Statistical Analysis Plan

Title: A Phase 3, Open-label, Multi-center, Single-arm Study to Assess Contraceptive Efficacy and Safety of the Nomegestrol Acetate + 17β-estradiol Combined Oral Contraceptive (OG-8175A) in Premenopausal Females Aged 14 to 35 Years (Inclusive)

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STATISTICAL ANALYSIS PLAN

OG-8175A-023

A Phase 3, Open-label, Multi-center, Single-arm Study to Assess Contraceptive Efficacy and Safety of the Nomegestrol Acetate + 17β-estradiol Combined Oral Contraceptive (OG-8175A) in Premenopausal Females Aged 14 to 35 Years (Inclusive)

AUTHOR: [redacted]

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STATISTICAL ANALYSIS PLAN SIGNATURE PAGE

Statistical Analysis Plan Version 1.1 (Dated ddMMMYYYY) for Protocol OG-8175A-023.

	Name	Signature	Date (DDMMYYYY)
Author:	[redacted]		

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.

	Name	Signature	Date (DDMMYYYY)
Approved By:			
Position:			
Company:	[redacted]		
Approved By:	[redacted]		
Position:			
Company:			

MODIFICATION HISTORY

Unique Identifier for this Version	Date of the Document Version	Author	Significant Changes from Previous Authorized Version
Version 1.0	02 Dec 2023	[redacted]	Initial version
Version 2.0	23 Apr 2024	[redacted]	Updated following TLFs per Organon team review. • Updated Table 14.1.1.1 Participant Disposition, clarified the calculation of percentages. • Removed Tables 14.3.4.1 Markedly abnormal lab test. • Added Tables 14.3.4.1 through 14.3.4.3 Actual and change from baseline in lab tests by visit in hematology, chemistry, and urinalysis. • Added Listing 14.3.5.1 Markedly Abnormal liver function tests. • Corrected/updated Section 16 Appendix A. • Changed the definition of treatment compliance in Table 14.1.7.1. • Just keep two visits of baseline and last measurement and remove other visits in

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LIST OF ABBREVIATIONS

Abbreviation	Term
AE	Adverse Event
APS	Allocated Participants Set
ATC	Anatomical Therapeutic Chemical
BMI	Body Mass Index
CTMS	Clinical Trial Management System
DBP	Diastolic Blood Pressure
eCOA	electronic Clinical Outcome Assessment
eCRF	electronic Case Report Form
ECI	Event of Clinical Interest
ENR	All Participants Enrolled
EOS	End Of Study
EOT	End Of Treatment
MedDRA	Medical Dictionary for Regulatory Activities
MES	Multiple Enrollment Set
PT	Preferred Term
SAE	Serious Adverse Event
SAF	Safety Analysis Set
SAP	Statistical Analysis Plan
SBP	Systolic Blood Pressure
SI	International System of Units
SOC	System Organ Class

Abbreviation	Term
TEAE	Treatment-Emergent Adverse Event
WBC	White Blood Cells
WHODrug	World Health Organization Drug Dictionary

1. INTRODUCTION

Due to early termination of the study, the sponsor decided to report study results in a synoptic report focusing on safety data. This document describes the rules and conventions to be used in the presentation and analysis of safety data for protocol OG-8175A-023. It describes the data to be summarized and analyzed, including specifics of the statistical methods and analyses to be performed.

This statistical analysis plan (SAP) is based on protocol Amendment 2, dated 30AUG2022.

1.1. IMPORTANT DEFINITIONS

Treatment cycle: A treatment cycle is defined by the period between 2 start dates of a blister, as recorded in the participant's e-Diary.
Evaluable cycle (at risk): cycles with duration 22 to 35 days (inclusive) with affirmed heterosexual vaginal intercourse and lack of additional contraception use. In cases of a confirmed pregnancy, cycles that start after the estimated date of conception (as determined by the investigator based on gestational age from an ultrasound) will not be considered "at risk".

On-treatment period for pregnancies: the period from the first date of intake of study treatment up to and including 7 days after the last date of study treatment intake.

