical Assessment of Akathisia responses will be classified as 'worsened', 'unchanged', or 'improved', relative to a subject's Baseline response to this item. A higher score than that of the Baseline would be classified as 'worsened'. Conversely, a lower score would be classified as 'improved'. If the score is equal to that of Baseline, the score will be classified as 'unchanged'.

BARS is assessed at these study visits: Visit 2, Visit 3, Visit 5, Visit 10, and Visit 17.

Change from Baseline in BARS total score at each scheduled visit (Week 1/Visit 3, Week 4/Visit 5, Week 24/Visit 10, Week 52/Visit 17) will be analyzed using an MMRM similar to the model described in Section 16.1.1.1 with Baseline BARS total score as the covariate. In addition, the MMRM analysis will be performed for subgroups of subjects based on whether the subject took concomitant medications for treatment of movement disorders during the study, which is similar to the model described in Section 16.1.1.4.

Change from Baseline in BARS total score at each scheduled visit (Week 1/Visit 3, Week 4/Visit 5, Week 24/Visit 10, Week 52/Visit 17) will be analyzed using an ANCOVA model similar to the model described in Section 16.1.1.3 (Analysis of covariance (including LOCF)) with Baseline BARS total score as the covariate.

The observed BARS total score and the change from Baseline values will also be summarized descriptively by treatment group and visit. In addition, the observed BARS total score and the change from Baseline values will be summarized descriptively by the subgroups of concomitant medication use for treatment of movement disorders.

Change from Baseline in BARS global clinical assessment score at each scheduled visit (Week 1/Visit 3, Week 4/Visit 5, Week 24/Visit 10, Week 52/Visit 17) will be analyzed using MMRM and ANCOVA models similar to the model described in Section 16.1.1.1 and Section 16.1.1.3 (Analysis of covariance (including

LOCF)), with Baseline BARS global clinical assessment score as the covariate.

Lastly, the observed BARS item scores and the change from Baseline values will be summarized descriptively by treatment group and visit. In addition, the frequency distribution of each BARS item will be summarized descriptively by treatment group and visit. Post-Baseline changes in BARS global clinical assessment score (Worsened/Unchanged/Improved) will be summarized descriptively by treatment group and visit.

17.6.4 MODIFIED SIMPSON-ANGUS SCALE (SAS)

The SAS is a clinician-rated assessment of neuroleptic-induced Parkinsonism consisting of 10 items. Items are anchor-based, rated on a 5-point scale (ranging between 0 and 4), and address rigidity, gait (bradykinesia), tremor, akathisia, shoulder shaking, glabellar tap, and salivation.

SAS mean score is defined as the average of all 10 items and ranges between 0 and 4. Lower values of the SAS mean score indicate milder symptoms. If one or more of the SAS items are missing at a visit, the SAS mean score will be set to missing for that visit.

The SAS mean score at each visit will be classified as 'abnormal' if it exceeds 0.3 (Rush, et al., 2000). Otherwise, the non-missing SAS mean score will be classified as 'normal'.

SAS is assessed at these study visits: Visit 2, Visit 3, Visit 5, Visit 10, and Visit 17.

Change from Baseline in SAS mean score at each scheduled visit (Week 1/Visit 3, Week 4/Visit 5, Week 24/Visit 10, Week 52/Visit 17) will be analyzed using an MMRM similar to the model described in Section 16.1.1.1, with Baseline SAS mean score as the covariate. In addition, the MMRM analysis will be performed for subgroups of subjects based on whether the subject took concomitant medications for treatment of movement disorders during the study, which is similar to the model described in Section 16.1.1.4.

Change from Baseline in SAS mean score at each scheduled visit (Week 1/Visit 3, Week 4/Visit 5, Week 24/Visit 10, Week 52/Visit 17) will be analyzed using an ANCOVA model similar to the model described in Section 16.1.1.3 (Analysis of covariance (including LOCF)), with Baseline SAS mean score as the covariate.

The observed SAS mean score and the change from Baseline values will also be summarized

descriptively by treatment group and visit. In addition, the observed SAS mean score and the change from Baseline values will be summarized descriptively by the subgroups of concomitant medication use for treatment of movement disorders.

Shift from Baseline in SAS mean score category (Normal/Abnormal) to each post-Baseline scheduled visit (Week 1/Visit 3, Week 4/Visit 5, Week 24/Visit 10, Week 52/Visit 17) and to the overall post-Baseline period (including both the double-blind treatment period and the follow-up period up to and including 9 days after the last dose of study drug) will be summarized descriptively by treatment group.

17.6.5 HEALTHCARE RESOURCE UTILIZATION

Healthcare resource utilization is assessed at these study visits: Visit 2, Visit 7, Visit 10, Visit 13, and Visit 17.

The frequency and percentage of subjects with physician's office visits, ER visits, and hospitalizations (for any reason and those related to schizophrenia) at Baseline and at each post-Baseline scheduled visit (Week 12/Visit 7, Week 24/Visit 10, Week 36/Visit 13, Week 52/Visit 17) (capturing the information during the past 3 months) will be summarized. The number of physician's office visits, ER visits, and hospitalizations (for any reason and those related to schizophrenia) per month at Baseline and at each post-Baseline scheduled visit (Week 12/Visit 7, Week 24/Visit 10, Week 36/Visit 13, Week 52/Visit 17), as well as the average length of hospital stays (for any reason and those related to schizophrenia) at Baseline and at each post-Baseline scheduled visit (Week 12/Visit 7, Week 24/Visit 10, Week 36/Visit 13, Week 52/Visit 17), will be summarized. The frequency and percentage of subjects receiving unpaid care at each time point, along with the average number of hours a caregiver spends per week helping the subject, will also be summarized.

The change in the number of physician's office visits, ER visits, and hospitalizations per month, the average length of hospital stays, and the average number of hours a caregiver spends per week helping the subject from Baseline at each post-Baseline scheduled visit (Week 12/Visit 7, Week 24/Visit 10, Week 36/Visit 13, Week 52/Visit 17) will be summarized.

Shift from Baseline to each post-Baseline scheduled visit (Week 12/Visit 7, Week 24/Visit 10, Week 36/Visit 13, Week 52/Visit 17) in whether the subjects receive unpaid care will also be summarized.

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19 DATA NOT SUMMARIZED OR PRESENTED

The variables and/or domains not summarized or presented are:

- Subject initials

- Any data collected on screen failures other than disposition, basic demographics, and pre-treatment events.

- Any data collected during previously failed screening(s) for randomized subjects who were screened more than once except Adverse Events.

These domains and/or variables will not be summarized or presented but will be available in the clinical study database and SDTM datasets.

20 REFERENCES

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Marder, S., Davis, J., & Chouinard, G. (1997;58:538–46). The effects of risperidone on the five dimensions of schizophrenia. *J Clin Psychiatry* .

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Rush, A., Pincus, H., First, M., Blacker, D., Endicott, J., Keith, S., . . . Zarin, D. (2000). *Handbook of Psychiatric Measures.* American Psychiatric Association.

APPENDIX 1. PROGRAMMING CONVENTIONS FOR OUTPUTS

IQVIA OUTPUT CONVENTIONS

Where applicable, the appendix_compilation_working_Guidelines_ 21Jun2017 Global Final.pdf document – provided by Sunovion – will be followed.

In addition, the following output conventions are to be followed:

- General presentation:

  - The first row in the body of the table or listing should be blank

  - Rounding should be done with the SAS function ROUND.

  - Numbers in tables should be rounded, not truncated.

  - Alphanumeric output should be left aligned.

  - Numbers should be decimal point aligned when possible. When more than 1 statistics is presented per row, alignment on the first value only will be done.

  - Text values should be left aligned.

  - The first letter of a text entry should be capitalized. Title case should be used in headers.

- Univariate Statistics: If the raw data has N decimal places, then the summary statistics should have the following decimal places:

  - Minimum and maximum: N

  - Mean, median, Q1, and Q3: N + 1

  - SD: N + 2

  - For lab data only, in the rare case where raw data has more than 3 decimal places, summary statistics will be presented for the scenario of N = 3. All decimals will be presented in Listings.

  - For UPSM scores, 3 decimal places will be presented for mean, median, Q1, Q3, LS mean, LS

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mean difference, and 95% CI; 4 decimal places will be presented for SD and SE; 2 decimal places will be presented for min and max. Up to 2 decimal places will be presented in Listings.

- Frequencies and percentages (n and %):

  - Percent values should be reported inside parentheses, with one space between the count (n) and the left parenthesis of the percentage. Parentheses should be justified to accept a maximum of 100.0 as a value and padded with blank space if the percent is less than 100.0.

  - Percentages will be reported to one decimal place, except cases where percent <100.0% but >99.9% will be presented as '>99.9%' (eg, 99.99% is presented as >99.9%); and cases where percent <0.1% will be presented as '<0.1%' (eg, 0.08% is presented as <0.1%). Rounding will be applied after the <0.1% and >99.9% rule.

  - Where counts are zero, no percentage should appear in the output.

- Confidence Intervals:

  - Confidence intervals and estimates are presented to one place more than the raw data, and standard errors to two places more than the raw data.

  - Confidence intervals should be justified so that parentheses displayed on consecutive lines of a table "line up".

  - Boundary values of confidence intervals should be separated by a comma.

  - Boundary values should be padded as necessary to accept negative values and to allow alignment of the decimal place.

- P-values should be reported to three decimal places, except values <1.000 but >0.999 will be presented as '>0.999' (eg, 0.9998 is presented as >0.999); and values <0.001 will be presented as '<0.001' (eg, 0.0009 is presented as <0.001). Rounding will be applied after the <0.001 and >0.999 rule.

- Ratios should be reported to one more decimal place than the raw data.

- Enough spaces should be left between column to easily distinguish which text pertain to which column.

- Missing values:

  - A "0" should be used to indicate a zero frequency.

  - A blank will be used to indicate missing data in an end-of-text table or subject listing.

- Figures:

  - Figures should be provided in RTF files using the SAS Output Delivery System (ODS), as Computer Graphics Metafile (CGM) formatted graphical output generated by SAS.

  - The image should be clear and of high quality when viewed in the Word document, and when printed.

  - In general, boxes around the figures should be used.

- Footers should be defined as follows:

  - Table footnotes should be defined using compute statements in the proc report, and should appear directly after the body of the table.

  - If text wraps across more than one line (for a note), the first letter for all lines of text after the first one will be indented to align beneath the first letter of the text in the first line.

DATES & TIMES

Depending on data available, dates and times will take the form yyyy-mm-ddThh:mm:ss .

SPELLING FORMAT

English US.

PRESENTATION OF TREATMENT GROUPS

For outputs, treatment groups will be represented as follows and in that order:

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Treatment Group	For Tables (Column Order)	For Listings and Graphs (Order)
SEP-363856 50 to 100 mg/day	SEP-363856 50 to 100 mg/day (1)	SEP-363856 50 to 100 mg/day (1)
Quetiapine XR 400 to 800 mg/day	Quetiapine XR 400 to 800 mg/day (2)	Quetiapine XR 400 to 800 mg/day (2)
	Total (3)	

LISTINGS

All listings will be ordered by the following (unless otherwise indicated in the template):

- Actual treatment group, displaying SEP-363856 50 to 100 mg/day first and then Quetiapine XR 400 to 800 mg/day. Randomized subjects who did not receive any study medication will be presented at the end and labelled "Not Treated".

- Subject ID

- Visit (where applicable)

- Original date/time (where applicable)

APPENDIX 2. PARTIAL DATE CONVENTIONS

The actual dates as collected on the CRF will be presented in the listings. Imputed dates will not be presented in the listings unless otherwise specified.

ALGORITHM FOR ADVERSE EVENTS:

As a general rule, if the start date of an AE is available and the start time of the AE is not available, the AE will be considered to have started after the study drug dose administered on the day of the AE start date.

In case of partial or missing AE start and/or end dates, impute partial or missing event start and/or end dates (if not ongoing) using the algorithm below. If an AE has some missing components in both the start and end dates, first impute the end date.

AE end date imputation

- If year and month (YYYY-MM) of AE end date are known, then impute the missing day part to be the last day of the month.
- If only year (YYYY) of AE end date is known, then impute the missing month and day part to be 31st December.

If AE end date is completely missing and AE is not ongoing, then impute AE end date to date of last contact.

AE start date imputation

- If year and month (YYYY-MM) of AE start date are known and YYYY-MM = year and month of 361-304 study med start date, then impute AE start date to the earlier of 361-304 study med start date and AE end date (if non-missing).
- If year and month (YYYY-MM) of AE start date are known and YYYY-MM ≠ year and month of 361-304 study med start date, then impute AE start date to YYYY-MM-01.
- If only year (YYYY) of AE start date is known and YYYY = year of 361-304 study med start date, then impute AE start date to the earlier of 361-304 study med start date and AE end date (if non-missing).

- If only year (YYYY) of AE start date is known and YYYY ≠ year of 361-304 study med start date, then impute AE start date to YYYY-01-01.

- If AE start date is completely missing, then impute AE start date to the earlier of 361-304 study med start date and AE end date (if non-missing).

Using the full or imputed event dates, assign events into pre-treatment events vs. AE as described below.

If both event start date/time and 361-304 study med start date/time are available:

- If event start date/time < 361-304 study med start date/time, then pre-treatment event.

- If event start date/time ≥ 361-304 study med start date/time, then AE.

If (event start date is available and time is not available) and/or (361-304 study med start date is available and time is not available):

- If event start date < 361-304 study med start date, then pre-treatment event.

- If event start date ≥ 361-304 study med start date, then AE.

ALGORITHM FOR PRIOR / CONCOMITANT / POST-TREATMENT MEDICATIONS:

The concept of "date" below should also include time information whenever time is available for both comparators.

For the case where the medication start date is known and is equal to SEP-363856/Quetiapine study med end date and the medication start time is unknown, or the case where the imputed medication start date is equal to SEP-363856/Quetiapine study med end date:

- If CRF question '*Started after last dose of study medication?*' = *No*, then assign as concomitant.

- If CRF question '*Started after last dose of study medication?*' = *Yes*, then assign as post-treatment.

In case of partial or missing medication start or end dates, the following algorithm will be used for determining if a medication is prior, concomitant, or post-treatment. If a medication has some missing components in both the start and end dates, first impute the end date.

Impute stop date as latest possible date:

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- If only day unknown, impute as last day of the month.
- If month and day unknown, impute as to the earlier of 31st December and date of last contact.
- If end date is completely unknown and medication is not ongoing, impute to date of last contact.

Impute start date as earliest possible date:

CRF questions: 'Started prior to first dose?' = Yes; 'Started after last dose of study medication?' = No.

- If only day unknown, impute as the later of (first day of the month; date of birth [if full date is available]).
- If month and day unknown, impute as the later (1st January; date of birth [if full date is available]).
- If start date is completely unknown, impute to earlier of (date of informed consent, medication end date [if not missing]).

CRF questions: 'Started prior to first dose?' = No; 'Started after last dose of study medication?' = Yes.

- If only day unknown, impute as the later of (first day of the month; 361-304 study med end date + 1).
- If month and day unknown, impute as the later of (1st January; 361-304 study med end date + 1).
- If start date is completely unknown, impute to 361-304 study med end date + 1.

CRF questions: 'Started prior to first dose?' = No; 'Started after last dose of study medication?' = No.

- If only day unknown, impute as the later of (first day of the month; 361-304 study med start date).
- If month and day unknown, impute as the later of (1st January; 361-304 study med start date).
- If start date is completely unknown, impute to 361-304 study med start date.

Then assign a medication into prior, concomitant, or post-treatment

The concept of "date" below should also include time information whenever time is available for both comparators.

- If medication stop date < 361-304 study med start date, assign as prior.
- If (medication stop date ≥ 361-304 study med start date or medication is ongoing) and medication start date ≤ 361-304 study med end date, assign as concomitant.
- If medication start date > 361-304 study med end date, assign as post-treatment.

<u>Overriding rule</u>

For the case where the medication start date is known and is equal to 361-304 study med end date and the medication start time is unknown, or the case where the imputed medication start date is equal to 361-304 study med end date:

- If CRF question '*Started after last dose of study medication?*' = *No*, then assign as concomitant.

- If CRF question '*Started after last dose of study medication?*' = *Yes*, then assign as post-treatment.

PARTIAL DATE IMPUTATION RULES FOR INITIAL ONSET OF SCHIZOPHRENIA

For subjects with partial onset date of schizophrenia, impute the onset date using the following rules:

- If only day unknown, impute as the earlier of: 15th of the month, or date of ICF.

- If both month and day unknown, impute as the earlier of: June 30th of the year, or date of ICF.

PARTIAL DATE IMPUTATION RULES FOR SCHIZOPHRENIA DIAGNOSIS

For subjects with partial date of schizophrenia diagnosis, impute the date using the following rules:

- If only day unknown and the known year and month is earlier than the year and month of ICF, impute as the later of: 15th of the month, or date of initial onset of schizophrenia (actual or imputed).

- If only day unknown and the known year and month is the same as the year and month of ICF, impute as the later of: earlier of (date of ICF, 15th of the month), or date of initial onset of schizophrenia (actual or imputed).

- If both month and day unknown and the known year is earlier than the year of ICF, impute as the later of: June 30th of the year, or date of initial onset of schizophrenia (actual or imputed).

- If both month and day unknown and the known year is the same as the year of ICF, impute as the later of: earlier of (date of ICF, June 30th of the year), or date of initial onset of schizophrenia (actual or imputed).

PARTIAL DATE IMPUTATION RULES FOR LAST ACUTE EXACERBATION OF SCHIZOPHRENIA

For subjects with partial date of last acute exacerbation of schizophrenia, impute the date using the

following rules:

- If only day unknown and the known year and month is earlier than the year and month of ICF, impute as the later of: 15th of the month, or date of initial onset of schizophrenia (actual or imputed).

- If only day unknown and the known year and month is the same as the year and month of ICF, impute as the later of: earlier of (date of ICF, 15th of the month), or date of initial onset of schizophrenia (actual or imputed).

- If both month and day unknown and the known year is earlier than the year of ICF, impute as the later of: June 30th of the year, or date of initial onset of schizophrenia (actual or imputed).

- If both month and day unknown and the known year is the same as the year of ICF, impute as the later of: earlier of (date of ICF, June 30th of the year), or date of initial onset of schizophrenia (actual or imputed).

PARTIAL DATE IMPUTATION RULES FOR FIRST HOSPITALIZATION

For subjects with partial date of first hospitalization for treatment of schizophrenia, impute the date using the following rules:

- If only day unknown, impute as the earlier of: 15th of the month, or date of ICF.

- If both month and day unknown, impute as the earlier of: June 30th of the year, or date of ICF.

PARTIAL DATE IMPUTATION RULES FOR FIRST ANTI-PSYCHOTIC DRUG THERAPY

For subjects with partial start date for the first anti-psychotic drug therapy of at least 2 weeks duration intended for treatment of schizophrenia, impute the start date using the following rules:

- If only day unknown, impute as the earlier of: 15th of the month, or date of ICF.

- If both month and day unknown, impute as the earlier of: June 30th of the year, or date of ICF.

RULES FOR ASSIGNING DOSEON/DOSEA

- In general, DOSEON/DOSEA should be the dose level immediately before the start of an AE or an

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assessment. In case the AE or the assessment start date/time coincides with the first dosing start date/time of the study, the DOSEON/DOSEA should be assigned to the dose level associated with that first dosing start date/time. In case the AE or the assessment start date/time coincides with a dosing start date/time other than the first dosing start date/time (collected or imputed for Week 1 as specified in Section 14.1), the DOSEON/DOSEA should be assigned to the dose level associated with the previous dosing start date/time.

- In case of missing AE start time, missing assessment (start) time, and/or missing dosing start time, DOSEON/DOSEA should be assigned using the algorithm in the table below.

Scenario	Data	Rules
Dosing start date and start time both available	Adverse Events	If AE start date is available and AE start time is missing, dose on the same day as AE start should be assigned as DOSEON.
	Scales/Questionnaires, Vitals, Labs, ECG	If assessment start date is available and assessment start time is missing, dose on the previous day of the assessment should be assigned as DOSEA.
Dosing start date available but start time missing	Adverse Events	Regardless of whether AE start time is available, dose on the same day as AE start should be assigned as DOSEON.
	Scales/Questionnaires, Vitals, Labs, ECG	Regardless of whether assessment start time is available, dose on the previous day of the assessment should be assigned as DOSEA.

- In case of partial or missing AE start date, the imputed AE start date will be used for the purpose of assigning DOSEON.

APPENDIX 4. EXTRAPYRAMIDAL ADVERSE EVENTS

To ensure comprehensive and consistent selection of terminology used for analyses of extrapyramidal signs and symptoms in ongoing / planned studies of SEP-363856, MedDRA PTs were identified from the following source:

- MedDRA version 22.0 SMQ: Extrapyramidal syndrome [20000095], Broad, including all 4 sub-SMQs (Akathisia [20000096], Dyskinesia [20000097], Dystonia [20000098], and Parkinson-like events [20000099])

Description:

All PTs listed in the MedDRA version 22.0 SMQ for Extrapyramidal syndrome [20000095] were included. The table below depicts the PTs by sub-SMQ.

Table 5: Extrapyramidal Syndrome SMQ Using MedDRA v 22.0

Akathisia		Dyskinesia		Dystonia		Parkinson-like	
PT	Code	PT	Code	PT	Code	PT	Code
Akathisia	10001540	-	-	-	-	-	-
-	-	-	-	-	-	Akinesia	10001541
-	-	Athetosis	10003620	-	-	-	-
-	-	Ballismus	10058504	-	-	-	-
-	-	-	-	-	-	Bradykinesia	10006100
-	-	Buccoglossal syndrome	10006532	-	-	-	-
-	-	Chorea	10008748	-	-	-	-
-	-	Choreoathetosis	10008754	-	-	-	-
-	-	-	-			Cogwheel rigidity	10009848
-	-	Dopamine dysregulation syndrome	10067468	-	-	-	-
-	-	-	-	Dopa-responsive dystonia	10080034	-	-
-	-	Dyskinesia	10013916	-	-	-	-

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Akathisia		Dyskinesia		Dystonia		Parkinson-like	
PT	Code	PT	Code	PT	Code	PT	Code
-	-	Dyskinesia neonatal	10013922	-	-	-	-
-	-	Dyskinesia oesophageal	10013924	-	-	-	-
-	-			Dystonia	10013983		
-	-			Dystonic tremor	10073210		
-	-	-	-	Early onset primary dystonia	10076668	-	-
-	-	-	-	Emprosthotonus	10014566	-	-
-	-	-	-	-	-	Freezing phenomenon	10060904
-	-	Grimacing	10061991	-	-	-	-
-	-	-	-	-	-	Hypertonia	10020852
-	-	-	-	-	-	Hypertonia neonatal	10048615
-	-	-	-	-	-	Hypokinetic dysarthria	10082243
-	-	-	-	Meige's syndrome	10027138		
-	-	-	-	-	-	Muscle rigidity	10028330
-	-	Oculogyric crisis	10030071	Oculogyric crisis	10030071		
-	-	-	-	-	-	On and off phenomenon	10030312
-	-	-	-	Opisthotonus	10030899	-	-
-	-			Oromandibular dystonia	10067954	-	-
-	-	-	-	-	-	Parkinsonian crisis	10048868
-	-	-	-	-	-	Parkinsonian gait	10056242
-	-	-	-	-	-	Parkinsonian rest tremor	10056437
-	-	-	-	-	-	Parkinsonism	10034010
-	-	-	-	-	-	Parkinsonism hyperpyrexia syndrome	10071243

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Akathisia		Dyskinesia		Dystonia		Parkinson-like	
PT	Code	PT	Code	PT	Code	PT	Code
-	-	-	-	-	-	Parkinson's disease	10061536
-	-	-	-	-	-	Parkinson's disease psychosis	10074835
-	-	Pharyngeal dyskinesia	10070912	-	-	-	-
-	-	-	-	Pharyngeal dystonia	10081226	-	-
-	-	-	-	Pleurothotonus	10035628	-	-
-	-	-	-			Propulsive gait	10082328
-	-	Protrusion tongue	10037076	-	-	-	-
-	-	Rabbit syndrome	10068395	-	-	-	-
-	-	Respiratory dyskinesia	10057570	-	-	-	-
-	-	-	-	-	-	Resting tremor	10071390
-	-	-	-	Spasmodic dysphonia	10067672	-	-
-	-	Tardive dyskinesia	10043118	-	-	-	-
-	-	-	-	Torticollis	10044074	-	-
-	-	-	-	Trismus	10044684	-	-
-	-	-	-	Writer's cramp	10072249	-	-
-	-	Abnormal involuntary movement scale	10075002	-	-	-	-
-	-	-	-	-	-	Action tremor	10072413
-	-	-	-	Blepharospasm	10005159		
-	-	-	-	-	-	Bradyphrenia	10050012
-	-	Chronic tic disorder	10076661	Chronic tic disorder	10076661	-	-
-	-	Complex tic	10076663	Complex tic	10076663	-	-

Akathisia		Dyskinesia		Dystonia		Parkinson-like	
PT	Code	PT	Code	PT	Code	PT	Code
-	-	Drooling	10013642	Drooling	10013642	Drooling	10013642
-	-	-	-	-	-	Dysphonia	10013952
Extrapyramidal disorder	10015832	Extrapyramidal disorder	10015832	Extrapyramidal disorder	10015832	Extrapyramidal disorder	10015832
-	-	-	-	Facial spasm	10063006	-	-
-	-	-	-	-	-	Fine motor skill dysfunction	10076288
-	-	-	-	-	-	Gait disturbance	10017577
-	-	-	-	Gait inability	10017581	-	-
Hyperkinesia	10020651	-	-	-	-	-	-
Hyperkinesia neonatal	10020652	-	-	-	-	-	-
-	-	-	-	-	-	Hypokinesia	10021021
-	-	-	-	-	-	Hypokinesia neonatal	10021022
-	-	-	-	-	-	Laryngeal tremor	10078751
-	-	-	-	Laryngospasm	10023891	-	-
-	-	-	-	-	-	Micrographia	10057333
-	-	-	-	-	-	Mobility decreased	10048334
Motor dysfunction	10061296	Motor dysfunction	10061296	Motor dysfunction	10061296	Motor dysfunction	10061296
Movement disorder	10028035	Movement disorder	10028035	Movement disorder	10028035	Movement disorder	10028035
-	-	Muscle twitching	10028347			-	-
-	-	-	-	Muscle contractions involuntary	10028293	-	-
-	-	-	-	Muscle spasms	10028334	-	-
-	-	-	-	Muscle spasticity	10028335	-	-
-	-	-	-	Muscle tightness	10049816	-	-

Akathisia		Dyskinesia		Dystonia		Parkinson-like	
PT	Code	PT	Code	PT	Code	PT	Code
-	-	-	-	Muscle tone disorder	10072889	Muscle tone disorder	10072889
-	-	-	-	Muscle twitching	10028347	-	-
-	-	-	-	Musculoskeletal stiffness	10052904	Musculoskeletal stiffness	10052904
-	-	-	-	Oesophageal spasm	10030184	-	-
-	-	-	-	Oropharyngeal spasm	10031111	-	-
-	-	-	-	Posture abnormal	10036436	-	-
-	-	-	-	-	-	Postural reflex impairment	10067206
-	-	-	-	-	-	Postural tremor	10073211
-	-			Posturing	10036437	-	-
-	-	Provisional tic disorder	10076694	Provisional tic disorder	10076694	-	-
Psychomotor hyperactivity	10037211	-	-	-	-	-	-
		-	-	-	-	Reduced facial expression	10078576
Restlessness	10038743	-	-	-	-	-	-
-	-	-	-	Risus sardonicus	10039198	-	-
-	-	Secondary tic	10076702	Secondary tic	10076702	-	-
-	-	Tic	10043833	Tic	10043833	-	-
-	-	-	-	Tongue spasm	10043981	-	-
-	-	-	-	Torticollis psychogenic	10044076	-	-
-	-	-	-	-	-	Tremor	10044565
-	-	-	-	-	-	Tremor neonatal	10044575
-	-	-	-	Uvular spasm	10050908	-	-
-	-	-	-	-	-	-	-
-	-	-	-	-	-	Walking disability	10053204

APPENDIX 5. UNCORRELATED PANSS SCORE MATRIX (UPSM)

PANSS	UPSM-POS	UPSM-DIS	UPSM-NAA	UPSM-NDE	UPSM-HOS	UPSM-ANX	UPSM-DEP
PANSS01	0.5792730597	-0.1547126840	-0.0828932650	0.0071927220	-0.0593031510	-0.0735449620	0.0020484408
PANSS02	0.0292444390	0.1975824582	-0.0260173260	-0.0234753800	-0.0368756010	-0.0012396240	-0.0361645050
PANSS03	0.2065788330	-0.0179419820	-0.0250663450	-0.0133031880	-0.0300507070	0.0001506005	0.0293001724
PANSS04	-0.0336790630	0.0115284348	0.0011652392	-0.0723891460	0.1379358628	0.1108194656	-0.1045224460
PANSS05	-0.0341508580	-0.0301875430	-0.0041019560	-0.0233459100	-0.0069204000	-0.0313277060	0.0308288417
PANSS06	0.3537254634	-0.0626270750	0.0477329954	0.0012126712	0.0192067437	-0.0161398140	0.0063264235
PANSS07	-0.0383468990	-0.1767919370	-0.0299340700	0.0314652864	0.5025411101	-0.0997121200	0.0573604084
PANSS08	-0.0054230270	-0.0291400280	0.0568702938	0.2474176209	-0.0388464000	0.0188235393	-0.0091524870
PANSS09	-0.0315765690	-0.0243925850	0.3317907576	-0.0228204580	-0.0507096280	-0.0145653830	0.0112689069
PANSS10	-0.0742072890	-0.0401313020	-0.0097485120	0.0161513666	0.0245536353	-0.0176161520	-0.0172218040
PANSS11	-0.0943532590	-0.0856364190	0.4611503804	-0.0286825100	-0.0189062390	-0.0185825180	-0.0130433890
PANSS12	0.0043338689	0.1062496353	0.0255910591	-0.0301470410	-0.0133497570	0.0096065791	-0.0686802390
PANSS13	0.0041274699	0.0051521898	0.0009558861	0.2576813501	-0.0085004640	0.0194235006	-0.1037459520
PANSS14	-0.0111267300	0.1462268689	-0.0276416260	0.0023017188	-0.0055291270	-0.0118427800	0.0040128786
PANSS15	-0.0356272010	0.0552508287	-0.0382627720	0.0110152489	-0.0309176290	0.0444944076	0.1059845189
PANSS16	-0.0331052830	-0.0821894470	-0.0327376640	-0.0533178140	-0.0386473380	0.4576579818	0.1197800301
PANSS17	-0.0368854600	-0.0004363100	-0.0020681500	-0.0407976460	-0.0272172130	-0.0253163640	0.2459654614
PANSS18	-0.0931367690	-0.0332617600	-0.0132943930	0.0231904701	-0.0287529750	0.5123850161	-0.0312522560
PANSS19	-0.0455199430	0.0494113554	-0.0324174560	0.1026255664	-0.0136676190	0.0293507269	-0.0441735260
PANSS20	-0.0344751890	-0.0688197670	-0.0412738350	0.0381793764	0.0042219619	-0.0635101090	0.4514426846
PANSS21	-0.0348890020	-0.0366137810	-0.0779782830	0.4409895205	-0.0073240410	-0.0192655290	0.0464131877
PANSS22	-0.0803690920	0.0334025939	-0.0088488890	-0.0200483170	0.2858700784	-0.0567167860	-0.0531076130
PANSS23	0.1428966744	0.0939213700	-0.0326143600	-0.0367524640	-0.0675856980	-0.0209072840	-0.0177890070
PANSS24	-0.0383047770	-0.0324584080	-0.0255393890	-0.0180115340	-0.0266180700	-0.0210068530	-0.0176029110
PANSS25	-0.1036311520	0.2814367260	-0.0478918640	0.0029986238	0.0037656449	-0.0226520240	0.0401351054
PANSS26	0.0142987589	0.1548635741	-0.0306089330	-0.0331581690	0.0262295986	-0.0576293550	-0.0626180490
PANSS27	-0.0573513270	0.1867914227	-0.0143489160	0.0581534153	-0.0145494330	-0.0371788310	0.0455412078
PANSS28	-0.0748387810	0.0166272025	-0.0267498020	-0.0031632780	0.2546669938	-0.0201249190	-0.0076420280
PANSS29	-0.0520812460	0.2912295497	0.0029775475	-0.0324350460	-0.0442337350	-0.0047991290	0.0567191230
PANSS30	-0.0112030990	-0.0007246980	0.2860136812	-0.0606201430	0.0183598393	-0.0302347770	0.0370748725

APPENDIX 6.   EQ-5D-5L INDEX VALUE CALCULATION

EQ-5D-5L health states, defined by the EQ-5D-5L descriptive system, may be converted into a single index value using an appropriate EQ-5D-5L value set. If a standard EQ-5D-5L value set is not available, but an EQ-5D-3L value set is available, a "crosswalk" value set can be used to derive the index value. For multiregional trials, EuroQol recommends applying a single standard value set (or crosswalk value set) to all study sites. For this study, the US EQ-5D-5L standard value set will be used for all countries.

Please refer the following EuroQol website for EQ-5D-5L value sets and further information.

https://euroqol.org/eq-5d-instruments/eq-5d-5l-about/valuation-standard-value-sets/

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APPENDIX 7.   ADVERSE EVENTS OF POTENTIAL DRUG ABUSE AND DEPENDENCE

To ensure comprehensive and consistent selection of terminology used for analyses of drug abuse and dependence in ongoing / planned studies of SEP-363856, MedDRA PTs were identified from the following sources:

- FDA Guidance for Industry: Assessment of Abuse Potential of Drugs (CDER, 2017; noted that the Guidance reflects MedDRA version 20.0 terminology)

- MedDRA version 22.0 SMQ: Drug abuse and dependence [20000101], Broad

- FDA FMQ: Study Agent Abuse Potential, Broad (released at FDA public workshop "Advancing Premarket Safety Analytics", held September 14, 2022)

Description:

Preferred terms were tabulated using MedDRA version 22.0 from the sources listed above. All PTs within the FDA Abuse Potential Guidance were included. All PTs listed in the MedDRA version 22.0 SMQ for Drug abuse and dependence [20000101] were included. For the FDA Study Agent Abuse Potential FMQ: No associated MedDRA PT was found for the term "Hypnogogic hallucination", and this is therefore not included. Sunovion evaluates 'Drug withdrawal' as a unique medical concept using MedDRA version 22.0 SMQ for Drug withdrawal [20000102] (Broad); any overlapping PTs from the Drug withdrawal SMQ which are listed in the FDA Study Agent Abuse Potential FMQ are not included. All other PTs listed in the FDA FMQ were included.

The table below depicts the PTs by source.

Table 6: Drug Abuse and Dependence Preferred Terms Using MedDRA v 22.0

FDA Guidance 2017		SMQ 20000101		FDA FMQ	
PT	Code	PT	Code	PT	Code
-	-	Accidental overdose	10000381	Accidental overdose	10000381
-	-	-	-	Acute psychosis	10001022
Aggression	10001488	-	-	-	-

FDA Guidance 2017		SMQ 20000101		FDA FMQ	
PT	Code	PT	Code	PT	Code
Behavioural addiction	10081939	-	-	-	-
Confusional state	10010305	-	-	-	-
-	-	-	-	Delusion of grandeur	10012241
-	-	-	-	Delusional perception	10012258
Dependence	10012335	Dependence	10012335	Dependence	10012335
-	-	-	-	Depersonalisation	10012357
-	-	-	-	Derealisation disorder	10077810
-	-	-	-	Detoxification	10061814
-	-	-	-	Disinhibition	10013142
Disorientation	10013395	-	-	-	-
-	-	Disturbance in social behaviour	10061108	-	-
Dizziness	10013573	-	-	-	-
Dopamine dysregulation syndrome	10067468	Dopamine dysregulation syndrome	10067468	-	-
-	-	Drug abuse	10013654	Drug abuse	10013654
-	-	Drug abuser	10061111	Drug abuser	10061111
-	-	Drug dependence	10013663	Drug dependence	10013663
Drug dependence, antepartum	10013675	Drug dependence, antepartum	10013675	Drug dependence, antepartum	10013675
Drug dependence, postpartum	10013676	Drug dependence, postpartum	10013676	Drug dependence, postpartum	10013676
-	-	Drug detoxification	10052237	Drug detoxification	10052237
-	-	Drug diversion	10066053	Drug diversion	10066053

FDA Guidance 2017		SMQ 20000101		FDA FMQ	
PT	Code	PT	Code	PT	Code
-	-	Drug level above therapeutic	10061132	-	-
-	-	Drug level increased	10013722	-	-
-	-	Drug screen	10050837	-	-
-	-	Drug screen positive	10049177	-	-
Drug tolerance	10052804	Drug tolerance	10052804	-	-
Drug tolerance decreased	10052805	Drug tolerance decreased	10052805	-	-
Drug tolerance increased	10052806	Drug tolerance increased	10052806	-	-
Drug use disorder	10079381	Drug use disorder	10079381	Drug use disorder	10079381
-	-	Drug use disorder, antepartum	10079382	Drug use disorder, antepartum	10079382
-	-	Drug use disorder, postpartum	10079383	Drug use disorder, postpartum	10079383
-	-	-	-	Energy increased	
Euphoric mood	10015535	-	-	Euphoric mood	10015535
Feeling abnormal	10016322	-	-	-	-
Feeling drunk	10016330	-	-	Feeling drunk	10016330
-	-	-	-	Feeling jittery	10016338
Feeling of relaxation	10016352	-	-	Feeling of relaxation	10016352
-	-	-	-	Flight of ideas	10016777
Hallucination	10019063	-	-	Hallucination	10019063
Hallucination, auditory	10019070	-	-	Hallucination, auditory	10019070
Hallucination, gustatory	10019071	-	-	Hallucination, gustatory	10019071

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FDA Guidance 2017		SMQ 20000101		FDA FMQ	
PT	Code	PT	Code	PT	Code
Hallucination, olfactory	10019072	-	-	Hallucination, olfactory	10019072
Hallucination, synaesthetic	10062824	-	-	Hallucination, synaesthetic	10062824
Hallucination, tactile	10019074	-	-	Hallucination, tactile	10019074
Hallucination, visual	10019075	-	-	Hallucination, visual	10019075
Hallucinations, mixed	10019079	-	-	Hallucinations, mixed	10019079
Inappropriate affect	10021588	-	-	Hallucination, gustatory	10019071
-	-	-	-	Hypersomnia	10020765
-	-	-	-	Hypervigilance	10048533
-	-	-	-	Hypnagogic hallucination	10020927
-	-	-	-	Hypnogogic hallucination	No such code
-	-	-	-	Hypnopompic hallucination	10020928
-	-	-	-	Inappropriate affect	10021588
-	-	-	-	Infant sedation	10082187
-	-	-	-	Intentional misuse of drug delivery system	10081675
-	-	Intentional overdose	10022523	Intentional overdose	10022523
-	-	Intentional product misuse	10074903	Intentional product misuse	10074903
-	-	Intentional product use issue	10076308	-	-
-	-	-	-	Mania	10026749

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FDA Guidance 2017		SMQ 20000101		FDA FMQ	
PT	Code	PT	Code	PT	Code
-	-	Maternal use of illicit drugs	10026938	-	-
-	-	Medication overuse headache	10072720	-	-
-	-	-	-	Mixed delusion	10076429
Mood altered	10027940	-	-	Mood altered	10027940
Mood swings	10027951	-	-	-	-
-	-	Narcotic bowel syndrome	10072286	-	-
-	-	Needle track marks	10028896	-	-
-	-	Neonatal complications of substance abuse	10061862	-	-
-	-	-	-	Neonatal oversedation	10050395
-	-	Overdose	10033295	-	-
-	-	-	-	Paranoia	10033864
-	-	-	-	Post-injection delirium sedation syndrome	10072851
-	-	Prescription drug used without a prescription	10076639	-	-
-	-	Prescription form tampering	10067669	Prescription form tampering	10067669
-	-	-	-	Psychomotor hyperactivity	10037211
Psychotic disorder	10061920	-	-	-	-
		Reversal of opiate activity	10039004	-	-
-	-	-	-	Sedation	10039897

FDA Guidance 2017		SMQ 20000101		FDA FMQ	
PT	Code	PT	Code	PT	Code
-	-	-	-	Sedation complication	10079741
Somnolence	10041349	-	-	Somnolence	10041349
-	-	-	-	Somnolence neonatal	10041350
-	-	-	-	Stupor	10042264
-	-	Substance abuse	10066169	Substance abuse	10066169
-	-	Substance abuser	10067688	Substance abuser	10067688
-	-	Substance dependence	10076595	Substance dependence	10076595
-	-	Substance use	10070964	-	-
Substance use disorder	10079384	Substance use disorder	10079384	Substance use disorder	10079384
-	-	Substance-induced mood disorder	10072387	Substance-induced mood disorder	10072387
-	-	Substance-induced psychotic disorder	10072388	Substance-induced psychotic disorder	10072388
-	-	-	-	Suspected product tampering	10079404
Thinking abnormal	10043431	-	-	-	-
-	-	Toxicity to various agents	10070863	-	-
-	-	-	-	Transient psychosis	10056326
-	-	-	-	Withdrawal hypertension	10048007

APPENDIX 8. PREDEFINED POTENTIALLY CLINICALLY SIGNIFICANT (PCS) CRITERIA IN SI UNITS

Category
  Parameter Name
    Age/Sex Restriction, if any
	PCS Low	PCS High

HEMATOLOGY		
WBC	≤2.8 x 10^9/L	≥16 x 10^9/L
Neutrophils (abs)	<0.5 x 10^9/L	>13.5 x 10^9/L
Lymphocytes (abs)	N/A	>12 x 10^9/L
Monocytes (abs)	N/A	>2.5 x 10^9/L
Eosinophils (abs)	N/A	>1.6 x 10^9/L
Basophils (abs)	N/A	>1.6 x 10^9/L
Neutrophils (relative)	≤0.15	>0.85
Lymphocytes (relative)	N/A	≥0.75
Monocytes (relative)	N/A	≥0.15
Eosinophils (relative)	N/A	≥0.10
Basophils (relative)	N/A	≥0.10
Hemoglobin		
Male	≤115 g/L	≥190 g/L
Female	≤95 g/L	≥175 g/L
Hematocrit		
Male	≤0.37	≥0.60
Female	≤0.32	≥0.54
RBC	≤3.5 x 10^{12}/L	≥6.4 x 10^{12}/L
Platelet Count	≤75 x 10^9/L	≥700 x 10^9/L

SERUM CHEMISTRY		
Sodium	<130 mmol/L	>150 mmol/L
Potassium	<3 mmol/L	>5.5 mmol/L
Chloride	≤90 mmol/L	≥118 mmol/L
Calcium	<1.75 mmol/L	≥3.1 mmol/L
Phosphate	<0.65 mmol/L	>1.65 mmol/L
Bicarbonate	<15.1 mmol/L	>34.9 mmol/L
Magnesium	<0.4 mmol/L	>1.23 mmol/L
AST	N/A	≥3 x ULN
ALT	N/A	≥3 x ULN
Alkaline Phosphatase	N/A	≥1.5 x ULN
CK	N/A	>2.5 x ULN
Creatinine	N/A	≥177 umol/L
BUN	N/A	≥10.7 mmol/L
Total bilirubin	N/A	≥34.2 umol/L OR >2 x ULN
Total protein	≤45 g/L	≥100 g/L
Albumin	≤25 g/L	N/A
Total Cholesterol	N/A	>7.76 mmol/L
HDL-Cholesterol	<0.78 mmol/L	N/A
LDL-Cholesterol	N/A	>4.9 mmol/L
Triglycerides	N/A	>3.42 mmol/L
Uric acid		
Male	N/A	>595 umol/L
Female	N/A	>476 umol/L
Glucose	<2.78 mmol/L	>13.9 mmol/L
HbA1c	N/A	≥0.075
Prolactin	N/A	≥5 x ULN
URINALYSIS		
RBC	N/A	>25 hpf
WBC	N/A	>25 hpf

APPENDIX 9. SCHEDULE OF EVENTS

Table 7: Schedule of Assessments

Study Visit Number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17 (EOT/ ET)[a]	18
Study Week	Screening/ Washout[b]	Baseline[c]	1	2	4	8	12	16	20	24	28	32	36	40	44	48	52	Follow-up[d]
Study Day[e]	-21 to -1	1	8	15	29	57	85	113	141	169	197	225	253	281	309	337	365	7±2 d after last dose
Obtain informed consent	X																	
CCI																		
Review inclusion/exclusion criteria	X	X																
Prior/concomitant medication review	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Randomize (IWRS) to treatment		X																
Dispense study drug[f]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
Study drug accountability			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Demography	X																	
Medical history	X																	
Psychiatric history	X																	

Study Visit Number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17 (EOT/ ET)[a]	18
Study Week	Screening/ Washout[b]	Baseline[c]	1	2	4	8	12	16	20	24	28	32	36	40	44	48	52	Follow-up[d]
Study Day[e]	-21 to -1	1	8	15	29	57	85	113	141	169	197	225	253	281	309	337	365	7±2 d after last dose
Tobacco use information		X					X			X							X	
SCID-CT[g]	X																	
Telephone contacts[h]			Telephone calls to the subjects will be made at Weeks 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, 33, 34, 35, 37, 38, 39, 41, 42, 43, 45, 46, 47, 49, 50, and 51. Unscheduled visits may occur at the discretion of the Investigator.																
Physical and neurological examinations	X				X		X			X			X				X	X
Vital signs[i]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

Table 7:   Schedule of Assessments (Continued)

Study Visit Number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17 (EOT/ ET)[a]	18
Study Week	Screening/ Washout[b]	Baseline[c]	1	2	4	8	12	16	20	24	28	32	36	40	44	48	52	Follow-up[d]
Study Day[e]	-21 to -1	1	8	15	29	57	85	113	141	169	197	225	253	281	309	337	365	7±2 d after last dose
Weight (including BMI[j])	X	X			X		X			X			X				X	
Height	X																	
Waist circumference		X			X		X			X			X				X	
12-Lead ECG	X	X	X		X		X			X			X				X	
Hematology, chemistry, urinalysis[k]	X	X	X		X		X			X			X				X	
Blood sample for hepatitis screening	X																	
Serum FSH[l]	X																	
Serum β-hCG, females of childbearing potential	X																		
CCI																		

Study Visit Number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17 (EOT/ ET)[a]	18
Study Week	Screening/ Washout[b]	Baseline[c]	1	2	4	8	12	16	20	24	28	32	36	40	44	48	52	Follow-up[d]
Study Day[e]	-21 to -1	1	8	15	29	57	85	113	141	169	197	225	253	281	309	337	365	7±2 d after last dose
CCI																		
Plasma cotinine level[o]		X					X		X								X	
Urine drug screen[p]	X	X	X		X		X		X		X						X	
Urine β-hCG, females only[q]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

Table 7: **Schedule of Assessments (Continued)**

Study Visit Number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17 (EOT/ ET)[a]	18
Study Week	Screening/ Washout[b]	Baseline[c]	1	2	4	8	12	16	20	24	28	32	36	40	44	48	52	Follow-up[d]
Study Day[e]	-21 to -1	1	8	15	29	57	85	113	141	169	197	225	253	281	309	337	365	7±2 d after last dose
PANSS[v]	X	X	X		X	X		X		X		X		X		X	X	
BNSS		X	X		X	X		X		X		X		X		X	X	
MADRS		X	X		X	X		X		X		X		X		X	X	
C-SSRS	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
CGI-S	X	X	X		X	X		X		X		X		X		X	X	
SAS[r]		X	X		X					X							X	
BARS[r]		X	X		X					X							X	
AIMS[r]		X	X		X					X							X	
EQ-5D-5L		X															X	
ESS		X								X							X	
BACS		X					X			X							X	
UPSA-B		X					X			X							X	
SLOF		X					X			X							X	
MSQ	X[s]																X	

Study Visit Number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17 (EOT/ ET)[a]	18
Study Week	Screening/ Washout[b]	Baseline[c]	1	2	4	8	12	16	20	24	28	32	36	40	44	48	52	Follow-up[d]
Study Day[e]	-21 to -1	1	8	15	29	57	85	113	141	169	197	225	253	281	309	337	365	7±2 d after last dose
Healthcare resource Utilization		X					X			X			X				X	

Table 7:   Schedule of Assessments (Continued)

Study Visit Number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17 (EOT/ ET)[a]	18
Study Week	Screening/ Washout[b]	Baseline[c]	1	2	4	8	12	16	20	24	28	32	36	40	44	48	52	Follow-up[d]
Study Day[e]	-21 to -1	1	8	15	29	57	85	113	141	169	197	225	253	281	309	337	365	7±2 d after last dose
Pretreatment / AE monitoring[t]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Duplicate subject check[u]	X																	

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Abbreviations: AE = adverse event; AIMS = Abnormal Involuntary Movement Scale; BACS = Brief Assessment of Cognition in Schizophrenia; BARS = Barnes Akathisia Rating Scale; β-hCG = human chorionic gonadotropin; BMI = Body Mass Index; BNSS = Brief Negative Symptom Scale; CGI-S = clinical global impression – severity; C-SSRS = Columbia Suicide Severity Rating Scale; ECG = electrocardiogram; EDC = electronic data capture; EOT = end of treatment; EQ-5D-5L = EuroQual-5D-5L; ESS = Epworth Sleepiness Scale; ET = early termination; FSH = Follicle stimulating hormone; IWRS = interactive web response system; MADRS = Montgomery-Asberg Depression Rating Scale; MSQ = Medication Satisfaction Questionnaire; PANSS = Positive and Negative Syndrome Scale; CCI ; SAS = Simpson-Angus Scale; SCID-CT = Structured Clinical Interview for DSM-5, Clinical Trials version; SLOF = Modified Specific Level of Functioning scale; UPSA-B = UCSD Performance-Based Skills Assessment – Brief Version; US = United States.