- Pre-treatment pregnancies: pregnancies with an estimated date of conception before the first date of study treatment intake. Also, all pregnancies in participants in which all dispensed trial treatment is returned unused (per investigator's record) will be considered pre-treatment.
- On-treatment pregnancies: On-treatment pregnancies are pregnancies with an estimated date of conception between the first date of intake of study treatment up to and including 7 days after the last date of study treatment. In the absence of an ultrasound, the earliest positive serum/urine test date will be utilized to classify pregnancy category. In this case, an on-treatment pregnancy is defined as a positive serum/urine pregnancy test date that is more than 7 days after the first pill and not more than 14 days after the last pill.
- Post-treatment pregnancies: Post-treatment pregnancies are pregnancies with an estimated date of conception after the on-treatment period as defined above. In the absence of ultrasound results, post-treatment pregnancy is defined as a positive serum/urine pregnancy test date that is more than 14 days after the last pill.

Final determination for pre/during/post treatment will be made by the clinical team.

2. OBJECTIVES AND ENDPOINTS

Only safety objectives and endpoints will be analyzed as outlined in Table A.

Table A Study Objectives and Endpoints

Objectives	Endpoints
Primary	
To assess the safety and tolerability of the NOMAC-E2 COC	• Proportion of participants who had an adverse event • Abnormalities in clinical laboratory assessments, vital signs, and physical examination • Proportion of participants who prematurely discontinued study treatment due to adverse events

Abbreviations: COC=combined oral contraceptive; NOMAC-E2=Nomegestrol Acetate + 17β-estradiol

3. STUDY DESIGN

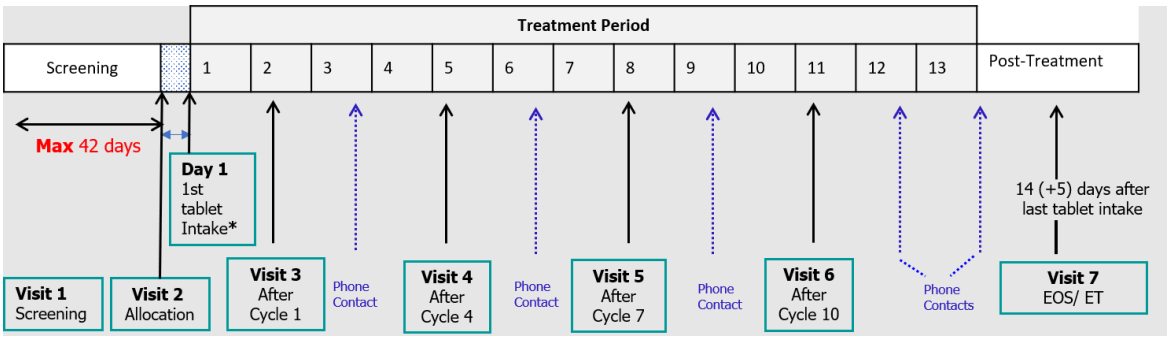
3.1. GENERAL DESCRIPTION

This is an open-label, single-arm, multi-center study to assess the contraceptive efficacy and safety of the NOMAC-E2 COC in postmenarcheal premenopausal women aged 14 to 35 years (inclusive) at the time of study entry.

The total duration of study participation will be up to 60 weeks, which includes a Pre-treatment Period of maximally 6 weeks, a Treatment Period of 52 weeks, and a Follow-up Period of 2 weeks after the last intake of study treatment. Schedule of activities can be found in Section 1.3 of the protocol.

All participants will receive NOMAC-E2 COC. Participants will take one tablet of study treatment per day for thirteen 28-day treatment cycles. The NOMAC-E2 COC active tablets contain 2.5 mg NOMAC and 1.5 mg E2 and will be used in a 24/4 regimen, i.e., 28-day cycles with 24 days of active tablet intake followed by 4 days of placebo tablet intake.

Study Schema



Abbreviation: EOS=End of Study; ET=Early Termination; Max=maximum.
* Time between Visit 2 and Day 1 will depend on the onset of menstruation or the completion of the pre-study contraceptive.

3.2. CHANGES TO ANALYSIS FROM PROTOCOL

Only safety analyses will be performed for this study. Efficacy and PK analyses will not be performed. Consequently, the Safety Analysis Set (SAF), Allocated Participants Set (APS), and Multiple Enrollment Set (MES) as described in Section 5 will be used.

The protocol (footnote to Table 11) specifies that laboratory and vital will be analysed up 28 days after last tablet intake; however, the protocol also specifies that the follow-up visit occurs 14 days (+5 days) after the last tablet. Therefore, this is now corrected in the footnote of Table B of the SAP.