[a] If a subject discontinues from the study, all Early Termination (ET) procedures should be performed at the ET visit, within 48 hours of last study dose.

[b] Subjects screen fail may be re-screened once after consultation with the Medical Monitor. Screening assessments may occur over multiple days. The Screening Period may be extended for up to 7 days after approval from the Medical Monitor. Subjects may be hospitalized for up to one week prior to randomization during the Screening/Washout Period, if deemed clinically necessary by the investigator. Further hospitalization during Screening/Washout will require approval from the Medical Monitor.

[c] Subjects may be hospitalized for the first 7 days of the Treatment Period, if deemed clinically necessary by the Investigator.

[d] All Subjects will have a safety Follow-up Visit (7 [± 2]) days after their last dose of study drug. While every effort should be made to complete the Follow-up Visit in the clinic, AEs and concomitant medications may be collected by telephone contact if subject is unable to come to the clinic for the Follow-up Visit.

[e] Visit windows are as follows: + 2 days for Visit 3; ± 2 days for Visits 4 and 5; ± 3 days for Visit 6 through Visit 17.

[f] All study drug will be taken once daily in the evening at bedtime by mouth without food or with a light meal.

[g] The SCID-CT will be used to support the DSM-5 diagnosis and must be administered by a qualified rater listed on Form 1572 with at least 2 years' experience with the population under study.

[h] Telephone calls will be made by a member of the research staff to the subject between scheduled study visits that are more than one week apart to collect AEs and concomitant medications, as well as to remind subject about adherence to study drug administration and upcoming visits.

[i] Vital signs will include respiratory rate, oral body temperature and supine and standing measurements of blood pressure and heart rate.

[j] BMI will be calculated and recorded in the eCRF at the clinical site at Screening. For other visits, BMI will be derived in the EDC system.

[k] Subjects must be fasted (no food or drink except water at least 8 hours prior to specified blood tests). Serum prolactin results will be blinded after the Screening visit. A list of laboratory tests are provided in Protocol Section 21.

[l] Blood samples for follicle stimulating hormone (FSH) will be collected for post-menopausal women or if menopause is suspected.

[m] CCI

[n] Sample collected at Baseline will be pre-dose. The time and date of the 3 previous doses of study drug prior to blood sampling and the time and date of blood sampling must be recorded. The remaining plasma samples, after PK measurement is completed, CCI .

[o] Blood samples taken at Baseline and Weeks 12, 24 and 52 for study drug concentration measurement will also be used for the measurement of cotinine levels. No separate blood samples will be collected for cotinine.

[p] Urine drug screen may be ordered at other visits as deemed clinically appropriate. These results should be discussed with the Medical Monitor.

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[q.] Any positive urine β-hCG test should be confirmed by a serum β-hCG test.

[r] Unscheduled BARS, AIMS, and SAS scales should be administered if a subject develops extrapyramidal symptoms (EPS) requiring treatment.

[s] To be completed at the Screening Visit only for those subjects who were currently treated with an antipsychotic medication.

[t] Events occurring prior to first dose of study drug are programmatically identified as pretreatment events. Events occurring after first dose of study drug are programmatically identified as adverse events.

[u] Duplicate subject check will be performed (where allowed by local/regional regulations). Subject consent is required.

[v] The PANSS-Informant Checklist (PANSS-IC) form will be completed as part of the PANSS.

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APPENDIX 10. INTERNATIONALLY AGREED ORDER FOR SYSTEM ORGAN CLASS

Internationally Agreed Order
Infections and infestations
Neoplasms benign, malignant and unspecified (incl cysts and polyps)
Blood and lymphatic system disorders
Immune system disorders
Endocrine disorders
Metabolism and nutrition disorders
Psychiatric disorders
Nervous system disorders
Eye disorders
Ear and labyrinth disorders
Cardiac disorders
Vascular disorders
Respiratory, thoracic and mediastinal disorders
Gastrointestinal disorders
Hepatobiliary disorders
Skin and subcutaneous tissue disorders
Musculoskeletal and connective tissue disorders
Renal and urinary disorders
Pregnancy, puerperium and perinatal conditions
Reproductive system and breast disorders
Congenital, familial and genetic disorders
General disorders and administration site conditions
Investigations
Injury, poisoning and procedural complications
Surgical and medical procedures
Social circumstances
Product issues

APPENDIX 11. IDENTIFICATION OF SUICIDALITY, HOMICIDALITY, AND/OR RISK OF HARM TO SELF OR OTHERS

Condition	Data Source	Criteria
Suicidality or Risk of Harm to Self	Adverse events	• AEs with preferred term of "Assisted suicide", "Completed suicide", "Suicide attempt", "Suspected suicide", or "Suspected suicide attempt" • Medical review of all AEs contained in the MedDRA SMQ of "Suicide/self-injury (SMQ)"
	C-SSRS	• C-SSRS findings of at least one occurrence of suicidal ideation (Item 4 and/or Item 5) or at least one occurrence of suicidal behavior • C-SSRS findings of self-injurious behavior, defined as a "Yes" answer to the following question in the Suicidal Behavior section: Has subject engaged in Non-Suicidal Self-Injurious behavior?
Homicidality or Risk of Harm to Others	Adverse events	• AEs with preferred term of "Aggression", "Anger", "Antisocial behaviour", "Belligerence", "Defiant behaviour", "Homicide", "Homicidal Ideation", "Hostility", "Physical abuse", "Physical assault", or "Violence-related symptom" contained in the MedDRA SMQ of "Hostility/aggression (SMQ)" • AEs with a verbatim term that contains text of "homicid*", "kill*", or "murder*".

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Author:	PPD	Version Number:	0.6
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Effective Date: 02Dec2019			

APPENDIX 12. CLASSIFICATION OF PATIENT TYPE FROM UPSM FACTOR SCORES

Guided machine learning via linear support vector machine (L-SVM) algorithm in MATLAB will be used to classify subjects into 5 patient types based on UPSM factor scores. There are 5 distinct patient types described in the table below.

• TYPE	• PATIENT TYPE
• 1	• Prominently Disorganized
• 2	• Prominently Negative
• 3	• Prominently Hostile
• 4	• Prominently Positive
• 5	• Prominently Affective

The classification will occur in two steps:

Step 1: Train L-SVM in MATLAB to classify subjects into 1 of 5 patient types using 7 columns of UPSM data. Training dataset is given in the table below.

Step 2: Use the now trained classifier function in MATLAB to classify subjects into 1 of 5 patient types using 7 columns of UPSM data.

Table 8: Training Dataset

UPSM-HOS	UPSM-DIS	UPSM-POS	UPSM-NAA	UPSM-ANX	UPSM-NDE	UPSM-DEP	TYPE
0.110138	1.960813	0.478927	3.298293	1.382828	2.114771	0.391504	1
1.431769	1.616874	3.310726	2.225812	0.541127	1.542821	0.22721	4
0.537462	2.293898	3.358519	2.713077	2.582309	1.584137	2.762624	5
1.458801	0.51371	3.162632	4.179415	2.367169	0.687056	2.014098	5
0.491282	1.47429	0.583566	2.633944	4.227873	1.12837	3.735909	5
2.124307	2.621508	2.553096	1.81619	1.463642	0.857061	1.801388	3
0.229749	4.356682	3.900132	2.980611	1.59104	2.825456	2.487569	1
0.65872	1.492003	3.98728	1.558729	1.721153	1.716735	2.567419	4
4.311785	3.13258	3.26397	-0.53456	3.583895	0.246863	3.063737	3
1.673673	2.982224	2.381804	0.168301	2.017634	2.223616	2.420761	3
-0.28911	1.117716	3.325504	4.394722	0.710643	2.619891	1.77449	4
-0.40258	1.164411	3.68884	2.699136	3.395212	2.032147	2.131544	5
0.120462	2.660464	3.395254	2.078197	2.900268	0.261296	2.725002	4
1.361992	3.411795	4.64508	0.18819	1.223746	2.532468	1.366811	4

3.667904	3.136446	2.321715	2.125103	3.409371	1.537432	-0.2218	3
4.879887	3.475862	2.076838	-0.59349	1.113849	1.688076	0.123996	3
-0.02164	2.41729	2.779121	3.079331	2.108443	1.951256	1.676715	1
-0.3092	2.157215	2.674034	2.803489	1.084307	0.996332	1.994321	4
0.196083	2.475004	2.878793	1.351682	1.201559	0.816825	2.181635	4
0.030238	3.526967	4.532129	0.380547	0.326149	1.986222	1.517082	4
2.275873	2.640193	3.251667	0.839343	2.051567	0.58417	2.170745	3
0.664909	2.042059	2.76595	2.366495	1.440192	0.733822	2.402925	5
1.243306	1.337145	4.074218	2.793057	2.698381	2.51747	3.318289	5
3.22947	2.860181	3.577492	3.502082	2.628584	0.298051	3.390157	5
0.901195	1.663412	2.142304	3.688469	1.330552	2.56257	2.640387	5
2.593164	3.648882	3.709823	3.206283	1.011247	1.094186	3.558644	3
-0.51118	2.448093	2.437806	1.15006	2.797663	3.063268	2.065887	1
-0.11226	1.666885	2.743509	1.415346	0.850013	2.305111	1.401516	4
0.461343	2.627467	4.224476	0.273361	1.87481	0.626399	1.981483	4
2.984818	3.119943	1.817018	0.766638	2.093436	1.529787	0.320228	3
3.77918	4.634406	1.565869	3.283619	0.239241	1.954698	0.044583	2
2.144653	2.782737	3.498727	0.538967	1.545457	0.710868	0.792113	3
0.894321	4.51713	0.328192	4.038478	0.461848	4.202648	0.153093	2
-0.36753	4.43122	3.945508	3.314841	3.447207	2.09228	1.277813	1
-0.54075	4.778543	0.863248	4.518782	2.584591	3.675675	1.102248	1
0.567503	3.24148	3.050335	3.616151	2.485309	1.23559	1.194027	1
-0.14361	3.811718	1.934878	4.106673	2.496619	1.883645	1.255909	1
2.074899	4.309083	3.67494	2.931829	2.158336	1.564656	0.532635	2
-0.19755	3.56726	2.443049	2.469007	2.522924	2.551866	4.876176	1
1.77413	1.53753	2.847139	1.882985	0.272108	1.812518	3.542881	5
1.620442	2.629055	2.66762	-0.09426	2.112038	0.781558	3.528088	3
0.284396	1.770956	2.033619	2.009207	3.469858	0.528655	2.227344	5
3.932854	4.528324	2.861762	1.430475	2.837778	1.200249	2.254885	3
-0.56969	0.692111	4.179689	2.437995	1.95239	1.874127	3.146663	5
4.750689	2.427282	4.856594	3.187711	1.452157	-0.41915	0.793141	3
3.405697	1.355663	3.002656	3.832785	3.044058	1.05007	2.012123	5
3.246586	1.094777	3.274349	3.670523	2.797322	0.536438	3.19334	5
-0.73954	2.073529	3.517236	4.06399	3.114689	3.682423	3.860445	5
-0.52019	1.761008	4.510467	2.327021	2.304678	3.148164	2.974405	4
2.014756	2.407895	2.295336	2.006102	1.24862	3.567501	2.040139	2

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0.617758	2.661608	1.536687	3.738151	1.672221	2.392486	-0.23323	2
2.207155	1.517604	2.625454	1.804154	0.763335	0.901574	1.873668	3
1.23422	2.210916	2.561197	2.528093	1.527851	1.183324	0.255261	4
0.021092	1.402188	2.331655	1.812051	2.72359	0.272525	2.258971	5
-0.954	5.328812	2.839309	3.194626	2.923765	1.602491	3.133907	1
3.167057	3.125152	1.146554	4.533739	1.648505	1.456163	2.409444	2
0.076614	2.337764	1.24781	1.632617	2.307237	1.494694	0.092505	1
1.769865	3.050355	3.584774	3.050455	0.435454	0.965985	1.414732	4
-0.14345	2.274485	3.363205	2.516223	1.298419	0.84683	0.939489	4
0.73008	2.109659	1.353254	2.267853	1.683644	1.547878	2.385081	1
1.99611	2.845866	2.776477	2.253987	2.519993	1.293208	0.830398	3
0.070748	2.973237	2.458206	2.670777	0.933532	0.498741	0.68469	4
0.876838	1.702267	2.500296	1.205238	1.988358	1.73428	1.88312	5
2.539879	1.866446	1.194986	2.380642	1.503776	2.970662	0.607604	2
1.394134	3.329297	3.029867	2.34767	2.089692	0.610036	3.175958	5
1.370158	3.673851	0.853038	2.542066	2.93799	2.377451	1.666476	1
1.873059	1.656544	2.282509	0.870666	2.632208	0.4312	1.362965	3
2.587309	1.766566	1.972871	2.451865	2.200703	1.026357	0.802177	3
3.83788	1.83301	2.241711	3.814479	1.270124	0.82664	0.010026	3
1.139727	1.009246	2.171023	2.861618	1.94202	1.469105	2.310987	5
0.399375	1.269958	3.185143	3.451366	2.536612	1.873559	3.891391	5
1.155282	0.720076	1.978406	2.550957	1.676011	2.227286	1.931072	5
1.344237	1.329165	2.176408	2.522749	2.36858	1.113254	1.862452	5
1.884397	0.811162	2.366897	3.193561	1.903167	0.529586	3.039549	5
0.857138	1.991846	4.143588	3.203741	2.567467	1.723389	2.662205	5
0.316037	0.913369	3.265191	3.908459	2.02769	2.805904	3.226179	5
0.941557	1.611534	3.550319	2.397795	2.465604	1.637112	2.268425	5
1.001373	0.053415	2.59386	3.243315	2.765545	1.745535	1.070277	5
0.503857	0.731232	2.859462	3.221411	1.999709	0.617281	0.785101	4
0.606582	1.644987	2.617478	3.87998	1.79895	0.52075	1.931541	5
0.028959	0.051636	2.679662	3.743596	1.258786	0.796158	2.684655	5
1.346641	0.874823	2.367707	3.081821	1.922213	0.204586	1.535142	5
1.860828	2.605349	3.667323	4.365784	-0.09249	1.265363	1.238416	2
3.841476	0.719424	2.257701	4.478491	1.331765	0.100831	1.896058	5
1.661837	1.572432	2.894384	4.184757	1.296394	0.92299	2.19499	5
1.639518	1.463103	2.652642	1.584517	2.156156	1.371609	1.96164	5

0.422721	1.235118	2.915662	1.806378	1.774961	1.461898	1.782514	5
1.706561	2.255214	2.013119	3.335592	1.432492	1.106246	0.37835	2
1.400759	1.11035	3.176518	2.727226	1.683432	1.484354	2.072159	5
0.261743	1.846856	2.95069	1.604365	1.313196	2.201688	2.045153	4
0.589363	1.63248	2.607093	3.117401	1.985862	1.962965	2.226981	5
-0.25198	1.221123	3.025169	3.361783	1.767464	1.630335	2.390124	5
2.291071	0.293838	3.270165	3.243712	2.442306	-0.00452	2.387481	5
1.537487	0.068818	3.108614	1.546074	2.023246	1.696579	2.706242	5
0.582496	1.908653	2.366867	2.51433	1.475041	0.41553	1.263473	4
2.181457	1.917974	2.429864	2.922081	1.514385	-0.21779	1.973444	3
2.263951	0.29547	3.331314	1.415383	2.346612	1.031364	2.892756	5
2.009356	1.113335	3.138889	3.341652	1.883817	0.109166	1.958678	5
0.172439	1.489999	3.292475	2.720522	1.176231	1.605558	2.641559	5
-0.17314	1.356652	4.442061	3.10633	2.049317	0.791991	1.912506	4
1.388335	1.095188	3.220865	1.628662	1.732311	1.352052	2.405447	5
1.205138	2.024409	3.791492	2.398941	3.006668	1.787416	2.920256	5
0.464397	1.684218	3.40262	2.726862	3.013933	1.189662	3.61535	5
1.628768	1.308049	2.95217	2.745054	1.327077	2.028925	3.357957	5
0.586597	2.536766	2.916748	3.252801	2.392646	2.207333	3.37449	5
0.668672	0.21496	3.401807	3.499059	2.747658	2.264928	3.708938	5
1.85842	1.032293	3.81473	3.017692	2.560804	1.060393	2.687179	5
0.421477	1.193203	3.072718	3.197042	2.410182	2.327653	3.342285	5
0.705007	2.094874	1.758942	2.993589	1.631168	1.769052	2.175233	1
1.341319	2.511154	2.487053	0.737579	1.309727	1.172314	2.21039	3
-0.10475	3.201991	2.494132	3.312053	0.911785	2.561984	0.543735	2
1.26418	1.34083	2.50963	3.164473	0.66512	1.883488	1.486237	2
2.135516	2.140969	2.155306	4.111724	2.433874	1.272746	2.910099	5
0.11181	3.029033	2.241817	4.074078	2.229162	1.485626	1.801666	1
0.57075	4.309476	3.042631	3.640668	1.121444	1.676763	0.985236	2
2.368828	2.078152	1.757995	3.68918	2.238158	0.832056	3.202517	5
0.460592	3.343601	1.369653	3.591892	3.052149	1.590111	1.853283	1
1.039519	2.73413	2.797452	4.794559	3.188477	1.32171	2.069804	1
-0.10856	3.283553	2.221476	2.861392	2.916771	1.670176	1.495856	1
1.635721	1.670994	2.776531	3.481021	3.648923	1.09168	3.517521	5
-0.28728	1.550428	3.027047	1.569179	3.495302	1.675143	3.72542	5
0.629977	1.356138	4.076404	1.705047	2.22813	1.423955	2.063269	4

2.307646	2.236448	2.680489	0.969736	2.569013	-0.08536	2.277701	3
2.477069	3.263651	2.163565	2.139497	1.721061	-0.00358	0.65799	3
1.243638	2.913075	4.107979	2.66461	0.995093	-0.14437	1.22687	4
0.527388	1.958446	1.279965	3.081775	0.643036	1.853639	2.172642	1
0.424628	2.137735	2.088917	1.156878	1.766872	1.219234	1.53977	1
2.527044	0.76957	4.013747	2.360512	3.03441	-0.3789	4.007144	5
-0.19304	1.261063	2.340497	2.776243	2.052291	1.922053	3.962693	5
0.533501	1.87061	4.417346	2.075672	3.323951	-0.27006	4.225107	5
2.411661	1.882853	4.355587	1.036112	1.98607	0.055844	1.311082	3
-0.48578	1.752793	4.45535	3.947321	1.094441	2.902358	2.033406	4
0.464869	3.413253	2.635796	2.121825	2.8906	1.996746	3.22642	1
4.132441	0.401081	2.381923	3.456109	0.953315	3.096096	0.555434	2
0.218247	3.435941	1.849422	1.196065	2.511003	1.363478	0.35237	1
-0.32981	4.544489	1.360392	3.024887	1.106194	2.727317	0.572736	1
0.544813	4.282196	2.116876	2.290366	2.541964	1.369559	1.818978	1
-0.47234	4.088985	0.577244	2.967936	2.63388	2.877609	2.381399	1
-0.55527	4.84008	1.960686	2.982342	2.094423	1.626178	1.184506	1
0.263513	3.736018	1.959549	1.758239	1.640343	1.004376	1.472666	1
0.705893	3.718196	2.301378	0.926439	1.774488	0.994932	1.79793	1
0.069405	3.026261	2.43983	3.17107	3.19792	2.883761	1.97275	1
-0.32695	0.330879	2.510527	3.441654	2.057765	2.304866	2.878307	5
2.690017	0.693133	1.730133	3.88509	2.562458	1.455035	1.213344	5
0.46547	1.287936	2.939181	1.394492	3.396399	2.015295	2.080734	5
1.394982	1.559578	2.471032	3.161232	2.57522	0.992441	2.406263	5
0.672309	2.393359	1.896502	2.598218	0.993053	3.154678	1.696235	1
1.693716	1.325886	0.880014	5.37448	1.164323	3.653433	2.895248	5
1.356159	2.406733	2.037301	2.919935	1.869511	3.465406	1.13788	2
1.027015	1.062603	0.659294	4.357499	2.82001	3.266347	4.132878	5
1.436698	-0.58649	1.964863	3.95011	3.191804	0.377813	4.488555	5
4.058956	-0.66886	1.317517	4.606702	1.160914	2.731827	3.099033	5
1.416783	1.490505	2.933091	1.730763	3.560499	0.430518	2.821162	5
0.824231	-0.19387	4.748215	0.202208	2.896445	0.69977	4.873985	5
-0.36924	2.678109	3.163096	1.596358	0.59506	3.346233	1.61617	4
2.327808	1.715927	3.390249	3.327197	-0.07099	1.647033	1.876406	2
1.146957	1.732186	2.467294	4.312694	0.967439	3.606223	2.364763	2
-0.08434	2.371234	1.923559	2.551661	2.780099	-0.41496	2.607441	5