4. PLANNED ANALYSES

Only a final analysis will be performed for this study. No interim analysis is planned.

4.1. DATA MONITORING COMMITTEE

There was no data monitoring committee for this study.

4.2. FINAL ANALYSIS

All final, planned analyses identified in this SAP will be performed by [redacted] Biostatistics following sponsor authorization of this SAP, analysis set determination, and database lock.

5. ANALYSIS SETS

Agreement and authorization of participants included/excluded from each participant-level analysis set will be conducted prior to database lock.

The all participants enrolled (ENR) set will include all participants who provided informed consent for this study and were entered in IRT correctly.

Allocated Participants Set (APS) will include all participants who were allocated to treatment regardless of if any dose was taken.

Safety Analysis Set (SAF) will include all participants allocated to treatment who took at least one dose of study treatment, as determined based on the Drug Accountability eCRF (i.e., participants are expected to either have a date of first dose or indicate that no study drug has been taken). The SAF population will be used for the analysis of all safety data in this study.

If some participants were enrolled in the study more than once, these participants will be excluded from all analysis sets mentioned above (except in pregnancies listing and AE listing).

6. GENERAL CONSIDERATIONS

6.1. REFERENCE START DATE AND STUDY DAY

Study Day will be calculated from the reference start date and event start date and will be used to show number of days since start/stop day of assessments and events relative to first dose of study treatment.

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

If the date of an event is on or after the reference date, the following will be calculated:
Study Day = (date of event – reference date) + 1.
If the date of the event is prior to the reference date, then:
Study Day = (date of event – reference date).

6.2. BASELINE

Unless otherwise specified, baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments). In the case where the last non-missing measurement and the reference start date coincide, that measurement will be considered pre-baseline with the following exceptions:
Adverse events (AEs) and medications commencing on the reference start date will be considered as either pre-baseline or post-baseline based on the collected eCRF assessment of whether the item started prior to the start of study treatment.

6.3. DERIVED TIMEPOINTS

The 'Last measurement' is defined as the last value obtained during the study.
Assessments collected at protocol visit V7 or ET will be displayed in listings as V7 for participants who started Cycle 13 and as ET for those who did not.

6.4. RETESTS, UNSCHEDULED VISITS AND EARLY TERMINATION DATA

In general, for by-visit summaries, data will be presented following the mapping described in Table B (section 6.5 of this SAP), including scheduled and unscheduled measurements, however only scheduled time points will be summarized. Additionally, unscheduled measurements will contribute to the 'Last measurement' value (defined in section 6.3).

In the case of a retest (same visit number assigned and same date), the last available measurement for that visit will be used for by-visit summaries. Listings will include scheduled, unscheduled, retest, and early discontinuation data.

6.5. WINDOWING CONVENTIONS

The on-treatment period for safety assessments will be defined as the period from the day of the first tablet intake up to and including the day of the last tablet intake, extended by 14 days after last tablet.
Windows shown in Table B will be used in the analysis of vital signs and laboratory parameters for analyses performed per visit. Values outside these visit windows, or outside the defined on-treatment period for post-baseline assessments, will be excluded from the analysis of that particular visit. However, no values will be excluded from listings or for the determination of markedly abnormal laboratory (unless outside the defined in-treatment period). If more than one observation is available within a specific visit window, the latest value will be used for analysis.

Table B Timeframe Used in the per Visit of Vital Signs and Laboratory Parameters

Definition	Visit	Visit window (treatment day)
Baseline	Visit 1 Screening	<1
On-treatment[a]	Visit 3 After Cycle 1	29 ± 28 days
	Visit 4 After Cycle 4	113 ± 28 days
	Visit 5 After Cycle 7	197 ± 28 days
	Visit 6 After Cycle 10	281 ± 28 days
	Visit 7 After Cycle 13	379 ± 14 days
	Last measurement	>1

a. From Day 1 until ≤14 days after last tablet intake; Day 1 is defined as day of first study treatment intake.

6.6. STATISTICAL TESTS

No statistical testing will be done.

6.7. COMMON CALCULATIONS

For quantitative measurements, change from baseline at Visit X will be calculated as:
Test Value at Visit X – Baseline Value

6.8. SOFTWARE VERSION

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

7. STATISTICAL CONSIDERATIONS

7.1. HANDLING OF MISSING AND INCOMPLETE DATA

Partial or missing dates for AEs and medications will be imputed as described in section 16 Appendix A of this SAP.