2.330935	1.249285	1.977942	-0.29365	1.750854	1.887952	3.34313	5
-0.29097	2.579936	4.03501	2.453226	1.223345	1.756084	1.578965	4
2.433418	1.586402	2.744031	2.943148	2.595221	-0.15045	4.456784	5
1.686219	2.133575	3.063004	2.625084	1.837615	0.138859	2.505072	5
2.182811	2.480894	3.512331	2.528045	3.359501	1.174893	2.358992	5
1.726701	2.611469	3.08875	2.914048	3.581237	1.05601	1.522262	1
0.604793	3.12306	2.124151	2.637198	2.7244	2.472494	1.200589	1
3.236433	3.290153	2.702033	2.314023	3.316992	0.3816	1.895082	3
1.425043	3.692046	3.472158	4.057196	2.405972	0.434079	2.869765	1
2.201707	3.084578	2.151076	4.021647	2.182574	2.301893	1.407549	2
1.815693	2.134869	4.303099	4.369005	1.882038	0.949098	1.847457	4
1.20209	3.064755	4.217095	3.649783	2.915971	0.357701	1.225159	4
0.046373	2.916968	4.455808	2.885248	3.107358	0.426352	2.008252	4
-0.01844	3.893585	3.026784	1.817709	0.913144	3.254477	2.670709	1
0.15412	3.328443	1.620771	1.879719	2.673819	2.668971	2.431268	1
-0.07332	4.359244	3.52468	1.723178	0.553973	1.862672	0.970363	4
0.708979	3.65687	2.295132	2.084227	1.178033	3.673556	0.603624	2
1.454947	3.430231	2.232895	2.447069	2.309456	2.631151	2.32591	1
0.583852	3.473869	2.416568	2.141427	0.479351	2.977283	1.947473	2
0.284904	3.74932	2.086627	3.204144	-0.07831	2.28367	1.519997	2
0.882449	3.863615	3.044836	2.195771	-0.10572	1.730727	0.181928	2
0.180445	1.883516	1.562047	2.663036	2.63216	2.250718	2.436309	1
0.378782	2.931791	1.708711	2.980852	2.771396	2.111069	0.610343	1
0.352732	1.89972	2.265854	3.230448	1.11399	1.21381	2.019503	5
-0.07905	1.7187	0.81324	3.213864	2.58132	2.072825	1.596053	1
-0.04268	2.161476	1.854841	2.9067	2.572292	2.05655	3.250114	1
0.532978	3.478254	2.049047	1.952408	2.807302	1.696268	1.824182	1
0.155656	3.999629	3.146047	1.349007	2.792547	1.478153	1.4613	1
0.796148	2.634837	3.132603	3.222581	2.680883	1.854805	2.030157	1
0.86594	2.609557	2.546813	1.751367	1.740951	1.533923	2.228512	1
1.01185	2.816307	2.912837	1.669116	2.542537	1.330716	1.168323	1
1.350645	1.989788	1.74757	3.198019	2.213117	0.804664	1.34773	1
0.349145	2.756305	1.716076	2.68973	2.739907	1.656974	1.623306	1
0.342705	1.679803	1.833402	2.032994	2.960676	1.663841	2.120364	1
1.484201	1.539412	1.50688	2.924464	2.475359	1.705127	1.683536	5
1.562951	3.030532	1.644437	2.014339	1.595521	1.644179	1.164406	1

3.029619	2.819386	1.874296	2.742982	1.788343	2.269874	1.542436	2
0.78352	1.877238	2.074483	2.627216	2.240644	2.194709	2.377748	5
0.710665	2.849776	2.364681	1.919057	2.747839	1.648826	1.233827	1
0.798178	2.933791	3.35471	2.705446	0.796685	3.192393	0.488374	2
1.905889	4.839237	3.456346	0.724097	2.164524	0.999083	1.83366	3
-0.42893	2.354318	2.48451	3.358162	0.714569	2.794577	2.607276	1
2.197681	2.953134	3.844426	1.086876	0.80736	-0.01227	2.050991	3
1.175299	4.850591	4.181569	1.539452	1.490182	0.734061	1.239397	4
-0.50935	3.131051	2.46547	2.550862	1.514948	3.740844	1.942203	1
-0.47872	2.432521	2.670089	3.345092	1.896522	3.066479	3.392814	1
1.647404	2.212889	0.922094	2.565279	2.766181	2.737955	1.599062	1
2.466112	2.010557	3.626749	3.847344	2.514457	1.560699	3.442844	5
3.004502	2.637176	2.798804	3.711184	2.463544	1.57843	2.123784	3
1.241437	2.778655	1.589605	2.563038	2.012834	1.91169	3.491985	1
2.391924	2.637746	2.374582	0.755083	2.629425	2.330716	2.941087	3
1.486578	3.128626	2.487837	1.743571	2.003073	1.737516	1.329548	1
2.586535	2.877124	2.287801	2.632841	1.387282	2.363598	2.453764	2
1.66655	2.838318	2.35911	1.973314	1.859279	2.225311	2.915387	1
1.589938	3.65255	2.956482	2.565466	0.975133	1.615948	0.499501	2
1.945618	3.050839	2.514292	3.234862	2.203473	1.822279	1.99805	1
1.755469	2.075945	3.480556	2.94479	1.519334	1.681199	0.758004	4
2.935053	2.718756	3.31552	2.504717	1.889886	1.201849	1.460136	3
2.119775	3.394806	2.506338	2.120552	2.614302	0.679575	0.89525	3
2.458961	2.329016	2.154788	3.310596	1.474675	2.59347	1.591725	2
1.244654	1.73021	1.827923	2.489334	1.383575	2.073081	1.360675	1
-0.20744	1.946772	4.276268	1.584494	1.25229	0.51958	1.276463	4
1.074974	1.973074	1.265671	1.897755	2.948865	0.870864	1.737043	1
-0.14189	-0.04374	3.164932	3.531256	1.980725	0.632499	3.87712	5
3.376984	0.831567	2.275181	2.779673	1.98059	1.308505	1.968036	5
0.410408	1.295473	3.211679	2.991182	2.99265	1.394861	2.979216	5
0.412831	0.728305	2.774347	3.476108	2.485126	0.143779	1.325316	5
0.395383	1.266636	3.547077	3.848593	2.41841	0.233631	1.330153	4
0.303011	0.68115	3.431149	2.896138	2.845076	0.290205	2.987518	5
0.623263	2.844467	2.011102	3.13837	1.748296	2.03984	2.51607	1
0.430849	2.024006	2.387261	2.938496	1.830338	1.725661	1.602135	1
0.302646	3.078668	1.809565	2.02404	2.874748	0.986561	3.022366	1

0.217969	2.234125	3.086551	2.801215	2.881359	1.925122	2.6483	1
1.148024	4.715529	1.712537	1.143191	1.448075	0.735696	1.255713	1
0.17321	2.714301	3.093773	2.731845	3.555077	0.30472	1.964692	1
1.628505	1.333563	2.279517	3.023174	2.166503	1.909445	2.062154	5
1.460183	2.173385	1.803192	2.793002	2.444099	0.941715	2.221664	5
0.443037	2.964066	1.915887	2.678915	1.792021	2.577074	1.45575	1
0.462123	1.136766	3.163593	3.69979	3.024302	-0.067	2.09806	5
-0.00933	2.530804	3.25533	3.315988	1.517136	0.677362	2.642933	4
1.040869	1.969233	2.705048	4.084591	2.318205	0.820581	2.483245	5
0.146118	1.409769	2.792843	2.852647	2.966719	0.792185	2.797111	5
0.957539	1.814681	2.711	3.043293	1.665616	0.197362	2.822844	5
1.552961	2.008691	3.036311	3.633731	2.497589	-0.00887	1.003566	4
1.250273	3.122429	2.403355	3.189958	1.795676	0.107745	0.924363	1
1.322036	1.215882	3.921602	3.003509	2.284119	-0.24933	1.806291	5
0.251952	2.113829	2.664782	3.034502	1.648737	0.259419	2.65026	5
0.59895	3.329155	2.836852	2.202842	1.497784	1.607472	2.583754	1
0.565399	5.191211	2.58232	2.271006	2.778369	1.798438	0.76725	1
1.891514	1.030671	2.378489	2.521739	2.470474	1.713408	1.830049	5
2.251343	1.964833	2.782653	2.173102	2.552897	0.928943	2.420509	5
0.827273	1.676045	1.79413	2.599383	2.936736	2.290989	1.069859	1
0.933062	4.872175	1.858903	3.41357	1.483246	3.481183	0.717352	2
1.319798	3.170397	2.467164	3.559172	3.259405	2.329196	0.779611	1
1.159981	2.887268	2.048998	1.864787	1.714485	1.964015	0.851252	1
2.594349	4.47202	1.935226	2.39397	0.807125	1.443819	1.010001	2
2.259674	2.817409	2.241478	3.232779	1.265977	2.904775	1.005764	2
3.853234	3.442007	3.483622	1.254111	2.035139	0.95848	2.220828	3
0.107242	2.316128	1.787862	2.913061	2.647041	1.852659	1.796499	1
4.540121	2.034294	1.273216	4.195778	0.812797	3.901634	2.414239	2
1.940409	1.744759	2.334533	3.048773	2.032325	1.673573	2.156116	5
1.771326	1.136763	2.607683	3.880771	1.931054	1.665451	2.462573	5
2.056638	0.596344	2.676342	3.652917	1.954028	1.575281	2.359132	5
1.998099	1.080433	2.593327	4.200915	1.916664	1.49471	2.380617	5
1.973644	0.455134	3.08072	4.16708	1.829094	1.683288	2.447056	5
1.836602	0.707831	2.460104	4.184537	1.830863	1.615467	2.488581	5
1.970747	1.071085	2.266924	3.64906	3.038635	1.177264	2.83891	5
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1.017331	2.182473	3.564923	0.448758	2.352833	2.376049	3.255035	5
1.725945	3.009119	2.694312	0.112874	3.046849	1.046677	2.597689	3
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1.826434	3.195578	1.861429	3.285702	2.60437	0.337541	1.982752	1
1.081747	2.024036	3.051124	2.759296	2.689623	2.411139	3.523435	5
1.726368	2.23849	3.132346	2.316369	2.459357	2.194413	2.921579	5
0.273047	2.916457	1.761402	3.342903	1.357142	2.447486	1.642088	1
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-0.44394	1.990884	2.120804	2.786634	1.973897	3.156599	3.453843	1
0.965206	1.901004	1.431642	3.042105	2.183742	2.33692	2.365446	1
1.658993	1.392341	3.179016	2.725544	1.270456	1.609023	2.18851	5
1.841815	2.190828	2.24286	3.811443	2.195616	0.758591	2.922796	5
1.22653	1.421029	2.261803	2.765931	2.425561	1.732311	3.372288	5
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1.32315	0.012205	4.865486	0.779994	1.714469	0.367159	2.011743	4
2.650652	1.224055	2.722871	2.274911	1.37163	1.630707	1.845764	3
1.607415	2.287416	2.580634	1.22177	2.238811	1.518263	0.841124	3

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1.956178	-0.46028	4.546977	2.448721	1.334782	1.148109	3.918205	5
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1.584827	0.935282	3.327166	1.94125	2.179968	0.358369	3.245291	5
0.928618	0.658035	3.076131	3.113168	2.172916	1.004145	3.430131	5
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3.807773	3.594538	1.889844	0.931891	1.714179	-0.22761	0.176671	3
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1.563126	0.95651	2.505286	2.57955	1.915208	0.43884	3.595415	5
0.166357	2.392899	3.069375	2.770552	1.708797	3.004771	0.534774	1
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1.419943	3.311596	2.146657	1.1977	1.445532	1.588575	0.49374	3
1.6282	2.717846	3.449848	2.08389	0.548107	3.320778	3.109258	2
0.74564	4.329717	3.465316	2.586558	0.874382	2.331343	0.952736	2
-0.53777	2.184301	1.465823	2.443865	3.215783	3.614718	3.522195	1
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1.925363	1.20103	1.434322	1.670427	2.831532	1.924301	2.443715	5
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-0.50069	3.784005	2.725673	3.553338	0.042037	2.158042	2.048815	2
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0.506534	1.782591	2.399148	2.907124	2.313644	1.898565	1.305203	1
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1.313982	1.203218	2.354178	3.867624	1.752954	2.803632	0.720678	2
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1.511414	2.714801	2.477878	2.356489	1.608225	2.422306	1.576296	1
3.784065	1.862054	1.713389	0.213838	2.933285	1.556042	1.609158	3
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3.780426	1.734454	3.849178	2.897637	2.083926	1.825276	1.092608	3
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3.757162	1.90669	4.023394	2.056548	2.092316	0.702579	2.357687	3
3.200396	1.822515	4.443242	2.109396	2.22672	1.391675	1.539029	3
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1.820917	1.750117	4.53634	2.28264	1.228009	2.070476	1.366165	4
3.837824	3.469015	3.399461	1.508111	2.106133	0.646965	1.877185	3
3.086287	3.311494	3.384577	1.007094	2.34214	0.704304	1.716368	3
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1.790911	3.020807	2.397504	2.504064	3.159573	2.110374	2.839354	1
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0.905829	3.986124	2.764364	2.658993	1.428778	2.003098	0.431219	2
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0.764445	3.897983	3.379027	3.055913	0.426009	3.234069	0.929019	2
3.687367	1.522458	4.258232	2.500019	0.945134	1.624383	0.883844	3
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4.672162	3.069382	3.688413	2.440952	1.405466	0.020889	1.708298	3
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1.991084	3.045781	3.097603	3.246524	0.560414	3.354772	2.362809	2
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0.745193	1.490097	3.379798	2.22975	2.245205	1.51202	1.55745	4
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1.884125	2.075508	2.16487	1.55485	2.294037	1.421776	2.021908	3
0.985738	2.323031	3.344249	2.186234	1.046613	1.139703	2.08681	4
1.339493	2.1716	2.640416	1.643363	1.890265	0.862075	2.452216	5
1.411204	1.768375	2.509155	2.071366	1.069819	1.270294	2.138543	5
1.603957	2.393124	4.600104	1.479665	0.3686	1.257599	1.671143	4
1.593894	1.808995	1.276598	2.542793	2.668689	1.234447	3.011351	5
0.437205	2.05325	2.233585	2.342777	2.863301	0.989024	3.132892	5
1.796248	1.921808	4.253712	0.987076	2.703099	0.264328	0.99685	3
1.637491	2.60536	2.78299	3.176663	3.185908	0.945942	1.681183	1
2.397302	1.887024	1.91816	2.197268	2.581808	1.771002	2.369984	5
2.328269	2.27798	2.125474	3.005204	0.099046	1.713398	1.026657	2

0.11416	2.396599	2.853036	3.178833	1.031306	1.899937	0.55292	4
0.646272	2.409414	3.949841	1.627033	1.13211	1.385222	1.246331	4
1.819873	2.572002	1.843449	1.60919	3.013846	0.301808	1.919204	3
2.893933	1.199162	2.164442	2.545358	2.839459	1.856562	2.979892	5
1.657387	-0.04104	2.817115	2.885721	2.252117	2.258384	3.244889	5
3.223918	1.104266	2.818893	1.829432	1.385741	2.348728	3.350843	5
1.567883	1.69097	2.678636	3.576635	1.69927	2.373808	1.665361	5
1.444466	2.164448	3.129106	2.105301	1.025459	3.286115	2.679373	5
0.789237	2.751414	4.503448	2.279741	0.594937	1.47052	1.258745	4
1.32103	1.739759	2.91269	1.970637	1.670966	2.325363	1.734543	5
1.417863	1.565313	2.942052	2.716931	2.031696	2.665588	1.504992	5
0.105744	2.701506	3.935611	3.081274	0.140042	2.612532	1.21387	4
0.093926	1.328851	3.657152	2.021215	2.748042	1.799659	2.503177	5
2.058253	1.409092	3.385514	1.720862	1.359984	2.940476	2.368557	5
0.610951	2.617612	2.618744	2.959006	1.079474	1.703607	0.602328	2
1.620419	1.452286	3.220025	2.04852	1.620619	2.70717	2.011157	5
1.26425	2.492492	2.254208	3.149003	0.20461	2.680442	0.963521	2
0.931603	0.778784	3.816232	2.411449	1.588901	1.749691	2.903384	5
1.883671	1.958262	2.662179	2.06722	1.593241	2.260557	1.932458	5
1.616866	1.148898	3.165864	2.700711	2.133769	2.779107	2.060409	5
1.96896	1.173538	3.408077	1.916709	1.627131	2.562472	2.227437	5
0.775019	3.539821	1.948109	1.474039	1.512137	2.192336	0.356982	1
-0.48434	2.801792	3.341801	1.253899	2.23096	2.792869	3.211511	1
1.735924	3.692729	4.176931	0.871424	2.20432	-0.09871	1.803309	3
2.436967	2.242692	2.95653	2.42781	1.861757	1.764807	2.614867	5
1.658166	2.250213	2.272366	3.709927	2.741535	2.928559	1.376769	1
1.333809	3.28714	1.923658	2.704404	1.874826	2.942094	1.95615	1
0.304445	2.431619	3.242846	1.164343	2.616041	2.179615	2.512263	1
1.093769	2.70846	3.188444	1.452049	2.704276	2.837869	3.558715	1
0.979075	2.932777	2.236762	1.834613	3.024493	1.92344	3.156133	1
1.504879	2.118966	1.74156	1.487179	3.392883	2.680421	2.117358	1
0.235742	1.514871	2.640203	4.244476	1.9561	1.274938	3.144923	5
0.721346	2.624908	2.503404	1.783081	2.070988	2.354757	2.050832	1
1.511873	1.611845	2.686757	2.24819	2.398428	0.857729	2.340673	5
1.483817	1.742122	2.38017	2.115277	2.46686	0.885315	2.411145	5
1.412824	2.023799	2.394205	2.244071	2.566338	1.066282	1.957895	5

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0.96656	1.956889	2.503954	1.889427	2.584678	0.635303	2.486109	5
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1.264227	1.559251	2.530892	2.351941	2.005204	1.908408	2.08316	5
1.300572	1.506208	2.456656	2.476265	1.930084	1.826288	2.238183	5
1.395494	2.681821	2.399638	1.861954	1.670527	2.336857	1.348026	1
1.071372	1.64587	2.335144	2.049403	2.134302	1.103433	2.192995	5
0.972549	2.213103	2.453235	1.965736	1.820293	1.210596	1.269824	1
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0.290952	2.170553	2.27139	3.121171	1.858355	1.795948	1.144805	1
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2.310326	1.084356	3.212852	0.991361	2.383933	1.0178	3.223335	5
0.538985	0.684544	2.87213	3.319863	0.471048	1.146485	3.037455	5
1.320483	0.370392	2.959414	2.893502	3.208969	0.487022	2.159851	5
0.632746	0.962392	3.786251	3.674781	1.636723	0.976119	0.43589	4
1.260572	1.114517	3.471529	3.147704	2.509499	0.784426	0.739571	4
1.81431	0.908937	3.437827	3.115334	1.089183	0.8543	1.536967	5
0.480491	1.603937	3.497161	3.171849	2.858567	1.045461	0.796103	4
2.448276	0.9507	3.11357	2.242604	2.513886	1.092078	1.001218	3
1.667621	0.720564	3.065787	2.789554	2.601914	1.00463	1.646084	5
1.36549	0.471031	3.670106	2.32908	2.812428	0.692981	2.377931	5
1.782831	0.668699	4.303075	2.950578	1.196954	1.473613	2.410163	5
1.779422	1.804898	2.372978	2.236031	1.796164	1.101095	2.408556	5
0.752197	1.221928	3.601867	1.913002	2.917384	0.485048	2.184378	5
1.090207	0.371767	3.657906	3.103313	2.695586	1.088557	2.130409	5
1.449626	1.446819	4.565353	2.201232	1.589811	1.28579	1.45593	4
1.538993	0.432944	3.880188	2.973588	2.369882	1.22025	3.079243	5
1.267368	0.956728	3.771335	2.573059	2.060642	1.354038	2.111837	5
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0.542068	2.551937	3.744826	2.376175	0.753738	3.505419	2.13489	4
0.372456	3.354352	3.712648	1.479283	0.715589	1.445332	0.635211	4
0.305215	2.289783	4.46517	2.340381	1.999469	2.164077	1.869376	4
2.755486	3.573517	3.853695	1.941299	2.051228	1.450862	2.118203	3
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0.873249	2.555248	2.54208	2.041056	2.167741	0.808359	1.213751	1
0.806786	1.256641	3.512638	2.772089	1.439192	2.428634	3.160887	5
0.026556	1.299047	2.254734	2.758667	2.102032	2.059072	2.925602	5
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1.531207	1.639334	2.208954	2.580159	1.424991	1.388167	2.864206	5
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1.062165	1.703427	4.137153	3.523577	-0.25471	0.274785	2.414101	4
1.613615	1.567968	2.01006	2.909649	1.084012	1.64672	3.082602	5
2.611317	1.360381	2.572052	3.842697	2.318571	1.267588	1.442266	5
0.244814	0.983054	2.619721	3.328562	3.670014	1.220171	3.959349	5
0.212633	1.470245	3.736618	2.26854	3.534922	1.163535	2.752749	5
0.210494	2.000189	3.356024	2.1878	2.134824	1.09907	3.104368	5
1.926494	2.720868	1.743791	1.398287	2.173038	3.352568	2.561924	1
1.072198	3.31218	4.423606	0.480775	1.247225	1.562622	3.173473	4
1.357499	2.189561	2.255633	3.35382	1.874947	3.258765	3.437023	5
1.497423	1.962183	2.210324	1.454927	2.617754	2.249815	2.748368	5
1.704547	1.358564	2.589937	2.18018	2.343222	1.467078	3.609101	5
1.339563	2.526236	2.490679	1.016699	2.780961	2.661584	2.361953	1
2.328581	2.394616	2.552002	1.14282	2.842293	0.484683	4.308226	5
1.85317	1.934251	3.869415	0.499016	2.363052	1.674276	1.029997	3
1.45469	2.190708	3.760847	1.722148	1.768372	3.116628	3.478788	5
3.470967	3.439438	3.360445	0.721942	-0.20575	-0.06164	0.009922	3
1.296298	2.090994	1.963986	3.324418	1.359161	1.950194	4.18974	5
0.814951	2.698575	2.986318	0.932067	2.782515	1.42676	0.998865	1
0.701812	2.816236	4.503632	3.118434	1.809571	2.136325	1.220668	4
-0.10962	4.748057	1.311358	3.02705	1.085849	3.705541	2.662043	1
1.458165	3.619007	2.461477	1.602822	1.411744	2.264779	2.547659	1
0.800917	4.262438	2.544643	2.894222	0.613533	3.956862	1.671726	2
0.717591	4.02109	1.879332	2.441721	1.49057	2.877834	0.429284	2
0.643691	3.855714	1.005858	3.175629	0.103246	3.558945	0.795806	2