Missing safety data will not be imputed.

An estimated date of conception is required from the investigator for all pregnancies and will be recorded in the eCRF. If the estimated date of conception cannot be determined, the pregnancy diagnosis and first/last dose date will be used to define a pregnancy as pre-treatment, on-treatment, or post-treatment.

8. OUTPUT PRESENTATIONS

Conventions for presentation of data in outputs will be included in the Programming Conventions for Outputs document.

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 [redacted] Biostatistics.

All data will be listed, and summary tables will be provided. Continuous variables will be summarized for the measured values and change from baseline values using the number of observations, mean, standard deviation, median, minimum, and maximum. Categorical variables will be summarized with counts and percentages for each category.

9. DISPOSITION AND WITHDRAWALS

All participants who provided informed consent will be accounted for in this study.

9.1. DISPOSITION

Participant disposition and withdrawals, and reasons for exclusion from each analysis set will be presented for the ENR set.

The number and percentage of participants who were screened, screen failed (including reason screen failed), allocated to treatment, completed or discontinued the Treatment Period (including reasons for early treatment discontinuation), and completed or withdrew from the study (including reasons for study withdrawal) will be presented. In addition, the primary reason for discontinuation for participants who were allocated to study treatment but discontinued prior to study treatment (non-treated participants) will be presented. Completion of treatment and completion of study are recorded on the End of Study Treatment and Disposition eCRFs, respectively.

9.2. PROTOCOL DEVIATIONS

The I[redacted]Clinical Trial Management System (CTMS) will collect protocol deviations and as per the Protocol Deviation Management Plan, where deviations will be assigned a clinical categorization of 'Critical/Major/Minor' and will be deemed as Important or not. To reduce potential bias from the review, participant ID and site ID will be hidden during review. All major and critical protocol deviations will be summarized for the SAF.

10. DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

Demographics and baseline characteristics include age (years), race, ethnicity (Hispanic or Latino), body weight (kg), height (cm), and BMI (kg/m^2). All variables will be summarized by descriptive statistics for the SAF populations. Substance use will be listed. BMI will be calculated in EDC as follows:
BMI (kg/ m^2) = weight (kg)/ height $(m)^2$

11. MEDICAL, GYNECOLOGICAL, AND CONTRACEPTIVE HISTORY

General medical history, gynecological and obstetric history, contraceptive history, and contraceptive status at Visit 1 and Visit 2 will be presented for the SAF population.

11.1. GENERAL MEDICAL HISTORY

Medical history will be coded using Medical Dictionary for Regulatory Activities (MedDRA) version 26.1 or higher. Medical history conditions are defined as relative conditions which are reported at screening and may or may not be ongoing as of the screening visit. Medical history will be listed using System Organ Class (SOC) and Preferred Term (PT).

11.2. GYNECOLOGICAL AND OBSTETRIC HISTORY

For the gynecological history, the time since menarche (in years) will be summarized, as well as the usual duration of menstrual flow (in days) and usual volume of flow without hormonal contraceptive use.

Information relative to the pregnancy history will present the number and percentage of study participants with previous pregnancies as well as descriptive statistics for the overall number of previous pregnancies (gravidity number) and the number of times the participant has given birth to a fetus with gestational age of 24 weeks or more (parity number).

11.3. CONTRACEPTIVE HISTORY

For the contraceptive history at Visit 1, the number and percentage of participants who have previously used a medical or barrier method of contraception in the 6 months prior to screening will be presented. The frequency of participants who used any of the following will also be presented: male condom, female condom, cervical cap, diaphragm, vaginal sponge, vaginal ring, vaginal spermicides, emergency contraceptive pills, contraceptive patch, contraceptive ring, contraceptive implant, contraceptive injection (overall and separately for 1 month, 2 months, and 3 months duration), combined oral contraceptive, progestin-only oral contraceptive, intrauterine device with/without hormone, or other contraceptive.

The contraceptive status at Visit 1 will be summarized in the same manner as contraceptive history. The contraceptive history will be presented for the SAF.

12. MEDICATIONS

Medications will be presented for the SAF population and coded using WHODrug Global B3 version 01March2023 or later; additional populations will be summarized as noted below.