0.460533	3.698006	2.572437	2.387381	2.850441	2.808884	3.094858	1
4.04329	2.578201	0.799226	1.244423	1.632081	1.311067	1.735986	3
1.774165	4.058947	4.405546	1.785724	2.283782	0.758058	0.79129	3
2.724334	4.789961	1.917886	3.663023	0.860011	2.905804	-0.22034	2
1.890045	3.070056	2.121002	2.630324	1.471761	1.45338	1.399154	2
1.179053	2.241616	2.464325	1.743874	2.39835	0.483349	2.739105	5
0.910327	1.109921	3.392557	1.840023	3.649984	0.230089	2.727363	5
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2.31223	2.140411	3.730239	2.46278	1.824992	1.428426	2.476548	3
2.000375	2.189982	3.724534	2.161509	1.635054	1.57342	0.200782	3
3.566437	0.913912	4.240227	1.9238	2.017575	2.399885	0.391107	3
1.62852	1.018615	3.425307	2.069394	2.752738	2.893608	1.471069	5
2.456128	1.924375	4.611679	1.543373	2.675139	1.215867	0.819487	3
2.955322	1.138264	3.747873	1.707216	2.573102	0.483788	0.805569	3
2.62885	1.755127	3.044607	2.3257	3.162495	2.415337	1.155672	3
2.310367	1.524535	3.543808	2.150572	2.369389	2.057397	0.899822	3
2.827557	1.951977	3.069947	1.919696	2.682531	1.73087	1.301477	3
2.354338	1.852527	4.186875	2.762147	2.727398	1.526546	1.348267	3
3.133866	1.126868	3.578091	2.250377	2.22218	0.989612	2.052883	3
3.902417	1.344091	2.9635	2.392058	2.238225	1.139263	1.925944	3
4.044799	2.560889	2.663006	2.169593	0.901192	1.77012	1.96679	3
4.155056	3.609037	2.424906	2.437343	0.670008	2.751403	1.023351	2
3.229569	3.060956	1.07279	2.674057	0.661189	2.715768	2.115442	2
2.921269	3.279488	2.066332	2.23657	1.842327	2.123827	1.809801	3
3.044779	4.07456	3.89887	1.460329	1.288036	0.384507	1.178261	3
2.740083	1.644629	2.55435	3.62446	1.955832	2.066756	0.815177	2
3.672096	3.42332	1.365735	3.932623	0.190274	3.855517	0.758265	2
3.179953	3.568001	2.620359	2.696917	-0.87467	3.369777	0.541363	2
2.519518	3.268074	3.607177	2.930387	1.07823	3.237732	2.437606	2
2.225039	3.775535	1.123748	3.689868	1.819697	3.939923	2.586388	2
3.709609	3.536046	2.146801	3.13129	1.525033	3.051844	1.077151	2
3.922836	3.537094	2.352621	3.817752	0.344085	3.99746	1.601192	2
2.559641	4.363924	3.081225	3.940225	1.04974	4.147581	1.955423	2
2.506535	3.511332	2.686218	2.671171	0.351229	3.135231	1.534423	2
3.611068	4.140873	2.759899	3.567679	0.327898	3.496142	1.915584	2

5.041109	4.030347	2.811553	1.898102	0.623562	2.481326	0.318056	3
3.987555	3.862457	2.73161	2.815862	0.253199	2.530565	0.116675	2
3.206587	3.376827	1.547706	3.04708	0.941526	3.026795	1.442369	2
2.687183	3.33638	2.737193	3.16023	0.407868	1.803257	1.018576	2
4.22479	4.024705	2.715407	2.974781	0.622469	2.100873	0.07855	2
3.485571	4.124516	1.799485	1.550554	0.865302	2.835845	0.512219	2
3.689093	2.992012	2.750544	2.126705	0.951029	1.841686	1.154485	3
1.507022	1.700048	3.643006	1.920586	1.721019	1.670477	0.88364	4
2.276998	1.872161	3.071937	1.551547	1.758093	1.456656	3.036033	5
1.722543	1.742988	3.195897	1.77644	1.623838	1.707611	1.691541	3
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1.74568	2.356083	3.455882	1.940336	1.498636	1.462326	1.919923	3
0.158772	2.513544	4.247838	2.551583	1.045512	1.299605	1.587535	4
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2.561767	1.359762	3.215666	1.723347	2.649111	1.506876	1.212116	3
2.008407	2.326931	2.699744	1.797094	2.059043	1.621615	1.595778	3
2.063938	2.29876	3.576087	1.683763	1.536197	1.5092	1.604547	3
1.870314	3.05033	2.832324	1.120539	1.534361	0.937647	1.53327	3
1.545386	2.699153	2.90158	1.987278	1.572393	0.979358	2.326712	3
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2.883239	1.229672	3.978406	2.649253	1.311891	0.28695	1.875801	3
3.555512	0.756289	4.859439	2.591224	-0.00136	1.007842	1.233879	3
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2.359152	2.995853	2.391476	2.378635	0.185879	0.813561	0.190325	2
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1.137828	1.970334	4.54537	1.77048	0.962424	1.676055	0.879076	4
1.978596	2.050605	4.222893	1.545038	2.620691	1.180971	2.380491	3
1.621695	1.681869	2.94142	2.467838	-0.34802	1.869441	0.368981	2
1.218523	1.811689	4.994002	2.11	-0.69899	2.880036	1.550563	4
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1.429912	3.253482	2.093267	3.097008	2.026439	2.325492	1.059837	1
1.462999	2.915668	2.516664	3.674496	3.004662	1.589824	0.748062	1
0.733537	2.892451	2.643295	3.09355	3.151582	1.65196	1.337782	1
0.791875	2.884693	2.779237	3.413417	2.44907	2.601256	1.424172	1
-0.10517	3.040316	3.360112	2.855718	2.873678	1.188593	0.322964	1
0.875719	2.924053	3.610616	2.741726	2.132826	1.585964	0.493479	4
2.176518	4.067647	1.934115	2.559868	2.254118	2.083677	1.380008	1
-0.17358	3.503438	2.423085	3.051185	2.147663	1.953754	2.706169	1
1.679471	2.53749	2.705387	2.011349	3.219434	1.704823	2.592947	5
-0.62134	3.307752	3.073545	2.275577	1.186566	2.329074	1.121935	1
-0.58953	4.10793	2.459029	3.07827	1.627415	1.960017	0.474559	1
-0.4566	3.748106	2.48163	1.703436	2.031344	2.439934	2.085523	1
-0.40305	4.629888	1.803605	2.719529	0.109098	2.449213	0.376085	2
-0.13362	3.298538	2.094871	2.657361	2.068097	2.119957	1.46328	1
1.051681	3.044125	1.860595	2.414682	1.750706	2.127842	0.624443	1
-0.46756	3.672684	2.609306	2.798242	2.727397	2.08414	1.927971	1
-0.22257	3.403974	3.992026	1.594233	0.951226	1.79945	1.564202	4
0.879599	2.559537	2.682985	2.436528	1.732751	1.685048	0.478358	1
2.068797	4.083433	2.641366	3.421411	2.299622	2.077696	0.331541	2
3.216228	3.0991	2.141928	3.095791	1.858518	2.550298	0.088065	2
3.29187	3.301854	1.867055	2.807832	2.601268	1.726811	0.402809	3
3.144054	3.6932	1.424622	1.494059	2.486708	2.370872	0.574533	3
2.457114	2.686718	2.077536	2.537355	2.735416	1.764817	0.329161	3
1.390182	3.449505	1.922259	2.738923	2.591671	0.9854	1.00846	1
2.120156	2.579095	2.882224	2.725341	2.006488	1.055209	0.117931	3
1.970891	3.700663	1.468186	1.396667	1.40279	2.8171	2.009906	1
2.336216	3.764322	2.473572	2.329863	2.576363	1.084098	1.365232	3
-0.10381	3.389959	2.547536	3.543453	2.283116	2.61914	1.589867	1
1.530012	3.427078	3.194501	2.701941	1.67882	0.968439	1.025129	4
0.857718	3.392356	0.472536	3.279675	2.230862	2.233642	1.218844	1
1.505968	2.621823	1.743091	2.215408	1.95822	2.639966	2.912557	1
0.725015	3.984839	1.182635	3.701695	1.594431	2.084002	1.741048	1
1.473229	3.459439	1.638031	3.406329	1.333691	1.702277	0.560334	2
1.060838	4.181436	2.247993	3.323963	1.172574	1.898132	0.339313	2
2.990401	2.281804	3.070215	3.687298	-0.31184	1.27937	0.285347	2
0.769166	3.840194	2.731756	3.841705	1.747542	2.137993	1.252245	1

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0.75415	3.558579	3.263125	2.647108	1.429326	2.333785	1.492619	1
1.303379	3.795161	1.530871	3.377136	2.072449	1.99248	1.083788	1
0.524407	3.859915	0.853766	3.074975	2.435645	3.317072	2.826819	1
0.12645	3.785307	2.629406	3.674972	1.265829	3.524083	1.271341	2
0.343963	3.983414	2.502811	1.906588	1.645706	0.417935	0.845107	1
1.710316	3.076969	2.060937	1.610017	1.059669	2.128205	0.703361	2
0.417446	3.648473	1.424328	3.711073	2.197958	3.114104	3.181453	1
2.04927	3.750571	1.462268	2.262071	2.189925	2.108657	0.792803	1
0.69803	2.205002	2.111445	2.568238	1.649992	2.488567	2.237445	1
0.951935	2.583197	3.095091	1.735256	2.707042	2.199157	0.645377	1
1.068594	2.818606	1.152625	2.573538	1.774493	3.034217	1.334008	1
1.308397	2.569901	3.080408	2.525086	2.007064	1.700561	0.976378	1
1.712708	2.433669	2.691373	2.580652	1.52399	1.378826	1.194658	3
0.91916	2.37196	2.775352	2.330603	1.599222	2.702074	0.89072	1
0.817149	3.12306	2.784622	2.661203	1.768797	1.560057	1.036902	1
0.791967	2.595179	1.847499	3.263682	2.414274	2.375985	1.818882	1
0.849967	2.071186	2.320527	2.101878	1.589166	3.016033	2.319835	1
1.60647	1.993996	2.891402	2.562998	2.438122	2.625546	1.083263	1
0.942826	2.975032	2.008094	2.730432	1.613834	2.493358	0.169133	2
1.07511	2.919006	2.379194	3.328983	1.773508	2.139629	0.766729	2
1.325045	2.690406	2.595724	1.726559	2.106144	2.474342	0.974182	1
1.411178	2.448139	2.713626	1.825376	2.091093	2.512333	0.987373	1
1.433908	3.131516	2.788815	2.250392	0.990708	2.570261	0.605752	2
0.880346	2.425598	2.678058	1.88785	2.024216	2.640519	1.366953	1
0.260364	2.906487	2.683074	2.969851	2.87145	1.602331	0.491496	1
0.423654	3.974504	2.400218	2.156817	1.89691	1.267873	0.473422	1
0.427651	3.447316	3.1171	2.700789	0.708482	1.333679	0.149171	4
0.579635	3.585689	2.21721	2.667774	2.940801	2.46273	0.537045	1
-0.02029	3.840243	2.522009	2.530284	1.500204	2.86294	0.081363	1
-0.06372	4.230166	3.597157	1.843047	0.983072	1.515249	-0.07676	4
-0.26029	3.873231	3.083164	2.437457	1.954143	1.404252	0.414916	1
-0.09942	2.776442	2.750918	2.707537	3.145203	1.570567	0.377695	1
0.275255	2.768954	4.02854	3.181462	2.991128	2.109993	1.402953	1
0.113402	2.605435	3.763227	2.119889	2.826393	0.865589	0.907433	4
0.149213	2.508363	3.846134	2.298856	2.899768	0.618085	1.543748	4
0.340557	2.541882	3.976928	2.681444	2.89268	1.145417	2.776941	5

-0.22202	2.844312	3.663467	3.049983	2.78542	0.617824	1.919961	4
-0.42178	2.192275	3.690923	2.891726	2.728776	1.202586	1.759638	4
0.457553	2.492178	3.576297	2.309842	2.744103	1.488316	0.765272	4
-0.07661	2.609934	2.688168	3.119072	3.314492	1.011728	2.009197	1
-0.30624	2.770384	3.647785	2.925661	2.651414	1.323014	1.751405	4
0.140752	2.594201	3.258795	3.069871	3.47017	0.903461	0.651931	1
1.494952	2.999964	2.300849	1.995311	1.425531	2.775196	1.773108	1
1.41039	2.949323	2.387595	1.69254	2.185164	2.487053	1.731274	1
1.118924	2.488969	3.415318	2.801899	2.178712	2.20894	1.709332	1
0.680572	3.258869	2.936039	1.918446	2.464094	2.07186	1.309618	1
1.141929	3.06936	2.624611	2.402971	2.363638	2.640456	1.426466	1
0.746483	3.534708	3.054122	2.286824	2.79205	2.205442	1.267024	1
1.011091	3.031657	2.571288	2.223547	2.575557	2.478644	1.656454	1
1.40917	2.33553	2.061849	1.689985	1.99935	1.701782	1.404149	1
0.768691	3.058953	2.917657	1.717871	2.803346	1.933463	1.826406	1
0.623259	3.10424	3.355942	1.998985	2.639103	2.307023	1.329493	1
1.357966	3.236041	1.628006	1.779124	2.009948	2.126546	2.923375	1
2.07341	2.95349	2.752977	0.969581	1.431418	1.74605	0.802422	3
0.792031	2.649246	3.21402	2.835091	2.391127	1.799076	1.483771	1
0.858457	3.130532	3.015193	2.654074	2.640759	1.527418	0.322885	1
0.80738	2.732501	1.65259	2.665072	1.627335	2.728416	2.013305	1
2.121461	3.110723	1.16904	2.698361	2.430201	1.879455	2.229385	1
1.359222	3.174655	1.435069	2.530789	2.244504	2.450394	2.122023	1
0.801118	3.074178	2.997585	3.838252	1.685823	1.335476	0.356832	2
0.080879	2.361793	4.274073	3.686526	2.221517	1.268115	0.479096	4
-0.17235	2.88178	4.48302	3.728202	1.719875	1.135475	0.350021	4
1.761006	2.297744	2.459649	3.053792	1.618949	1.878463	0.104232	2
0.216599	2.173008	3.770535	2.930397	2.304761	1.358994	0.372433	4
0.269085	2.048156	4.424645	2.43455	2.333657	0.970885	0.469465	4
0.065369	2.640117	2.597345	2.581476	2.209659	2.753815	1.558239	1
0.345163	2.569093	3.249664	3.07534	2.493951	1.078831	0.499263	4
0.052513	2.518404	3.110811	3.134081	3.319594	0.871954	0.68042	1
0.30771	3.104776	3.560694	3.132041	2.383767	0.800719	0.482138	4
1.154284	3.557102	1.593781	2.129454	2.591031	2.608611	1.732789	1
3.548581	3.065902	3.364989	2.870269	-0.19792	0.576981	0.807048	3
1.265666	2.865337	3.30641	1.610438	0.737536	0.923749	1.090937	4

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1.399631	3.450565	3.602698	2.993068	1.321121	3.436824	2.859307	2
2.071889	4.124985	2.273219	3.721401	1.332661	2.351524	0.687626	2
0.876012	3.10726	5.157052	2.502289	1.431415	0.674595	1.330972	4
2.349308	2.583863	1.776008	3.662912	2.041628	1.749898	2.531925	5
2.636519	2.334488	2.925445	2.995422	2.243155	2.308253	1.318905	3
2.987487	2.852596	2.434173	2.467237	1.838249	2.755136	1.358205	2
0.81905	1.825397	3.348165	4.522798	1.350309	1.59561	1.848665	5
1.774038	2.862877	2.685874	2.435596	2.107649	1.280506	0.910797	3
2.471096	2.604342	2.691034	2.817636	1.91936	2.006992	1.160133	3
3.060003	2.389687	3.987338	3.677606	1.309749	0.365417	0.614433	3
3.262966	3.396536	4.41932	0.726091	2.244941	0.726714	0.128801	3
2.494411	3.012345	4.550361	1.22457	1.950454	1.090167	0.322092	3
2.079433	2.14239	3.469334	1.070271	2.489137	1.932302	0.438562	3
2.268403	1.873654	4.282994	1.313821	1.418581	2.464574	0.276199	3
3.08802	1.748826	4.565023	-0.33519	2.055988	2.092309	0.217988	3
2.777448	1.078595	4.10723	2.455113	1.397793	2.134951	0.741937	3
3.102757	1.592921	3.055213	1.054164	2.005069	1.878598	0.214148	3
3.479759	1.33687	3.174094	1.2196	2.175686	2.51985	-0.06827	3
0.623457	2.841408	1.295385	3.855206	2.838636	3.356909	2.354045	1
1.847572	3.354191	3.861348	3.103105	0.405502	2.467452	1.557334	2
2.32006	2.266582	2.220428	2.264085	0.940936	1.327739	1.041959	3
2.959903	2.952272	3.331057	3.012319	0.19202	1.653348	0.098445	2
1.703666	4.825642	2.81377	-0.18771	1.279538	0.122421	0.405711	3
0.475181	2.03538	3.124756	3.793217	2.522743	3.14862	3.03574	5
2.204704	4.680761	3.398592	-0.06387	1.459862	0.056371	0.729264	3
2.002607	2.755353	3.376209	0.036351	1.407113	0.555023	2.247859	3
0.907119	1.708706	4.912416	2.140988	1.922985	2.28953	1.116472	4
1.825809	2.128214	4.741464	0.159796	1.636236	2.063124	0.352333	3
0.153648	2.889437	2.800667	0.352795	2.08095	2.082555	1.234468	1
0.587994	3.861874	2.269366	1.68284	1.605637	1.89417	0.802835	1
1.024508	3.664618	2.874202	0.661802	1.556209	1.204374	0.130695	3
0.283041	3.817617	2.288075	1.913851	1.877978	1.808863	1.815715	1
0.311823	3.273917	2.51415	3.816218	1.458316	2.762033	2.043699	1
0.718942	4.25634	4.459668	2.072599	1.638075	0.100716	1.716839	4
0.008545	2.195237	3.234108	2.99666	2.548574	1.681762	2.171549	1
-0.47133	4.246083	1.528641	2.336485	0.732913	3.646783	-0.41321	2

1.077048	4.530622	3.141172	1.851634	0.845131	1.322201	-0.08585	2
1.705065	3.239689	4.050878	1.401745	0.04819	0.238856	0.758254	4
2.025447	3.033307	2.675933	2.113983	1.52901	0.942658	2.129124	3
0.244751	4.092002	3.424906	1.330836	2.236125	0.876376	0.474374	4
0.151119	2.98758	3.568751	1.451563	1.656526	1.805595	1.468168	4
-0.24368	2.750309	3.5265	1.860395	1.715834	0.987104	1.895436	4
2.648074	3.621529	3.486606	2.933279	0.373718	2.709986	-0.22809	2
2.066586	3.066316	3.580333	2.246909	1.180946	1.055538	0.656804	3
1.944425	1.998555	3.567294	2.594938	1.536046	2.975502	0.613735	2
1.121274	2.724664	2.638417	2.486761	2.431015	2.384841	1.565011	1
2.850815	1.654452	3.992092	2.263066	2.418238	1.276869	1.221492	3
0.684173	2.59755	4.093945	1.046064	3.083327	0.362483	1.38296	4
0.174206	3.493588	3.316332	1.816635	2.951768	0.969128	0.733653	1
1.860815	1.680196	2.476973	1.941281	1.753742	1.344025	1.426395	3
1.752092	2.024168	2.66644	1.898802	1.6596	1.209577	1.477241	3
1.321311	2.063387	2.163432	2.908879	1.330973	1.88362	2.361532	5
1.647948	2.270076	1.86041	1.867999	1.454386	1.969179	2.568774	5
1.325019	2.361829	1.478412	2.266887	1.764518	2.642484	1.702186	1
1.088055	2.85659	2.246922	2.880238	1.555623	1.051089	1.817443	1
1.062752	2.864692	2.06805	2.854408	1.648133	1.414439	1.940907	1
1.898748	2.937805	2.14582	2.108399	1.533958	0.926171	1.734107	3
1.164505	3.039528	2.132053	2.855484	1.416871	1.0435	2.152127	1
1.217726	2.459069	2.369937	2.894859	1.596448	1.29165	1.294127	1
1.205169	2.99523	2.238958	2.69529	1.1099	1.645469	0.920897	2
2.247636	1.559871	2.359851	2.345988	0.75245	2.326831	2.011774	2
0.515809	3.209018	2.974778	0.088037	0.354395	2.184264	0.377669	4
2.664913	2.258446	2.453266	2.835131	0.94236	1.093029	1.450462	3
2.332702	2.904314	2.102263	3.80914	4.423846	2.545838	2.19781	1
0.858277	2.789032	2.675953	3.975471	2.940192	3.199923	1.756495	1
0.135326	3.130819	1.787072	3.322858	3.569177	3.067827	1.901571	1
0.210271	2.715819	3.337833	3.945324	2.118081	3.089931	2.290278	1
-0.10692	3.305084	3.883783	3.738765	2.271649	1.095572	2.372052	4
2.940514	2.045527	1.655645	3.337987	2.325931	1.995342	2.523698	5
0.017031	3.471114	2.781549	3.449273	3.063424	1.982684	2.810396	1
0.217045	3.102494	2.257095	3.712236	3.227408	2.424947	2.706707	1
1.168394	3.158382	2.397039	2.875788	3.195214	1.667232	2.237079	1

2.166365	2.328856	3.406558	3.882285	2.341709	1.610299	1.985158	5
1.207266	3.701287	3.536277	2.471503	2.445392	1.455107	1.94385	1
0.350961	3.216452	3.756608	3.369897	2.633468	1.71541	1.968044	1
2.142924	3.021736	4.265552	2.12064	0.265916	2.962148	1.455148	2
0.33667	1.944071	2.455792	1.119593	2.806737	2.954146	1.19752	1
-0.37456	4.684672	1.857995	2.673432	2.43409	1.675507	0.615034	1
-0.45765	2.951242	3.57413	2.673064	2.310049	1.494068	1.204785	4
2.241543	3.295219	1.761795	-0.46674	2.062207	0.658954	3.085202	3
2.274352	3.904877	0.965383	1.090103	2.177539	1.008027	1.615303	3
0.542086	1.246405	4.771957	2.932708	1.626256	0.35913	2.19558	4
1.405164	4.017422	2.502021	2.645762	2.199201	0.974838	1.105484	1
1.596445	2.820486	2.350912	1.453811	3.042025	1.647329	1.921859	1
-0.10552	2.818759	2.971996	3.080708	1.907297	0.083147	0.823936	4
-0.32487	3.260904	3.534991	2.253789	0.849691	0.516675	1.967281	4
-0.1682	2.358753	3.087227	0.986124	3.435746	2.779199	2.729604	1
2.247645	4.286214	0.019446	3.584856	2.068911	1.866873	0.807345	2
0.47302	1.446077	0.663542	3.750715	1.414859	3.605458	1.93925	1
-0.59701	1.675585	3.925224	1.716529	2.459564	3.219338	0.880136	4
0.861698	3.040857	2.553108	1.336346	1.43595	1.136466	0.604058	4
0.957117	2.787028	3.658154	0.801289	-0.61602	1.330431	0.835537	4
0.124301	2.421105	2.705534	2.460809	1.797187	2.180488	1.753949	1
1.006473	1.997175	1.029746	2.796541	2.776268	0.984417	2.779216	5
0.366053	2.322168	4.060788	1.559525	1.519204	0.253499	2.169938	4
1.583427	3.27796	2.562148	1.507864	2.014645	0.852825	2.43981	3
0.751172	3.492416	4.487172	2.507872	1.848005	0.476099	2.176782	4
0.859564	2.121968	3.57061	2.07186	1.694885	2.381739	1.771004	4
1.150281	2.229375	3.993247	1.538726	1.713609	1.263208	2.984529	4
1.009329	2.523104	3.632711	1.751953	2.49709	0.747835	1.973844	4
0.800092	2.313618	1.947549	2.129778	2.779523	2.736547	1.287074	1
0.507842	2.126182	3.709382	2.025182	2.014483	2.499448	1.949562	4
1.707627	1.784648	3.412401	2.081609	1.543876	1.982379	2.252024	5
1.520279	2.053032	3.102355	2.341057	1.547812	1.045763	2.045449	5
2.051176	1.709775	3.481137	1.391418	1.709236	1.635493	3.759327	5
0.911119	1.734922	3.484695	1.986006	2.121027	3.065789	1.925379	1
1.401215	1.524107	2.979994	1.938822	2.037472	0.806494	2.666591	5
1.082589	1.594227	3.461005	1.861188	2.047426	1.824083	2.205309	5