See Appendix A for 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 that started prior to the first dose of study treatment.
- 'Concomitant' medications are medications that started on or after the first dose of study treatment and started no later than 7 days following end of study treatment, with the exception that medications for contraceptive use after the end of study treatment will be excluded.
- 'Post' medications are medications that started more than 7 days following the last dose of study treatment, with the exception that all medications for contraceptive use starting any day after last dose of study treatment will be included.

Prior/concomitant/post-treatment medication use will be listed using preferred name and Anatomical Therapeutic Chemical (ATC) Level 3. If a medication is unable to be categorized to ATC Level 3, the most detailed level available will be used.

13. STUDY TREATMENT EXPOSURE

Exposure to study treatment in days will be presented for the SAF population. The date of first study treatment administration will be taken from the Drug Accountability eCRF. The date of last study treatment is taken from e-Diary.
Duration of exposure (days) = date of last study treatment administration – date of first study treatment administration + 1.

14. STUDY TREATMENT COMPLIANCE

Compliance with the use of study treatment will be presented for the SAF population. The intake of study treatment will be recorded daily in the e-Diary. The e-Diary will be the primary source for the calculation of compliance with the use of study treatment.

Non-compliance to study treatment intake within a cycle is defined as 4 or more days with forgotten tablets, or 2 or more consecutive days with forgotten tablets.

- Overall Compliance to study treatment will be calculated as following:

$$\frac{Number\ of\ days\ that\ at\ least\ one\ tablet\ was\ taken\ in\ the\ treatment\ period,as\ per\ e-Diary}{[\text{Date of last dose}-\text{date of first dose}+1]} \times 100$$

In addition, the number and percentage of participants who took 3 or more tablets on a given day, which is considered as an overdose, will be presented. Number of participants (and cycles) with evaluable cycles will be tabulated and listed.

15. SAFETY OUTCOMES

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

15.1. ADVERSE EVENTS

AEs will be coded using MedDRA coding dictionary, Version 26.1 or higher.

Treatment-emergent adverse events (TEAEs) are defined as AEs that started on or after the day of first dose of study treatment (or worsened in severity) and prior to the last date of study treatment + 14 days (inclusive). See Appendix A for handling of partial dates for AEs. In the case where it is not possible to define an AE as treatment emergent or not due to a partial start date, the AE will be classified by the worst case; i.e. treatment emergent. Pre-treatment AEs/SAEs starting before the on-treatment period, including those starting on the day of first dose of study treatment yet prior to the study treatment intake, will be excluded from the TEAE analyses. Pre- and post-treatment AEs will be identified in listings.

An overview table of number (%) of participants within each of the categories described in the sub-section below will be provided as specified in the templates. The broad AE categories consisting of the percentage of participants with any TEAE, a drug-related TEAE, a serious TEAE, a TEAE that is both drug-related and serious, and a TEAE leading to discontinuation of study treatment will be summarized. Similar Table by BMI group (<30 kg/m^2, ≥30 kg/m^2) will be provided. Listings will include all AEs (including participants who enrolled more than once).

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15.1.1. TEAEs

Incidence of TEAEs will be presented by SOC and PT, with SOC in alphabetical order and PT in order of decreasing frequency. The incidence of TEAEs will be broken down further by maximum severity and maximum relationship to study treatment.

15.1.1.1. Severity

Severity is classed as mild/ moderate/ severe (increasing severity). TEAEs with a missing severity will be classified as severe. If a participant reports a TEAE more than once within that SOC/ PT, the AE with the worst case severity will be used in the corresponding severity summaries.

15.1.1.2. Relationship to Study Treatment

Relationship, as indicated by the Investigator, is classed as 'unrelated', 'unlikely to be related', 'possibly related', and 'probably related' (increasing severity of relationship). A 'related' TEAE is defined as a TEAE with a relationship to study treatment as 'possibly related' or 'probably related' to study treatment. TEAEs with a missing or 'unknown' relationship to study treatment will be regarded as 'related' to study treatment. If a participant reports the same AE as both related and unrelated within that SOC/ PT, the related AE will be used in the corresponding relationship summaries.

15.1.2. TEAEs Leading to Discontinuation of Study Treatment

TEAEs leading to permanent discontinuation of study treatment will be identified by using the 'Action taken with study treatment' variable equal to 'Drug Withdrawal' from the Adverse Events eCRF. A summary of TEAEs leading to discontinuation of study treatment by SOC and PT will be prepared. A listing of all TEAEs leading to

discontinuation of study treatment will be provided, along with the details as to whether the event was related or was serious.

15.1.3. SERIOUS ADVERSE EVENTS

Serious adverse events (SAEs) are those events recorded as 'Serious' on the Adverse Events eCRF. A summary of serious TEAEs by SOC and PT will be prepared.

15.1.4. ADVERSE EVENTS LEADING TO DEATH

TEAEs leading to death are those events that are recorded as 'Fatal' on the Adverse Events eCRF. A summary and listing of TEAEs leading to death by SOC and PT will be prepared.

15.1.5. EVENTS OF CLINICAL INTEREST

ECIs, as defined in section 8.4.5 of the protocol, are those events recorded as 'ECIs' on the Adverse Events eCRF. A summary of TEAEs of Clinical Interest by SOC and PT will be prepared.

15.2. DEATHS

A listing of all fatal TEAEs will be provided. Details of the death as recorded on the Death Details eCRF will be presented in an appendix data listing.

15.3. LABORATORY EVALUATIONS

Results from the central laboratory will be included in the reporting of this study for hematology, biochemistry, and urinalysis. A list of laboratory assessments to be included in the outputs is included in Appendix 3 of the protocol (Table 10). For each parameter, normal reference ranges and safety ranges will be presented.

Presentations will use International System of Units (SI). Results will be converted as needed prior to the analysis. Quantitative laboratory measurements reported as '< X', i.e., below the lower limit of quantification (LLQ), or '> X', i.e., above the upper limit of quantification (ULQ), will be converted to X for the purpose of quantitative summaries, but will be presented as recorded, i.e., as '< X' or '> X' in the listings.

Actual and change from baseline in laboratory test values will be summarized by visit (including Baseline and last measurement) under each of hematology, biochemistry, and urinalysis. All available lab data will be included in the data listings.

In addition, markedly abnormal liver function-related laboratory tests will be summarized during all visits in the study based on the criteria listed below in Table C.

Table C Liver Function Markedly Abnormal Criteria

Liver Function Parameter	Criteria
ALT	≥ 3 x ULN
	≥ 5 x ULN
AST	≥ 3 x ULN
	≥ 5 x ULN
Total Bilirubin (in combination with ALT or AST criteria)	> 1.5 x ULN
	> 2 x ULN
Hy's Law Components	**Criteria**
ALT or AST	≥ 3 x ULN
Total Bilirubin	> 2 x ULN
Alkaline phosphatase	< 2 x ULN

15.4. VITAL SIGNS AND BODY WEIGHT

The following vital signs measurements will be listed:

- Systolic Blood Pressure (mmHg)
- Diastolic Blood Pressure (mmHg)
- Pulse Rate (bpm)
- Weight (kg)

- BMI (kg/m^2)

15.5. PHYSICAL, GYNECOLOGICAL, AND BREAST EXAMINATIONS

Clinically significant findings of general physical, gynecological, and breast examinations performed at EOS will be recorded as TEAEs by the Investigator; these findings will be included in the TEAE summaries, as appropriate.

15.6. PREGNANCIES

A listing of all pre-treatment on-treatment and post-treatment pregnancies will be listed for ENR (including participants who enrolled more than once).

16. APPENDIX A

16.1. ALGORITHM FOR TREATMENT EMERGENCE OF ADVERSE EVENTS:

AE START DATE	AE STOP DATE	ACTION
Known	Known/Partial/ Missing	If AE stop date is partial, impute AE stop date as latest possible date (i.e., last day of month if day unknown or 31st December if day and month are unknown). If AE start date < study treatment start date, assign as pre-treatment AE. If AE start date >= study treatment start date and <= study treatment stop date + 14 days, assign as TEAE. If AE start date > study treatment stop date + 14 days, assign as post-treatment AE.
Partial	Known/Partial/ Missing	If AE stop date is partial, impute AE stop date as latest possible date (i.e., last day of month if day unknown or 31st December if day and month are unknown). Impute AE start date as the study treatment start date, if: • the year of the AE start date is equal to the year of the study treatment start date and the AE stop date is later or equal to the study treatment start date or is missing. • the year and month of the AE start date is equal to the year and month of the study treatment start date and the AE stop date is later or equal to the study treatment start date or is missing. Otherwise, Impute AE start date as earliest possible date (i.e. first day of month if day unknown or 1st January if day and month are unknown). Then: If AE start date < study treatment start date, assign as pre-treatment AE. If AE start date >= study treatment start date and <= study treatment stop date + 14 days, assign as TEAE. If AE start date > study treatment stop date + 14 days, assign as post-treatment AE.