0.782273	1.504928	3.980124	1.198786	2.167906	1.904642	2.458123	4
1.130089	1.618194	3.558431	1.84232	1.224004	2.513945	1.961609	4
0.777959	2.330444	4.134831	2.302482	1.573921	1.895572	1.789862	4
1.708766	1.298943	2.563442	2.053514	2.096883	1.721538	2.927518	5
1.154063	2.688875	2.425242	2.718147	2.253345	1.159137	1.198447	1
0.809999	1.599301	2.619081	2.243507	1.198234	2.379065	3.111126	5
1.98482	1.356919	3.401547	2.87027	2.888688	0.917695	1.559026	5
2.623055	0.067936	2.551413	1.795425	2.420002	0.685113	3.023309	5
0.104503	0.941991	2.736113	4.900371	2.223849	2.112671	1.511158	5
1.397307	0.341324	2.840602	2.29184	2.505188	0.169115	3.259495	5
1.270621	0.496461	2.746452	2.312243	3.044293	0.303743	3.174375	5
2.274565	0.005369	2.76484	2.662452	2.414838	0.887809	2.310469	5
0.086942	2.180963	2.659627	3.723745	-0.4808	2.794365	2.358254	2
2.554201	2.382038	2.613128	2.197507	2.622773	0.417857	2.937588	5
0.665437	-0.15309	3.013491	3.591409	2.397752	0.910813	3.196063	5
0.219131	0.988948	2.949241	2.832939	2.812933	1.931909	2.337423	5
0.08191	1.904748	2.697057	2.395814	2.909281	0.849056	1.816543	1
-0.5757	2.364009	3.812397	1.903619	2.952605	1.246934	2.699965	4
0.281395	2.412998	4.491506	1.717264	1.527465	0.20048	1.743169	4
-0.37792	0.853802	3.500635	4.447944	1.770293	2.376319	2.945239	5
1.43101	1.729342	2.285234	3.594539	2.158406	1.41163	2.35083	5
2.242448	0.452776	2.03011	2.175292	2.960922	0.892266	3.490946	5
0.772287	1.044562	4.099495	2.099755	2.303216	-0.07957	3.408013	5
1.687683	0.705034	3.483106	3.50241	0.084663	1.296573	1.360677	4
0.08152	2.497989	2.633608	2.102286	1.992036	2.405288	2.854927	1
0.564148	0.290457	1.858481	3.457962	2.040157	2.621054	4.093532	5
1.432265	2.214134	2.28557	2.447828	3.114609	1.697488	0.560871	1
1.22986	4.209676	4.152368	1.648818	2.4148	1.380472	3.982964	1
1.798733	2.321707	1.944999	2.484884	2.09713	2.497045	3.945049	5
1.548915	2.98621	2.419907	4.166224	1.884883	3.007174	1.354243	2
1.736698	2.102224	2.781879	2.624937	1.287076	1.154947	2.066471	5
1.841468	2.779364	2.014616	1.952026	1.864021	0.832871	2.831117	5
1.850788	3.557185	1.247119	2.762191	2.367131	2.073187	2.334656	1
1.988117	1.848378	1.617975	3.235807	3.561746	0.849005	3.282251	5
2.963195	1.875433	2.294584	2.090209	1.373802	0.773446	1.733781	3
1.280458	3.577684	3.18186	2.344035	3.374431	2.15427	2.751256	1

0.884161	5.784644	3.534264	1.819497	2.386301	3.77747	0.141682	1
0.074259	3.574523	1.619785	2.533091	0.988846	2.903029	2.823716	1
3.04004	2.314318	2.13163	1.6602	1.868691	0.651936	2.527277	3
2.717961	1.981777	1.938336	2.53088	2.20996	0.227048	1.92194	3
1.469363	2.818761	1.884582	2.648021	2.089939	2.410461	1.996118	1
2.709623	2.493832	1.025723	2.408424	3.062117	3.46406	1.106719	1
2.161146	1.174376	2.314965	2.254531	3.234909	1.291243	2.520153	5
2.287607	1.838934	1.818019	2.927362	2.361122	0.866097	2.034928	5
3.353594	3.559703	2.04658	2.406643	-0.54042	0.195315	0.023831	3
1.392493	2.078828	2.6005	1.897844	2.84124	0.383242	0.947499	3
1.725897	3.336555	1.507295	1.7479	3.54761	2.859758	2.606246	1
1.2252	3.287465	2.245327	2.208732	1.496208	2.975495	2.753529	1
1.518102	2.010543	2.173446	2.299928	2.45509	2.839368	2.859943	5
1.289588	3.386302	4.211413	2.154531	1.303094	0.481756	2.964039	4
1.012439	4.384014	3.35423	2.879892	0.911968	4.236695	1.938896	2
-0.18313	2.332953	2.817455	2.991674	1.413407	2.469997	1.751645	1
-0.50824	2.851968	3.078299	3.017893	1.511157	3.204069	1.452336	1
2.015306	1.892684	3.122085	2.005002	1.28295	1.431305	2.252795	3
1.810405	2.313179	2.719985	2.289299	1.433045	1.995691	2.279748	5
-0.36417	2.441534	4.741204	2.029903	2.179041	1.560313	1.344052	4
1.612228	3.39865	3.771511	2.523235	1.798751	1.338797	1.638589	4
0.498329	2.028352	3.80679	2.242893	1.021459	2.388737	1.175935	4
-0.18434	2.373169	3.690509	2.559589	2.106675	1.890076	2.149593	4
1.521238	2.119707	2.963294	1.800389	1.566119	1.958181	0.758386	3
3.747659	1.227065	2.861703	2.434098	1.443798	2.781314	2.597393	5
-0.4823	1.90793	3.373967	2.878178	2.004723	3.40478	2.332985	1
0.899904	4.377078	2.276759	2.487403	0.184471	1.761139	0.685288	2
1.801516	3.019131	3.060307	2.431625	1.409738	1.490599	0.428911	2
0.524149	2.633798	3.796815	1.644169	0.667038	1.265146	1.836087	4
2.832446	3.170785	1.759903	1.961723	1.444286	1.823112	1.105778	3
-0.07634	2.224685	3.774898	3.031975	-0.1915	1.917331	1.714644	4
-0.00896	3.683818	3.356392	2.308612	1.307789	3.677818	0.323892	2
1.756645	2.94947	3.107809	2.888338	0.822709	3.959166	1.271949	2
2.132132	2.038671	2.938456	2.077305	1.016538	1.692268	1.867374	3
2.027801	2.090666	3.044967	2.391921	1.466157	2.999378	1.451428	2
2.365434	0.881948	2.909211	2.874983	1.970898	2.364969	2.719813	5

1.951106	1.417047	3.499015	3.274452	1.057297	1.360355	2.54604	5
1.155816	1.648827	3.136144	3.231095	1.479935	2.61277	2.369647	5
1.771195	1.978266	2.468392	2.849778	1.952468	2.637186	2.539566	5
2.175577	0.957878	1.749733	4.318935	2.408992	2.347051	3.083741	5
1.730574	1.460436	2.355927	2.801036	2.458172	2.805657	3.037723	5
1.625811	1.123879	2.555173	2.98834	1.932035	2.598875	3.107223	5
1.300338	1.27347	2.863889	2.670251	2.788495	2.009867	4.144211	5
1.058618	1.640886	3.14455	3.155436	1.597802	1.754571	2.858831	5
1.714292	1.198592	2.361832	3.655121	2.911294	2.190251	2.968629	5
1.240011	1.509991	2.984057	1.286569	2.708608	1.855332	3.967645	5
1.152672	1.764461	2.576472	2.889279	2.721701	1.695326	2.606245	5
1.255709	1.355849	2.521385	2.856854	2.597104	1.876426	3.207666	5
0.74156	1.575887	3.573962	3.438606	3.075308	2.406598	2.848083	5
1.487389	2.083264	1.877643	2.610233	2.580977	2.734694	3.221042	5
1.02402	0.666849	3.200515	3.967067	2.679366	2.374665	3.865079	5
0.904672	0.738232	2.490656	2.403095	2.3109	1.981781	2.503543	5
1.97023	1.764496	2.422681	3.936467	1.939548	2.512576	3.901476	5
2.676331	1.08356	3.41355	3.33541	0.698102	2.519931	3.287986	5
2.614462	4.775062	3.793557	-0.19917	-0.981	0.09312	1.252973	3
0.092529	2.213861	1.666891	3.141264	2.591698	3.012315	1.884515	1
0.62021	3.504931	2.630801	1.965301	1.737083	2.335864	1.035281	1
-0.10889	2.970387	2.077207	2.483217	2.67454	2.810844	2.125511	1
-0.28494	2.862408	4.948831	1.475156	1.273039	0.024325	2.188301	4
0.141229	1.826175	2.57906	3.825405	2.331338	2.178282	3.733651	5
-0.27393	1.798164	2.281096	1.096077	3.405163	2.22112	2.368599	1
1.889118	2.197416	2.662556	0.938291	1.45778	1.768633	1.850104	3
2.026809	1.43333	2.852578	2.062381	2.494402	2.510134	1.003418	3
0.4547	1.822873	1.642994	1.648994	2.465097	2.307406	2.260072	1
1.180574	1.979456	2.190599	0.638097	1.822171	1.684538	1.976499	1
-0.15376	2.113963	2.755861	2.31101	2.417009	2.151042	2.155638	1
2.937327	0.559019	3.293035	1.705683	1.755515	1.537882	2.362831	5
0.356661	2.212595	2.084012	1.942391	2.012923	1.77337	1.492639	1
1.257337	1.708001	1.806124	1.843787	2.280795	1.967791	2.486759	5
1.302175	2.292117	3.27532	2.309357	0.828285	1.952833	1.783675	4
1.714566	2.866174	2.614927	1.165569	2.346443	-0.46207	1.580056	3
2.336772	1.820066	2.107818	2.778122	2.028988	1.729201	2.644071	5

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-0.531	1.905626	2.663749	4.288357	2.308736	3.089625	4.707173	5
1.955097	2.75595	1.720104	1.485425	2.439215	0.383829	2.150109	3
0.424371	2.775628	2.618747	3.105367	1.291942	1.385739	1.814535	1
2.682818	1.975018	3.091693	2.359624	2.077224	1.058987	2.189526	3
1.640291	2.201269	3.686279	2.493968	3.027828	0.383334	1.950114	5
1.962298	2.543239	1.478078	2.839681	0.880412	1.964117	2.524755	2
1.518659	3.192809	2.697412	1.905137	2.597932	-0.15954	2.23207	3
1.834275	1.687792	3.803747	2.399916	1.433644	0.562578	1.025609	4
1.540272	1.983626	2.956717	3.394021	1.800051	1.677738	0.662117	2
1.509981	2.642669	3.116794	1.549859	1.938711	1.855646	1.954819	3
2.134296	1.907773	2.690553	3.23495	1.495158	0.775124	1.619342	3
0.427512	2.987253	2.561937	2.27099	1.3845	2.114721	0.565118	1
1.466702	2.301835	2.37308	2.599048	2.254712	1.407731	1.813743	1
1.027552	1.923318	3.15668	3.298839	1.721175	1.344687	1.461926	4
2.925279	2.151205	3.252401	2.148987	1.787043	1.139834	1.406604	3
1.803615	0.897055	2.381724	4.027319	0.612286	2.102622	0.497539	2
0.501035	1.594727	3.748318	3.202126	2.717837	1.217422	2.0056	5
1.135913	2.46013	2.699918	2.040346	1.05604	2.40855	1.437545	2
1.47729	1.576555	2.766053	2.486893	3.088382	0.238345	2.288514	5
2.322109	1.8903	1.856853	3.043669	1.448824	1.854425	2.292022	5
0.943979	2.865445	2.334755	2.361299	1.84453	1.57974	1.455633	1
1.09441	2.61972	2.570202	2.266813	0.822919	1.006511	1.137528	4
1.446558	2.894173	3.720822	2.312959	2.573729	1.242164	1.410237	4
0.736881	2.07327	3.906554	3.063998	1.881051	1.369881	0.160261	4
0.665234	2.183043	2.941374	2.995214	1.14126	3.139709	0.670783	2
1.431209	2.102447	2.877089	3.272383	1.528063	1.667444	0.597345	2
0.48805	2.199462	2.791748	3.053477	1.218693	3.241743	0.81835	2
1.729035	2.60887	2.382874	2.946179	1.154216	2.539631	0.705188	2
0.923982	2.09841	3.134973	3.049035	1.577602	2.226752	0.562968	2
0.473393	1.823634	2.603832	3.244876	2.472785	2.388323	0.70335	1
0.643718	3.162341	2.628687	3.124583	0.697315	3.489079	0.444281	2
1.231598	1.489925	2.575601	2.956323	1.393692	3.056498	2.419777	5
0.885313	3.604693	2.334157	2.907145	1.783189	2.383189	0.473879	2
1.486663	2.382557	2.521454	3.405304	0.122165	2.458242	1.897779	2
1.305746	2.536706	2.503103	2.726279	1.370371	2.271897	0.760181	2
-0.12128	2.931554	2.985789	3.448854	2.373757	3.0748	0.750214	1

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-0.3651	3.29011	2.870149	3.014172	0.790517	3.231845	1.216384	1
1.310901	2.905656	3.206514	2.745517	2.308938	2.328841	1.60868	1
0.8192	2.058696	3.311621	2.910875	2.063997	2.20247	1.529922	1
1.579844	2.31691	1.764519	2.700399	1.475303	3.338388	1.799588	2
1.650651	1.172353	2.25335	2.336537	1.40992	2.091142	1.840565	5
2.400323	0.610945	2.145213	1.814261	2.156261	2.594137	1.989301	5
1.337072	1.787411	2.435036	2.180727	1.476423	1.703351	2.390161	5
1.334314	3.493188	3.203095	0.739232	2.752471	1.577154	1.506409	3
2.395664	1.784892	2.990832	1.597801	3.454405	1.431834	2.221238	5
2.834376	1.372208	2.467716	1.487558	2.422688	2.178153	2.292664	5
1.271013	2.190323	2.02582	1.854061	2.466391	2.423069	2.725961	1
0.129491	1.944993	3.627968	1.689957	1.382203	2.063105	2.376668	4
0.915972	2.036587	2.390177	2.812893	1.865705	1.996444	1.482858	1
-0.29183	2.254987	2.829684	2.300647	0.747438	3.259114	1.744497	1
0.234823	3.984334	2.709338	3.583035	0.06296	3.288988	0.717452	2
-0.03279	1.956234	3.73337	2.42477	1.51287	1.496175	2.24365	4
-0.22374	3.954465	4.147648	3.000342	2.095893	1.375367	0.174058	4
4.446452	3.112146	3.834213	-0.56448	2.322335	0.081094	0.815274	3
0.254195	2.219487	2.347961	1.5985	2.939996	1.619148	2.003347	1
0.722066	1.84351	3.439109	3.028911	0.858413	2.820346	2.055325	4
-0.27786	1.621398	3.810628	3.493549	1.61931	2.388291	1.959439	4
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1.197751	1.139765	2.959802	3.724448	2.00368	1.870335	3.248781	5
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0.435803	0.030049	2.99525	5.212456	3.600696	2.278578	3.051625	5
0.896986	2.123555	1.956048	3.483763	3.273525	1.450855	1.995661	1
1.727307	1.314198	3.995778	4.880579	3.018966	2.337371	2.479633	5
1.007479	1.779471	4.011855	3.485044	1.019926	0.992437	0.427342	4
1.133501	3.612282	3.371249	4.166631	0.783912	2.980189	0.390786	2
0.447813	1.584168	4.595198	4.146647	1.49147	1.118816	2.154007	4

1.36141	0.164857	4.184602	4.615451	0.680796	2.828915	2.215485	5
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0.2899	2.425688	2.527741	1.688038	2.859624	1.102273	1.363903	1
0.012578	2.713523	2.772004	1.695502	2.556442	1.490683	1.172728	1
0.457526	2.242863	2.640553	1.38489	2.9747	1.112302	1.723175	1
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0.439565	3.695894	3.233887	3.19461	-0.65113	2.981872	0.096498	2
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2.046115	1.860467	4.503206	1.44212	0.944814	0.960159	1.702708	4
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2.838667	1.587802	3.139398	2.455651	1.986433	1.559845	2.010168	3
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3.333304	1.738452	3.145411	1.694157	2.436078	0.861111	2.058184	3
2.809199	2.201564	3.268227	2.439596	2.217548	2.20399	0.443276	3
3.232019	2.695417	3.21763	1.39774	1.641224	1.386497	0.029767	3
2.562955	1.649742	4.191257	1.75234	3.416616	0.008248	0.947485	3
2.653311	2.213077	2.654112	1.964367	0.998636	3.271016	3.047206	5
4.088227	3.519633	1.458443	1.578193	0.700923	2.177483	3.025567	3
1.621409	1.437943	3.781382	2.457539	0.583088	1.380606	1.395895	4

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2.902669	2.219219	2.532083	1.780608	1.705037	1.497211	1.210752	3
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1.784393	3.483958	1.901055	2.434483	0.562683	3.044089	0.828156	2
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3.346217	1.09885	4.812988	1.455227	0.212139	1.128825	1.865715	3
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3.557233	1.908423	3.907425	3.378859	0.393898	1.68292	1.077381	3
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1.154398	2.149252	1.965355	2.992882	1.978235	3.127639	0.860784	1
0.688774	2.974488	1.694827	3.193321	2.122084	3.338055	1.028929	1
1.131356	2.409504	3.316011	4.297027	-0.46325	1.780486	0.505052	2
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2.083689	3.657652	2.921747	3.583169	-0.01864	2.614121	-0.05174	2
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1.125582	2.252314	3.475507	3.005104	1.493761	0.598888	1.6825	4
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4.088323	4.086708	1.203542	3.401486	1.006494	1.889707	1.626608	2
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0.630253	2.095562	4.612635	3.10251	0.403171	0.586135	1.524354	4
1.172078	3.404195	2.258	4.688623	0.018005	3.749981	0.113934	2
4.007734	4.416939	3.65958	2.156696	1.668164	2.136666	-0.46751	3
1.868898	3.149336	2.275342	3.520585	0.30994	2.832434	1.386088	2
0.780472	3.074664	2.209664	2.923805	1.234535	3.130313	0.715847	2
4.848926	2.952455	3.823995	0.591641	1.587537	2.18594	-0.83412	3

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1.211911	3.276599	1.160352	3.7608	0.172588	3.302692	0.900316	2
1.345695	4.407982	2.247066	3.577123	1.592001	1.564087	2.094433	1
1.224475	3.147634	2.941942	3.798999	1.535248	2.344394	1.478652	2
3.814597	3.334847	3.097241	4.383301	1.594088	3.575003	2.193627	2
2.618453	3.317255	1.941214	3.630248	2.69847	3.52205	2.648051	1
1.294275	1.56371	3.043611	2.412047	2.498057	1.647309	1.693621	5
0.789672	3.383044	3.337881	3.451955	2.680502	1.791768	-0.33461	1
5.565368	3.181652	3.711348	1.365467	3.165442	0.633596	1.577293	3
0.669129	2.118351	2.117884	2.709941	1.785749	2.353919	1.396308	1
2.122874	2.370528	4.039168	0.044906	1.404239	0.054061	1.210217	3
-0.31367	1.429249	3.608487	3.153238	3.435385	2.595252	1.562	1
2.998431	3.071495	3.935008	-0.03663	1.493068	-0.0469	0.969036	3
1.208636	1.198679	3.797957	1.94229	3.154749	1.181498	1.587801	5
1.238483	2.984314	4.102558	1.020331	1.746735	0.210602	0.596202	4
0.721211	2.570974	4.789879	1.510915	0.470652	0.495575	0.773934	4
2.182478	2.318548	4.180739	2.217635	1.400813	1.181345	1.366411	3
4.973196	1.25845	3.181555	1.930606	1.754247	0.502145	0.808431	3
1.299859	3.358898	2.963783	2.996693	1.210242	2.837687	2.661287	1
1.721604	4.747844	2.938984	3.246941	0.280358	1.577821	-0.18553	2
2.151246	2.475189	2.327683	1.99312	0.50071	1.478181	2.367488	3
-0.52803	2.946022	3.74577	3.453622	1.366665	1.530891	2.898386	4
2.520474	2.840891	4.605005	2.492233	1.505935	0.933693	1.547949	3
1.953568	4.710961	2.059415	3.21843	0.404182	2.072298	-0.48158	2
0.67322	2.059827	3.378463	3.263051	1.593942	1.411997	3.478853	5
0.482849	1.669846	5.337114	3.92286	0.857681	2.098765	1.276031	4
1.436908	3.006341	2.111445	3.63576	1.17833	2.696489	-0.03468	2
-0.16469	3.037464	2.593747	2.19126	1.150814	1.183965	2.885273	1
3.098244	2.591925	4.55368	2.771836	0.409717	4.100465	1.1617	2
0.287138	2.638836	3.863141	2.410391	1.952481	0.480413	3.121472	4
0.88184	3.625722	4.892386	0.792852	-0.38779	0.599907	0.319505	4
2.150267	2.531001	1.798742	1.734505	2.569138	1.474977	1.943503	3
0.080232	1.944229	2.89941	3.091852	1.297553	1.130481	1.479588	4
1.307558	3.242025	3.928579	0.550179	0.489302	-0.2167	1.569607	4
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0.452287	4.095796	2.938024	2.755959	1.197267	1.736364	1.48946	1
0.333146	3.491975	2.998474	2.348185	2.863105	2.005441	1.99996	1