AE START DATE	AE STOP DATE	ACTION
Missing	Known	If AE stop date < study treatment start date, assign as pre-treatment AE If AE stop date >= study treatment start date, assign as TEAE
	Partial	Impute AE stop date as latest possible date (i.e., last day of month if day unknown or 31st December if day and month are unknown), then: If AE stop date < study treatment start date, assign as pre-treatment AE If AE stop date >= study treatment start date assign as TEAE If AE stop date >= study treatment stop date + 14 days, then post-treatment
	Missing	Assumed as TEAE

16.2. ALGORITHM FOR PRIOR / CONCOMITANT MEDICATIONS:

Medication START DATE	Medication STOP DATE	ACTION
Known	Known/Missing	If start date < study treatment date, assign as prior. If start date >= study treatment start date and start date <= end of treatment + 7 days, assign as concomitant except medications for contraceptive use. If start date > end of treatment + 7 days, assign as post study. For all medications for contraceptive use, if start date > end of treatment, assign as post study.

Medication START DATE	Medication STOP DATE	ACTION
	Partial	Impute stop date as latest possible date (i.e. last day of month if day unknown or 31st December if day and month are unknown), then: If start date < study treatment date, assign as prior. If start date >= study treatment start date and start date <= end of treatment + 7 days, assign as concomitant except medications for contraceptive use. If start date > end of treatment + 7 days, assign as post study. For all medications for contraceptive use, if start date > end of treatment, assign as post study.
Partial	Known/Partial/Missing	If stop date is partial, impute stop date as latest possible date (i.e., last day of month if day unknown or 31st December if day and month are unknown). Impute start date as the study treatment start date, if: • the year of the start date is equal to the year of the study treatment start date and the stop date is later or equal to the study treatment start date or is missing. • the year and month of the start date is equal to the year and month of the study treatment start date and the stop date is later or equal to the study treatment start date or is missing. Otherwise, impute start date as earliest possible date (i.e. first day of month if day unknown or 1st January if day and month are unknown). Then: If start date < study treatment date, assign as prior. If start date >= study treatment start date and start date <= end of treatment + 7 days, assign as concomitant except medications for contraceptive use. If start date > end of treatment + 7 days, assign as post study. For all medications for contraceptive use, if start date > end of treatment, assign as post study.

Medication START DATE	**Medication STOP DATE**	**ACTION**
Missing	Known	If stop date < study treatment start date, assign as prior If stop date >= study treatment start date, assign as concomitant
	Partial	Impute stop date as latest possible date (i.e. last day of month if day unknown or 31st December if day and month are unknown), then: If stop date < study treatment start date, assign as prior If stop date >= study treatment start date, assign as concomitant
	Missing	Assign as concomitant

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Certificate Of Completion

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Status: Completed
Subject: Complete with DocuSign: OG-8175A-023_SAP_v2.0_23Apr2024.pdf
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Security Level: Email, Account Authentication (Required)	Signature Adoption: Pre-selected Style Signature ID: EB7A8784-54D7-44C8-8DC8-9107CDEC260F Using IP Address: [redacted] With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	
Electronic Record and Signature Disclosure: Accepted: 5/31/2023 4:44:53 AM ID: 65e478ec-80a7-4f83-aa26-1ddb5864d0d5		
[redacted]		Sent: 4/23/2024 2:30:49 PM Viewed: 4/23/2024 2:31:14 PM Signed: 4/23/2024 2:32:23 PM
Security Level: Email, Account Authentication (Required)	Signature Adoption: Pre-selected Style Signature ID: A7C55067-9956-4931-BC92-CCC5D85ADA96 Using IP Address: [redacted] With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	
Electronic Record and Signature Disclosure: Accepted: 10/30/2020 6:08:15 AM ID: 23cd19c6-bf4f-476e-8831-fe81ea183c9f		