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1.27648	2.71056	3.416199	3.573639	1.124956	2.475951	1.110492	2
1.071622	0.058392	4.1753	3.035761	3.147516	0.463041	3.434267	5
0.767058	2.902141	2.81539	1.046366	3.481824	2.314722	3.456745	1
3.199205	1.794078	3.094138	0.666184	2.680831	0.969656	3.012809	3
0.381606	1.855712	2.180899	2.28543	2.69681	2.129198	3.061778	5
1.199252	1.771864	3.210781	2.048203	2.117378	1.37389	2.377955	5
0.91132	1.981741	2.199601	2.419341	2.215353	2.0596	2.989397	5
1.465285	2.997421	3.137443	1.03661	2.101259	0.412757	0.556006	3
1.445957	2.331573	1.916218	2.899514	1.818489	2.843057	2.654736	1
2.190434	2.781964	2.697725	2.215768	1.935821	3.086303	2.382583	1
3.060515	2.893715	3.843192	1.274351	2.77693	1.999967	1.625444	3
3.43918	4.685975	2.511207	0.606142	2.48964	0.899216	2.126643	3
2.248858	3.078349	2.536622	1.289691	2.240462	3.084218	2.519339	1
3.37998	3.32946	4.457823	2.144631	1.21309	0.40427	0.75011	3
1.485575	0.653133	3.573337	1.804786	2.614735	1.700206	2.294768	5
-0.11639	1.697496	3.894954	1.163997	2.803677	1.62084	3.170209	5
0.265337	0.794674	3.483188	3.196532	2.270673	0.733305	3.105335	5
0.487467	2.134018	3.509739	2.158815	1.670326	3.086941	1.766996	1
1.785974	2.325783	3.97547	1.09789	1.533602	0.00662	0.661087	3
2.199662	1.043731	3.230455	1.471481	1.594108	0.196087	1.699968	3
0.432774	0.473242	3.749216	2.000787	2.260527	2.0028	2.936089	5
-0.03225	1.823518	3.460935	2.026709	2.073493	1.822957	2.199521	4
2.922641	1.912792	2.869191	1.92473	2.23171	1.463312	1.771086	3
1.95851	2.620691	3.209711	2.40885	2.167502	1.410435	0.780651	3
1.673373	3.1535	3.384783	2.665686	2.386609	3.045046	1.306632	1
2.052142	2.801713	3.616672	2.376778	2.198514	2.571284	2.109671	1
2.398755	2.656117	3.599123	2.113145	1.85368	1.955369	1.029531	3
1.600749	2.772373	2.97559	2.356207	2.179088	2.727056	2.963031	1
2.407436	2.876793	3.588069	2.349736	2.603454	1.472847	1.481762	3
1.477092	2.367975	3.279323	3.706314	2.496294	1.970748	2.027569	5
2.117032	3.129461	3.33882	2.353723	1.303854	3.213898	2.046513	2
0.862852	1.787891	4.693773	3.920364	1.536504	1.598562	0.812846	4
2.124976	2.522997	2.142115	2.017715	1.329319	1.353485	2.01721	3
2.053942	1.282666	2.60817	2.173067	1.883355	1.446771	1.932743	5
1.051968	1.351924	2.743535	2.133289	2.15663	1.277404	1.947453	5

1.711215	1.470019	2.419263	1.720749	1.882597	1.273467	2.368535	5
2.929092	1.337477	2.249875	2.137536	0.784348	1.365049	2.001452	3
1.158983	1.4628	2.915975	1.823459	1.509886	0.551248	2.793893	5
2.091268	1.750324	3.37735	1.24898	0.459163	1.414763	2.315137	3
2.076045	1.774582	2.512304	2.256736	1.866886	1.14936	2.611307	5
0.888772	2.398703	2.96251	3.053851	0.409217	0.752585	2.749108	4
1.385868	2.726663	4.786969	1.926702	-0.29151	1.447619	0.300511	4
1.573504	1.385677	2.765509	1.797339	2.803497	0.70662	1.886113	5
1.36709	2.250416	2.120969	3.156059	0.953453	0.834286	0.332707	2
1.83963	1.020248	2.261243	3.005754	1.931713	0.376005	1.855818	5
1.601561	1.25261	2.891928	2.486944	1.195034	1.634183	1.888287	5
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2.273433	1.691484	4.048696	2.607554	3.589263	1.255111	0.435131	3
2.088968	1.147388	2.211211	2.663832	2.513624	1.159295	2.510907	5
1.671819	1.377036	3.442522	3.119088	2.535569	0.140997	2.209565	5
0.655599	2.044898	3.029	2.970167	1.316146	2.118602	2.10233	4
1.85728	0.119835	2.531109	2.346743	1.542376	2.049295	3.632266	5
0.810013	0.519835	2.208672	2.690966	1.793883	2.252788	3.340709	5
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0.912099	0.843401	3.863282	1.466242	1.900905	1.511621	3.068371	5
0.717642	1.816272	2.257425	3.060543	1.17801	1.755652	3.457668	5
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1.405381	2.577678	4.286141	1.980834	2.432689	-0.09613	1.148452	4
1.567328	2.933253	3.513708	2.585126	1.043179	-0.13341	2.420696	4
0.654842	2.497284	3.603089	3.237035	1.70472	1.099211	1.797649	4
1.512999	0.611854	2.683634	2.169291	2.81694	1.732635	3.711279	5
1.750541	0.9083	3.874494	4.076287	-0.0004	3.253308	1.558526	2
3.554138	3.798572	3.92936	3.171349	1.134508	-0.27824	2.674967	3
1.843493	2.035074	1.975868	1.991719	2.417606	0.563503	2.469965	5
1.717436	2.392262	3.051026	2.060343	2.753362	1.495397	3.641729	5
-0.42161	4.174919	2.381554	3.388356	0.438055	3.444924	1.033751	2
1.763247	1.821026	3.455334	0.63166	3.032002	1.410237	2.909767	5
1.676444	2.552671	2.604784	0.875316	1.878914	-0.17302	2.688803	3
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0.95825	2.322112	2.79394	1.357469	2.849933	1.464401	1.685897	1
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0.576465	1.683357	3.679851	3.021204	2.972976	2.905107	2.180476	5
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1.992158	1.887124	2.751854	4.05701	2.787676	3.611463	1.616108	1
2.188311	1.67236	3.624552	2.120629	2.385157	-0.40732	2.290743	3
1.103505	3.213246	3.56517	1.335934	2.322979	2.073316	2.533389	1
1.172266	1.179647	3.3055	0.938081	2.639	3.333973	2.398904	5
0.946777	1.12983	3.224024	2.29541	2.958102	2.775739	1.638153	5
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1.191219	1.61463	2.640179	2.097072	2.463071	2.923712	2.126753	5
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0.99619	1.012696	1.960564	3.89922	2.166986	3.011827	2.011537	5
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2.510542	2.017149	2.234838	3.722974	3.594265	1.538423	4.527227	5
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3.639972	2.296478	1.151978	4.058536	3.114612	3.240043	1.390437	2
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1.588088	1.83981	1.621011	2.296312	2.576374	1.595488	3.050562	5
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0.906972	2.341611	3.474023	3.766265	1.319244	2.054854	0.849818	2
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1.280015	2.513557	2.225763	1.868445	1.739776	1.374607	1.782267	1
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1.446411	3.638014	2.57226	2.162072	2.791145	2.57307	1.488721	1
1.167265	2.626558	2.203502	2.296486	1.842762	2.90644	1.855448	1
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1.40074	1.014476	4.221012	2.082268	2.397258	1.566852	2.246523	5
3.364591	1.251376	3.290845	2.500423	2.222562	2.499598	1.64981	3
2.129269	2.710131	2.313439	3.013249	3.038706	2.468915	1.469671	1
3.640786	2.112478	2.740796	2.354109	1.865754	1.397937	0.737311	3
1.421128	1.717524	3.14217	3.412806	1.643833	2.767619	1.014461	2
3.634259	3.829661	2.455371	1.544377	1.340034	3.256891	2.485461	3
2.697317	2.840325	2.636191	2.10339	1.209549	2.466469	1.862657	3
2.125605	1.718318	2.887255	2.48321	2.397532	1.066204	2.379777	5
3.792892	2.650793	2.764114	1.400925	1.851319	2.681576	2.986922	3
2.072001	3.045846	3.962105	2.177186	2.573999	0.25015	0.832666	3
3.47285	2.593043	2.890262	3.791422	0.974418	0.107865	1.905316	3
3.442853	2.49001	3.917911	2.182262	1.331236	0.624292	0.56678	3
2.219969	2.735774	2.653031	1.323758	1.209602	2.197175	1.866327	3
3.544702	2.323891	2.279193	1.803041	1.570909	2.167078	2.118647	3
3.420414	1.926201	3.185597	0.632802	0.632656	1.50262	1.384866	3
3.209916	2.705199	3.627112	1.981629	2.297275	1.142996	1.049544	3
3.048556	2.6651	3.121058	2.043578	1.409733	1.083988	0.612292	3
2.713898	2.765805	2.622923	3.012792	2.375676	2.068843	1.575362	3
2.443942	2.666966	2.428546	0.891082	0.771637	2.603498	1.684131	3
2.905297	3.397697	2.938849	1.225181	1.163792	1.690736	1.431206	3
3.593219	4.593676	2.85064	2.031216	0.486013	2.463427	1.85159	2
2.102827	2.396113	2.513477	3.23259	0.053848	0.624753	1.872851	2
1.064304	1.898978	2.016754	3.140289	0.964322	2.533744	1.1192	2
2.444071	2.783835	4.013843	2.538264	-0.99133	1.913701	1.514094	2
0.597051	2.841435	3.260321	2.331223	2.770425	1.762876	1.657292	1
1.277791	1.224479	4.027602	2.223094	1.528438	1.553553	1.985067	4
2.544969	1.139785	3.265251	2.26823	-0.46458	2.591822	0.882637	2
1.825547	1.669443	3.223452	3.179786	-0.42529	1.875906	1.452051	2
2.962217	3.600508	5.143498	1.353762	0.671814	0.235175	0.560646	3
1.456116	2.008452	4.33278	2.854759	0.605656	0.405156	2.166573	4

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0.626556	3.945301	3.324774	2.371494	-0.03127	1.118954	0.265501	4
-0.31383	2.113856	2.59672	1.908942	1.667484	2.524643	2.408832	1
1.228335	1.387955	5.154633	1.452413	1.155377	0.786883	1.862063	4
1.25387	2.254079	4.47892	1.999785	1.359129	0.771985	2.204713	4
2.077432	1.663845	5.072246	2.79507	-0.51169	0.56814	0.610627	4
0.599443	1.280542	4.815207	2.746904	1.803925	0.649366	2.415114	4
0.598819	1.589002	4.750287	3.058779	1.458149	1.533219	1.688224	4
0.931227	2.847927	4.160636	2.13367	0.982232	1.452196	1.729529	4
0.316014	1.483445	5.063682	1.620782	1.363688	0.744981	2.184789	4
1.805851	0.751263	4.905275	2.126935	0.927103	0.411213	1.870546	4
1.817658	1.874295	3.402797	2.738788	0.632739	3.089684	0.283125	2
2.080507	1.479588	3.698097	2.018675	1.102444	3.123037	0.499457	2
2.155577	1.737956	3.83843	2.286946	1.14978	2.696318	0.43201	2
1.608477	1.801606	3.90294	2.616016	0.307342	3.013917	0.867098	2
2.281242	0.685045	2.986646	2.985925	1.546753	3.087632	0.720522	2
2.214117	0.65798	3.986178	2.320973	1.01724	3.012481	0.405324	2
0.781439	0.915361	4.091384	2.741706	1.203266	2.853794	0.715125	4
1.727043	2.106237	3.150811	3.001749	0.701208	2.788492	0.486409	2
1.728331	1.779813	3.270322	2.618096	0.884794	3.065053	0.971797	2
1.749562	1.403262	3.229064	3.006373	1.472604	2.900566	0.640564	2
0.679291	1.950655	4.747832	2.835375	0.382722	2.499583	0.591783	4
1.147152	1.826271	4.035526	2.320126	-0.02238	3.159645	0.731292	2
1.941818	2.082537	2.989712	2.260192	-0.00818	2.787371	1.151937	2
1.249031	1.527114	4.299129	2.535885	-0.5818	2.879486	0.525447	2
1.19344	1.077144	4.43854	2.214834	1.010501	3.005332	0.498575	4
1.38946	2.086965	3.925157	2.506738	0.61587	2.518739	0.56424	4
1.877671	2.377552	3.591046	2.443115	-0.60871	2.798473	0.648804	2
2.957277	2.94879	2.629078	2.712291	2.437214	2.745738	2.306572	3
2.992108	2.599115	2.293851	3.124804	2.015908	3.133204	2.268303	2
3.921003	3.011791	1.363058	2.752717	2.051352	2.988232	2.550854	2
1.728135	3.382881	2.602387	3.073562	1.122538	2.970503	0.769473	2
0.89866	3.708311	3.08077	2.230172	1.323137	1.21315	0.775188	4
0.108157	3.703654	4.751098	2.833147	1.226326	1.494066	0.657168	4
0.949288	3.908633	4.21671	2.584499	1.12431	2.357137	1.324043	4
1.685074	3.335918	4.22883	2.169423	1.972558	2.209607	1.534274	4
2.355394	2.924333	3.329398	1.851904	1.452708	1.768292	1.320825	3

1.392201	2.646019	3.262224	3.078521	1.380314	2.171287	1.551109	2
1.872292	2.807496	3.365211	2.991789	1.430271	1.604211	1.31471	2
4.06007	1.952389	4.366534	2.666384	0.004945	2.058869	1.022499	3
2.515136	3.582175	3.164015	2.511792	0.303662	2.456513	1.106662	2
2.353872	2.84456	3.277328	3.030188	0.686356	1.732787	1.083689	2
3.092874	2.935414	3.090189	3.004494	0.234085	1.989451	0.991129	2
2.985002	3.046288	3.149261	2.913923	0.221522	2.037312	0.911563	2
2.991006	3.1423	3.128822	2.930944	0.71372	1.97819	0.9461	2
2.498692	3.030364	3.712698	3.228355	0.051874	2.453515	0.868749	2
2.932435	3.234334	3.266269	3.874878	1.708321	0.299856	2.488879	3
3.732834	3.443928	4.925664	2.483556	-0.84478	1.269878	-0.24187	2
2.764755	1.765644	4.289369	5.662817	1.16513	2.814028	1.745695	2
3.089919	3.356786	4.52097	0.52877	1.356926	0.340221	0.917349	3
2.476432	2.565019	4.555364	2.821781	-0.36831	1.590714	0.438113	2
2.910139	4.087892	3.980479	1.786325	-0.66089	0.481637	0.032882	3
3.135612	4.630961	3.628399	3.051233	-1.17422	0.352569	0.381981	2
2.872695	3.720954	4.51504	3.199279	-0.98896	1.381106	0.015064	2
2.089671	2.377447	6.417695	0.828802	1.741449	0.852393	0.681979	4
1.288354	2.713286	5.504821	0.619534	1.160781	1.224874	0.05934	4
2.068221	2.422813	6.131995	0.715511	2.167848	1.25567	0.822885	4
1.624061	3.815175	6.237579	2.066145	-1.00305	2.208537	0.277069	4
2.445324	3.714635	5.837543	0.946298	-0.31739	1.034344	0.393447	4
1.445021	2.958948	2.395126	3.098661	2.870223	0.928077	0.090669	1
2.375642	2.68096	2.183977	3.157854	2.235614	1.306861	0.393268	3
1.505374	2.723895	3.330147	2.767737	3.015288	0.696092	0.640706	3
1.567687	2.888448	2.295104	3.176463	3.193394	1.005992	0.495985	1
2.912557	2.523757	1.949625	3.107942	2.987511	1.188252	0.531214	3
1.851181	3.069879	2.227234	3.15	2.626483	1.087311	0.423944	1
2.377584	2.854885	1.961183	2.925096	3.283892	1.388586	1.156093	3
1.467044	2.694963	3.178889	2.979329	2.500077	1.289893	1.388323	1
1.415615	2.35197	2.874528	3.014931	2.432711	1.772328	0.987868	1
2.030281	2.431548	2.221421	3.091684	2.478228	1.352556	0.871416	3
2.553599	4.262361	1.874516	2.474586	2.511507	2.529192	0.508671	2
3.185728	3.696322	1.49651	3.046902	2.934443	2.880074	0.135186	2
2.850695	3.55922	2.511403	2.548477	2.859269	2.493715	0.459517	3
3.577836	3.580969	1.643502	2.802134	2.574489	1.719936	0.253408	3

2.958074	3.415299	2.264899	2.677293	2.42812	2.083265	0.589096	3
3.087259	3.61867	2.115313	3.326557	3.243235	1.954775	0.300382	3
2.751739	3.585996	2.497658	3.382737	2.407784	1.805826	0.848883	2
3.0043	3.158151	2.642835	2.811435	3.556004	2.073591	0.192526	3
2.70127	3.29477	2.061836	3.531687	2.321305	2.139039	0.260408	2
2.866981	3.461092	2.503888	3.076605	2.320136	2.322889	0.164261	2
3.02909	3.796378	1.622972	3.100696	2.428454	2.112373	0.302758	2
1.832561	3.035723	2.92606	3.152572	1.969182	1.66836	2.027277	1
0.391172	3.724756	1.959737	2.563242	2.126821	1.498965	0.513307	1
0.537508	3.205037	1.664459	3.411925	1.951163	2.136093	1.881294	1
-0.03323	3.496502	1.921167	2.296864	2.092613	1.947697	1.894757	1
-0.28869	3.535061	3.032781	1.687279	2.179816	1.986136	3.189025	1
0.043266	3.098997	2.935675	2.583162	0.79795	1.274482	1.279583	4
0.111472	3.729742	3.438625	3.315709	1.270037	1.351169	0.323621	4
1.824843	2.878876	2.439134	3.205687	2.056859	1.26008	0.245724	2
-0.34372	3.260611	1.669527	2.611259	2.802661	1.975953	1.996848	1
0.929042	4.229001	0.958476	1.837791	2.345441	0.85991	0.266006	1
0.835028	4.094564	1.624835	3.745215	0.676649	1.596787	0.633265	2
0.518017	3.482631	0.026971	3.232487	2.585949	1.714216	1.247258	1
2.142077	2.763266	1.717985	2.132657	1.981876	1.682524	1.359786	3
1.163136	2.278781	2.040656	1.66038	2.28934	2.245927	2.48422	1
1.773945	1.815762	2.296841	2.241036	2.003111	2.440107	2.329185	5
0.370864	1.828904	3.135938	1.977168	1.213476	1.233708	2.011518	4
1.286832	2.260544	3.247904	2.244789	1.087078	2.409808	1.666524	4
0.665569	2.919365	2.218953	2.267884	1.69468	1.892542	1.390264	1
0.499638	1.950232	2.077153	2.111414	2.362764	2.243769	2.65479	1
1.813017	3.779611	3.381505	1.889955	2.499938	1.561516	0.468737	3
0.397136	4.680782	2.396155	3.188569	3.35778	3.188256	1.316963	1
1.019573	2.844814	3.271878	1.693419	1.576868	2.980728	1.484369	1
-0.12102	2.640397	1.937596	2.509998	2.081944	2.465172	1.921706	1
0.52094	4.365047	0.079631	3.39627	0.649761	3.180026	0.097283	2
2.731117	3.182713	2.077638	3.00734	2.583772	1.26684	0.103849	3
1.771354	3.13086	2.349316	1.061821	2.445899	2.343069	1.002997	1
2.059941	3.055221	2.663597	1.88279	2.215695	1.325664	0.702866	3
1.303168	2.959174	2.820694	2.397158	2.033969	1.579769	2.122712	1
2.429935	2.785714	1.96915	1.688699	2.165227	2.253247	1.325774	3

0.891107	2.804571	3.191638	2.048713	1.508145	1.19412	1.88979	4
1.907596	2.544843	1.657253	2.422589	1.154796	1.183471	1.661215	3
2.385735	3.027558	1.489701	1.884331	0.99354	1.180347	1.127258	3
1.251581	3.68027	2.711777	2.1435	1.619374	1.509578	0.333364	2
0.798065	3.178204	1.337118	2.323722	1.813707	1.180386	0.886322	1
2.252769	3.452674	2.544877	4.622918	-0.07422	2.354946	0.115854	2
0.583991	1.996347	3.522147	2.550794	2.507082	2.036728	2.388671	5
-0.13509	2.898338	2.444281	2.521597	1.825635	2.888208	1.921385	1
-0.36838	2.995744	3.441612	2.97643	1.572292	2.68975	1.238128	1
-0.30352	3.100945	3.418419	1.915066	2.18415	2.148555	2.157188	1
1.244294	3.111563	2.930995	1.059978	0.847236	1.804209	0.909519	4
-0.14236	1.646401	3.496471	1.485099	1.650087	0.930843	2.037234	4
1.19828	2.207907	2.349218	1.552053	1.722359	1.499779	1.598663	1
0.38149	3.928541	1.372957	2.687336	1.838206	2.154214	0.524778	1
2.481611	3.481827	2.197603	2.130881	1.476809	2.260437	1.234254	2
0.481608	2.39286	2.337152	1.8301	3.06498	1.393734	2.654131	1
2.037414	2.085096	1.496653	2.455538	3.879859	1.623686	2.888888	5
1.550216	3.153218	1.742108	1.904519	1.712383	1.807038	1.351736	1
1.648021	2.673175	1.638725	3.046737	1.692765	2.351428	1.857887	1
1.374126	2.435089	2.234815	2.18588	1.898093	2.19479	0.889646	1
1.019342	2.647679	2.648263	2.498198	1.115062	0.804325	2.647109	4
2.736435	0.551078	3.752571	1.417281	1.549031	0.691697	3.033024	5
1.076616	4.06708	2.069281	1.842046	1.935288	1.900541	2.868004	1
1.33195	2.484582	2.416758	2.379112	1.760003	3.692732	0.736447	2
2.77427	3.355737	2.304729	1.78513	0.741504	2.762615	1.853789	2
1.110734	3.632882	3.21394	1.776796	1.612268	0.850391	0.641557	4
2.389185	2.881695	1.795131	3.20699	0.41942	3.494308	1.27316	2
0.730482	2.662928	2.413819	2.880268	1.47977	2.413753	1.470869	1
1.544426	3.943903	2.727814	1.735903	0.3283	1.153388	0.127138	2
1.279774	1.859157	2.630356	2.828011	0.364033	1.515973	1.979112	4
1.793325	3.012943	1.797364	3.337012	0.706964	2.779247	1.325387	2
2.238936	3.999729	2.426756	1.92557	2.32772	3.174616	1.094697	2
1.328915	2.584895	2.436472	2.695512	0.404388	2.423566	0.966932	2
0.949881	2.271697	2.870003	1.331377	3.139382	1.581926	2.831327	5
1.447089	4.561358	2.758321	1.890039	1.155236	2.090646	-0.24765	2
1.559906	3.743831	2.957692	2.926744	0.70788	3.029807	1.492514	2

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0.037952	2.623521	2.977699	2.60586	1.7889	1.516554	1.752384	1
0.544136	2.470642	3.054143	1.796674	2.630448	1.995703	1.006744	1
1.103825	2.393463	3.065722	1.774394	2.428612	1.982995	0.895501	1
1.399663	2.370678	3.102827	1.824285	1.496074	2.043118	0.86195	4
0.897121	2.54747	3.141174	1.854219	1.595786	2.011652	0.804589	4
1.201974	2.640957	2.332992	2.627714	2.533396	2.930975	1.314934	1
1.363306	2.722	2.897964	1.712665	1.587274	2.16176	0.545037	2
0.723609	3.782392	3.074652	2.64536	2.840634	1.366008	0.711355	1
0.719305	3.75657	2.379346	3.293745	1.618362	3.079174	0.353328	2
0.328069	3.287281	2.131284	2.691661	1.991577	1.488309	0.506056	1
-0.64046	2.981621	2.625653	2.987986	1.415446	2.682281	2.372283	1
0.787829	3.43195	2.429392	3.333081	1.33786	2.979558	0.795472	2
0.227007	3.521006	2.724771	3.137629	0.03393	2.165901	0.06169	2
-0.40163	3.609939	2.626096	3.870232	-0.36079	2.958831	0.209338	2
1.965187	3.49462	2.311837	3.878262	-0.49392	1.852627	-0.02262	2
1.791554	2.700887	2.96369	2.574842	1.361732	1.22905	0.905313	3
0.592842	2.498902	3.325384	1.998149	2.970382	1.484991	2.433574	1
0.93449	3.04107	3.092865	3.005954	3.044192	1.088331	1.023012	1
0.003281	2.687613	3.929499	2.543304	2.892851	2.191037	3.148313	1
1.068601	3.440496	2.803361	2.066853	2.684096	1.392016	0.972695	1
0.253151	3.366974	3.134181	2.849601	1.98879	1.665742	1.794241	1
0.568625	2.599822	3.489269	2.403426	2.2514	1.457632	1.842686	4
0.00812	2.891183	3.527231	2.837727	2.056235	2.082804	1.521558	1
0.032748	2.470632	2.393383	2.203077	2.552633	2.522461	3.323862	1
0.542252	2.924785	2.188542	1.648248	1.714741	2.188392	2.210163	1
0.489436	2.782794	2.799251	2.348694	2.562243	2.045669	2.597358	1
0.598497	3.537035	2.270759	1.885296	2.640754	1.931446	1.9822	1
2.684479	4.627392	1.323444	2.104489	3.085864	1.524276	4.186668	1
0.655399	2.42486	2.702211	1.692073	2.686051	2.115035	1.992235	1
1.00012	2.63573	1.946578	1.927783	2.474008	2.149825	2.785688	1
0.803679	2.576829	1.90842	2.733659	2.142713	2.062206	2.425543	1
1.362799	2.747179	1.705736	1.951721	2.795911	2.423492	1.966459	1
0.963135	3.36129	1.576244	2.275032	2.391988	1.914535	2.548146	1
0.957478	3.325917	2.675156	2.401962	0.999558	1.423449	0.931414	2
0.847499	2.932603	2.498088	1.810525	2.707284	2.590633	2.0517	1
1.234055	2.177802	2.697905	2.809799	2.466852	1.403281	2.495561	5

2.015017	3.586158	1.209095	0.797506	1.692396	1.815927	1.146375	3
1.555804	2.938869	1.394756	0.825921	2.281687	1.885865	1.503032	1
1.919184	2.652597	2.006072	1.579702	1.47809	1.927411	1.892786	3
1.164025	3.354408	1.683151	2.741454	2.56621	1.453452	2.74602	1
0.86959	2.681597	1.65861	2.77981	2.819379	1.416855	2.724348	1
1.043517	2.337804	1.855299	2.055885	2.697255	1.476669	2.311822	1
2.083676	4.361556	1.724352	2.17223	2.581234	2.50454	1.35888	1
2.615128	3.571862	0.682013	3.528703	2.241834	3.449389	2.821293	1
2.085683	3.602037	1.088369	2.923386	2.205792	2.28507	2.979874	1
1.898764	3.276854	1.77007	2.506758	1.517037	2.607894	1.089812	2
2.5278	2.059308	1.713481	3.124673	1.225085	3.026174	3.025545	5
2.864402	3.013686	1.637174	1.573196	2.441859	1.623372	1.120725	3
2.072019	3.282316	0.870472	2.358488	2.208217	2.802844	1.730093	1
1.63954	3.096221	2.814322	2.561726	2.063223	1.377709	1.451547	1
2.309299	3.454196	1.661915	2.559652	1.830277	1.966368	0.014157	2
0.72982	2.395892	2.585869	2.750007	2.132678	2.026769	1.971763	1
2.549466	3.574283	2.038015	3.583879	1.986217	2.118853	0.140961	2
2.083922	3.433225	1.320953	2.441424	2.589508	2.780382	1.209729	1
1.293829	3.273937	1.462928	2.817106	1.721652	3.104604	2.554968	1
1.195288	3.769418	1.210908	2.98681	1.044027	2.749903	0.60132	2
2.061813	2.704437	2.316068	2.554463	2.553281	3.014762	2.00189	1
2.468648	2.98751	2.060243	3.21991	1.330698	2.781815	2.311667	2
0.936901	2.780699	1.501068	3.119347	1.893182	1.345022	1.445776	1
2.096261	3.729782	2.528279	2.942293	2.272058	1.668373	0.184038	2
-0.06866	2.323305	2.466225	3.008179	2.310103	1.806849	1.758138	1
2.600323	1.57889	2.767321	2.701491	1.678983	0.431804	0.746914	3
1.904414	1.941858	2.790823	1.733361	1.862784	0.627279	1.648438	3
1.596553	2.69657	2.367887	2.664833	1.633339	1.978123	0.121749	2
1.07667	1.205244	2.672278	1.959053	2.384767	1.783993	3.279252	5
1.595228	3.077974	2.380944	2.815531	1.774421	1.243553	0.373183	2
3.05165	1.742192	3.165878	2.403648	1.464842	0.801114	0.72373	3
2.207574	2.570317	1.919201	3.671462	-0.20097	2.181307	0.583058	2
1.136287	2.834087	3.186852	2.882391	1.934227	0.932035	1.06899	4
3.138606	1.675005	3.392111	2.846753	0.800305	1.366669	0.36267	3
3.006056	1.788769	2.430313	2.210938	2.343229	0.8086	1.471998	3
3.301842	2.534269	2.727616	1.645315	2.297743	1.398658	0.504945	3

1.045698	3.34271	2.926759	2.671772	-0.54325	3.05828	1.151877	2
1.474318	3.49987	3.358005	2.668088	-0.34163	0.727697	0.198376	2
1.418577	3.540259	1.859501	1.848117	0.758087	1.62029	1.178268	2
1.792042	3.571176	2.781245	2.623082	2.059251	2.687523	0.663873	2
2.246787	3.973687	2.288619	2.616655	0.964431	2.932953	0.383798	2
2.557149	3.009742	3.015698	2.63141	1.263235	2.701192	0.65265	2
2.406639	2.86216	2.747641	2.887785	2.069158	2.148691	0.371257	2
2.144278	3.008093	3.211825	4.019281	0.030605	2.866497	0.860084	2
2.555363	2.579017	3.075949	2.0346	2.256304	2.102979	0.446911	3
2.53739	3.435742	2.628374	3.319847	1.749244	2.053878	1.172975	2
2.645764	3.632515	2.547884	2.116629	2.961363	2.525557	0.751793	3
2.167688	3.177878	2.822987	2.693744	2.104781	2.348668	0.571723	2
1.225418	2.761464	2.284974	2.906629	1.555919	2.234763	1.344509	1
2.549378	1.883245	4.847159	-0.38613	2.328991	0.399031	0.899669	3
0.835491	3.410214	3.238864	2.174315	1.569618	3.313993	1.048845	1
0.197072	3.720005	3.210243	1.462301	1.715089	3.289458	0.349891	1
0.956348	1.634326	4.496375	2.859105	1.713968	2.541391	0.572134	4
2.710831	2.895985	4.542081	1.117162	1.602833	0.638402	1.605333	3
0.468519	2.775847	4.793864	1.572114	2.577669	2.142251	0.374559	4
0.801185	3.856247	4.476053	1.102946	1.665504	2.180561	1.051688	4
1.396774	2.38184	3.159023	2.272422	1.642917	2.218226	0.494604	2
1.029972	1.815946	3.624451	2.805185	1.766394	1.950249	0.557906	4
2.351785	2.454701	1.492669	4.377274	1.452214	3.421769	1.610619	2
2.32405	3.466859	1.816886	2.125494	2.298043	2.802006	1.772149	1
1.22715	2.873227	2.457041	2.742809	1.886899	1.460491	1.371267	1
1.281567	3.046454	2.498313	1.471574	2.914418	2.038731	1.977465	1
0.288136	1.74727	3.931425	2.686452	2.618377	2.564444	2.479821	5
2.522687	2.759939	1.745555	1.6985	2.060347	0.322064	1.304326	3
0.543637	2.544981	3.348045	1.906861	2.258307	1.031273	1.44175	4
1.620347	3.401088	2.574342	-0.41533	2.252736	0.219513	1.438078	3
1.842942	3.37822	2.328411	1.420737	2.466913	0.174455	2.317012	3
0.948361	3.600731	3.023847	2.142095	2.757594	0.861544	1.1149	1
1.868794	3.629237	1.867504	3.675692	1.405051	3.091689	0.902801	2
0.109365	3.572819	2.384525	2.616362	1.429333	1.794456	1.190442	1
2.186493	1.83317	2.188746	1.631281	2.02835	1.133724	2.584236	5
-0.19669	3.080497	2.427698	1.772721	1.871182	2.58294	1.963527	1

1.045365	3.084264	2.502615	1.233211	2.190984	1.398955	2.304011	1
0.498219	3.184056	3.006726	1.873029	1.272331	2.277158	2.527363	1
0.064184	3.279553	2.142248	1.683496	2.028901	1.967967	2.81393	1
1.294706	3.528197	2.401889	2.620905	1.628489	2.505685	1.915161	1
1.237893	4.214992	3.247795	1.255129	1.727378	1.922664	1.535637	1
0.895371	2.295853	2.195042	3.304022	1.494507	2.228977	1.607169	1
-0.15976	2.294287	3.693329	1.853443	2.346265	2.371389	1.889254	4
0.765196	3.619231	3.406026	2.56884	1.039612	2.176356	1.173186	2
0.040116	2.078193	3.350767	1.54803	2.515734	2.492502	1.961021	1
-0.01981	2.391736	2.677275	2.01822	2.822933	2.111246	2.320911	1
2.137868	3.088558	2.695161	1.66284	2.394352	1.829432	2.164855	3
2.081211	1.547291	3.061405	1.85112	1.647561	2.145304	1.606017	3
2.045868	2.033077	4.076113	2.57444	2.231006	2.358381	2.016695	5
1.758938	3.006452	2.01326	0.699399	3.04425	1.384979	0.665989	3
1.237003	2.523978	2.330382	2.049435	1.997275	1.271707	0.498445	1
0.667497	2.718609	2.958894	1.611983	2.782766	2.031715	2.059987	1
2.0786	2.254637	2.013767	2.860412	1.253703	2.580455	1.367255	2
1.137981	2.2767	2.173088	2.474196	1.543822	2.78904	1.474368	1
0.83508	2.375671	2.923106	2.319775	1.112637	1.568078	1.782344	4
1.532628	2.452578	4.199479	2.184313	1.28271	1.39555	1.30231	4
2.832667	3.229237	2.248558	5.046877	-0.14981	3.168044	0.514728	2
2.804329	3.544024	3.281753	1.443864	0.979548	1.515588	2.244697	3
4.176895	3.853278	3.442913	3.436163	-0.20598	1.787425	0.697663	2
1.447793	1.661014	4.651958	1.638069	0.705343	1.763816	0.192127	4
0.837814	3.230974	2.320599	3.009408	0.461031	2.905844	1.343623	2
1.802944	1.716569	3.558995	2.552908	0.4513	2.238213	-0.50813	2
0.957177	1.475594	3.511604	2.462799	0.950496	1.55846	1.053852	4
1.767879	2.111048	3.558412	1.886744	-0.32273	1.971333	-0.18521	2
0.567263	0.795808	2.30941	2.196065	2.747347	1.982559	2.3133	5
1.47234	2.608456	2.826792	2.398996	1.022706	2.533647	0.7236	2
1.025226	2.719732	2.423171	2.797212	2.343007	2.681939	1.803731	1
1.665459	0.517428	3.510286	1.925527	2.679155	2.339655	2.32634	5
0.626203	3.278759	4.570286	1.802226	1.454045	0.984405	1.873493	4
0.989795	3.025333	2.064807	1.322011	2.195479	2.639946	1.743527	1
0.748755	2.27195	2.717904	3.103542	2.114782	3.677446	1.694106	1
-0.54808	3.454881	2.794786	0.243503	2.598806	2.136147	2.934898	1

1.73608	2.049779	2.363716	2.801236	2.019415	1.639227	1.9725	5
2.540272	3.227549	3.596597	2.319795	1.413479	2.179313	0.192601	2
4.283287	3.240125	2.663105	2.760057	0.818601	1.64212	1.574151	3
1.391141	2.810916	2.450279	2.953166	2.210613	2.323273	1.154374	1

APPENDIX 13. IDENTIFICATION OF EXACERBATION OF THE UNDERLYING ILLNESS OF SCHIZOPHRENIA

Psychosis and psychotic disorders (SMQ)

English	Code	Level	Scope	Category	Weight	Status	Addition Version	Last Modified Version
Acute psychosis	10001022	PT	Narrow	A	0	Active	10.1	10.1
Alcoholic psychosis	10001632	PT	Narrow	A	0	Active	10.1	10.1
Alice in wonderland syndrome	10001666	PT	Narrow	A	0	Active	10.1	10.1
Brief psychotic disorder with marked stressors	10048549	PT	Narrow	A	0	Active	10.1	10.1
Brief psychotic disorder without marked stressors	10056395	PT	Narrow	A	0	Active	10.1	10.1
Brief psychotic disorder, with postpartum onset	10006362	PT	Narrow	A	0	Active	10.1	10.1
Charles Bonnet syndrome	10063354	PT	Narrow	A	0	Active	10.1	10.1
Childhood psychosis	10061040	PT	Narrow	A	0	Active	10.1	10.1
Clang associations	10009232	PT	Narrow	A	0	Active	10.1	10.1
Cotard's syndrome	10059591	PT	Narrow	A	0	Active	10.1	10.1
Delusion	10012239	PT	Narrow	A	0	Active	10.1	10.1
Delusion of grandeur	10012241	PT	Narrow	A	0	Active	10.1	10.1
Delusion of reference	10012244	PT	Narrow	A	0	Active	10.1	10.1
Delusion of replacement	10012245	PT	Narrow	A	0	Active	10.1	10.1
Delusional disorder, erotomanic type	10012249	PT	Narrow	A	0	Active	10.1	10.1
Delusional disorder, grandiose type	10012250	PT	Narrow	A	0	Active	10.1	10.1
Delusional disorder, jealous type	10012251	PT	Narrow	A	0	Active	10.1	10.1
Delusional disorder, mixed type	10012252	PT	Narrow	A	0	Active	10.1	10.1
Delusional disorder, persecutory type	10053195	PT	Narrow	A	0	Active	10.1	10.1
Delusional disorder, somatic type	10012254	PT	Narrow	A	0	Active	10.1	10.1
Delusional disorder, unspecified type	10012255	PT	Narrow	A	0	Active	10.1	10.1
Delusional perception	10012258	PT	Narrow	A	0	Active	10.1	10.1
Dementia of the Alzheimer's type, with delusions	10012295	PT	Narrow	A	0	Active	10.1	10.1
Depressive delusion	10063033	PT	Narrow	A	0	Active	10.1	10.1

Derailment	10012411	PT	Narrow	A	0	Active	10.1	10.1
Epileptic psychosis	10059232	PT	Narrow	A	0	Active	10.1	10.1
Erotomanic delusion	10015134	PT	Narrow	A	0	Active	10.1	10.1
Flight of ideas	10016777	PT	Narrow	A	0	Active	10.1	10.1
Hallucination	10019063	PT	Narrow	A	0	Active	10.1	10.1
Hallucination, auditory	10019070	PT	Narrow	A	0	Active	10.1	10.1
Hallucination, gustatory	10019071	PT	Narrow	A	0	Active	10.1	10.1
Hallucination, olfactory	10019072	PT	Narrow	A	0	Active	10.1	10.1
Hallucination, synaesthetic	10062824	PT	Narrow	A	0	Active	10.1	10.1
Hallucination, tactile	10019074	PT	Narrow	A	0	Active	10.1	10.1
Hallucination, visual	10019075	PT	Narrow	A	0	Active	10.1	10.1
Hallucinations, mixed	10019079	PT	Narrow	A	0	Active	10.1	10.1
Hypnagogic hallucination	10020927	PT	Narrow	A	0	Active	10.1	10.1
Hypnopompic hallucination	10020928	PT	Narrow	A	0	Active	10.1	10.1
Hysterical psychosis	10062645	PT	Narrow	A	0	Active	10.1	10.1
Ideas of reference	10021212	PT	Narrow	A	0	Active	10.1	10.1
Illusion	10021403	PT	Narrow	A	0	Active	10.1	10.1
Jealous delusion	10023164	PT	Narrow	A	0	Active	10.1	10.1
Loose associations	10024825	PT	Narrow	A	0	Active	10.1	10.1
Mixed delusion	10076429	PT	Narrow	A	0	Active	18.0	18.0
Neologism	10028916	PT	Narrow	A	0	Active	10.1	10.1
Neuroleptic-induced deficit syndrome	10075295	PT	Narrow	A	0	Active	17.1	17.1
Paranoia	10033864	PT	Narrow	A	0	Active	10.1	10.1
Paranoid personality disorder	10033869	PT	Narrow	A	0	Active	10.1	10.1
Parkinson's disease psychosis	10074835	PT	Narrow	A	0	Active	17.0	17.0
Paroxysmal perceptual alteration	10063117	PT	Narrow	A	0	Active	10.1	10.1
Persecutory delusion	10034702	PT	Narrow	A	0	Active	10.1	10.1
Postictal psychosis	10070669	PT	Narrow	A	0	Active	13.1	13.1
Post-injection delirium sedation syndrome	10072851	PT	Narrow	A	0	Active	16.0	16.0
Posturing	10036437	PT	Narrow	A	0	Active	10.1	10.1
Psychosis postoperative	10065617	PT	Narrow	A	0	Active	10.1	10.1
Psychotic behaviour	10037249	PT	Narrow	A	0	Active	10.1	10.1
Psychotic disorder	10061920	PT	Narrow	A	0	Active	10.1	10.1
Psychotic disorder due to a general medical condition	10061921	PT	Narrow	A	0	Active	10.1	10.1
Reactive psychosis	10053632	PT	Narrow	A	0	Active	10.1	10.1
Rebound psychosis	10074833	PT	Narrow	A	0	Active	17.0	17.0

Schizoaffective disorder	10039621	PT	Narrow	A	0	Active	10.1	10.1
Schizoaffective disorder bipolar type	10068889	PT	Narrow	A	0	Active	12.0	12.0
Schizoaffective disorder depressive type	10068890	PT	Narrow	A	0	Active	12.0	12.0
Schizophrenia	10039626	PT	Narrow	A	0	Active	10.1	10.1
Schizophreniform disorder	10039647	PT	Narrow	A	0	Active	10.1	10.1
Schizotypal personality disorder	10039651	PT	Narrow	A	0	Active	10.1	10.1
Senile psychosis	10039987	PT	Narrow	A	0	Active	10.1	10.1
Shared psychotic disorder	10040535	PT	Narrow	A	0	Active	10.1	10.1
Somatic delusion	10041317	PT	Narrow	A	0	Active	10.1	10.1
Somatic hallucination	10062684	PT	Narrow	A	0	Active	10.1	10.1
Substance-induced psychotic disorder	10072388	PT	Narrow	A	0	Active	15.0	15.0
Tangentiality	10043114	PT	Narrow	A	0	Active	10.1	10.1
Thought blocking	10043495	PT	Narrow	A	0	Active	10.1	10.1
Thought broadcasting	10052214	PT	Narrow	A	0	Active	10.1	10.1
Thought insertion	10043496	PT	Narrow	A	0	Active	10.1	10.1
Thought withdrawal	10043497	PT	Narrow	A	0	Active	10.1	10.1
Transient psychosis	10056326	PT	Narrow	A	0	Active	10.1	10.1
Waxy flexibility	10047853	PT	Narrow	A	0	Active	10.1	10.1
Abnormal behaviour	10061422	PT	Broad	A	0	Active	10.1	10.1
Abulia	10050013	PT	Broad	A	0	Active	10.1	10.1
Affect lability	10054196	PT	Broad	A	0	Active	10.1	10.1
Affective ambivalence	10077173	PT	Broad	A	0	Active	18.1	18.1
Affective disorder	10001443	PT	Broad	A	0	Active	10.1	10.1
Alcohol withdrawal syndrome	10053164	PT	Broad	A	0	Active	10.1	10.1
Anosognosia	10068346	PT	Broad	A	0	Active	11.1	11.1
Apathy	10002942	PT	Broad	A	0	Active	10.1	10.1
Asocial behaviour	10003472	PT	Broad	A	0	Active	10.1	10.1
Behaviour disorder	10004207	PT	Broad	A	0	Active	10.1	22.0
Bipolar I disorder	10004939	PT	Broad	A	0	Active	10.1	10.1
Blunted affect	10005885	PT	Broad	A	0	Active	10.1	10.1
Bradyphrenia	10050012	PT	Broad	A	0	Active	10.1	10.1
Catatonia	10007776	PT	Broad	A	0	Active	10.1	10.1
Constricted affect	10010778	PT	Broad	A	0	Active	10.1	10.1
Disorganised speech	10076227	PT	Broad	A	0	Active	18.0	18.0
Dyslogia	10054940	PT	Broad	A	0	Active	10.1	10.1
Echolalia	10014127	PT	Broad	A	0	Active	10.1	10.1
Echopraxia	10014128	PT	Broad	A	0	Active	10.1	10.1

Emotional poverty	10014557	PT	Broad	A	0	Active	14.0	14.0
Flat affect	10016759	PT	Broad	A	0	Active	10.1	10.1
Grandiosity	10018671	PT	Broad	A	0	Active	10.1	10.1
Hypomania	10021030	PT	Broad	A	0	Active	10.1	10.1
Idioglossia	10068366	PT	Broad	A	0	Active	11.1	11.1
Illogical thinking	10021402	PT	Broad	A	0	Active	10.1	10.1
Impaired reasoning	10071176	PT	Broad	A	0	Active	14.0	14.0
Inappropriate affect	10021588	PT	Broad	A	0	Active	10.1	10.1
Incoherent	10021630	PT	Broad	A	0	Active	10.1	10.1
Intrusive thoughts	10077275	PT	Broad	A	0	Active	19.0	19.0
Lack of spontaneous speech	10023615	PT	Broad	A	0	Active	10.1	10.1
Logorrhoea	10024796	PT	Broad	A	0	Active	10.1	10.1
Magical thinking	10025429	PT	Broad	A	0	Active	10.1	10.1
Major depression	10057840	PT	Broad	A	0	Active	10.1	10.1
Malignant catatonia	10080149	PT	Broad	A	0	Active	20.1	20.1
Mania	10026749	PT	Broad	A	0	Active	10.1	10.1
Mutism	10028403	PT	Broad	A	0	Active	10.1	10.1
Obsessive rumination	10056264	PT	Broad	A	0	Active	10.1	10.1
Paralogism	10077175	PT	Broad	A	0	Active	18.1	18.1
Perseveration	10034703	PT	Broad	A	0	Active	10.1	10.1
Poverty of speech	10036467	PT	Broad	A	0	Active	10.1	10.1
Poverty of thought content	10036468	PT	Broad	A	0	Active	10.1	10.1
Presenile dementia	10036631	PT	Broad	A	0	Active	10.1	10.1
Pressure of speech	10036649	PT	Broad	A	0	Active	10.1	10.1
Senile dementia	10039966	PT	Broad	A	0	Active	10.1	10.1
Social avoidant behaviour	10041243	PT	Broad	A	0	Active	10.1	10.1
Speech disorder	10041466	PT	Broad	A	0	Active	10.1	10.1
Suspiciousness	10042635	PT	Broad	A	0	Active	10.1	10.1
Tachyphrenia	10064805	PT	Broad	A	0	Active	10.1	10.1
Thinking abnormal	10043431	PT	Broad	A	0	Active	10.1	10.1
Vascular dementia	10057678	PT	Broad	A	0	Active	10.1	10.1
Verbigeration	10047313	PT	Broad	A	0	Active	10.1	10.1
Withdrawal catatonia	10081010	PT	Broad	A	0	Active	21.0	21.0

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