In Person Signer Events	Signature	Timestamp

Editor Delivery Events	Status	Timestamp

Agent Delivery Events	Status	Timestamp

Intermediary Delivery Events	Status	Timestamp

Certified Delivery Events	Status	Timestamp

Carbon Copy Events	Status	Timestamp

Witness Events	Signature	Timestamp

Notary Events	Signature	Timestamp

Envelope Summary Events	Status	Timestamps
Envelope Sent	Hashed/Encrypted	4/23/2024 2:30:49 PM
Certified Delivered	Security Checked	4/23/2024 2:31:14 PM
Signing Complete	Security Checked	4/23/2024 2:32:23 PM
Completed	Security Checked	4/23/2024 2:39:07 PM

Payment Events	Status	Timestamps

Electronic Record and Signature Disclosure

Electronic Record and Signature Disclosure created on: 3/3/2020 11:03:57 AM
Parties agreed to: [redacted]

CONSENT TO ELECTRONIC DELIVERY AND EXECUTION OF DOCUMENTS

From time to time, [redacted] ("we" or "us") may provide you certain written contracts, notices, disclosures, authorizations, acknowledgements or other documents (collectively, the "Documents") electronically. Please read this consent form carefully. It explains the terms and conditions under which such Documents are provided by us and executed by you electronically through your DocuSign, Inc. ("DocuSign") user account. If you consent to the delivery and execution of such Documents electronically, please click the "I Agree" button.

Documents will be sent to you electronically

If you consent to electronic delivery, Documents will be sent to your DocuSign user account. You may request a paper copy of documents previously made available through your DocuSign user account, but an additional charge may be incurred. Alternatively, you can download and print documents sent to your DocuSign user account. Unless otherwise noted, you can access a Document up to 30 days from the date we first sent the Document to you.

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If you withhold consent to electronic delivery or execution, or withdraw your consent at a later date, all Documents will be sent to your mailing address following our receipt of notice of such action. The following sections explain the consequences of withholding or withdrawing your consent to electronic delivery and execution of Documents, and also the procedures you must follow in order to effectuate delivery to your mailing address.

Consequences of Withdrawing Consent

By electing to only receive and execute Documents sent to your mailing address, we will not be able to carry out transactions or services as efficiently. For instance, some transactions or services require your express consent. We can perform these transaction or services only if we first receive an acknowledgement that indicates you received and consent to the Document related to the proposed transaction or service.

To withhold consent now or withdraw consent at a later date, please sign DocuSign's "Withdraw Consent" form on the signing page of your DocuSign user account. This will indicate that you have withdrawn your consent to receive Documents electronically. Once you sign the "Withdraw Consent" form, you will no longer be able to use your DocuSign user account to execute Documents electronically and we will send Documents to your mailing address. Withdrawal of consent does not affect the validity of any Documents previously executed electronically prior to such withdrawal of Consent. In addition, should you execute any Documents electronically, your execution of such Documents shall indicate your continued consent to execute such Documents electronically.

How to contact [redacted]

If you would like us to send the Documents to a different e-mail address, request paper copies of Documents you have previously received electronically, or withdraw your consent to receive electronic documents, please follow the instructions below. If you have any other questions, please contact: [redacted]

1. To advise [redacted] **of your new e-mail address**

If you would like your Documents sent to a different e-mail address, you must send an e-mail message to [redacted] . In the body of the e-mail please state the following: (i) your previous e-mail address, and (ii) your new e-mail address. No other information is required.

In addition, you must notify DocuSign of your new e-mail address. Please log into your DocuSign user account, and follow the instructions to update your e-mail address.

2. To request paper copies from [redacted]
To request paper copies of Documents you have received previously through your DocuSign user account, send an e-mail to [redacted]
In the body of the e-mail please state the following: (i) your e-mail address, (ii) full name, (iii) U.S. Postal address, and (iv) telephone number. Additional charges may apply for such paper copies.

3. To withdraw your consent with [redacted]

To withdraw your consent to receiving and executing Documents in an electronic format, you may do one of the following:

i. decline to sign a document from within your DocuSign user account, and on the subsequent page, select the check-box indicating you wish to withdraw your consent; or
ii. send us an e-mail to [redacted] and in the body of such request you must state your e-mail, full name, US Postal Address, telephone number, and account number. No additional information is necessary.

Required hardware and software

Operating Systems:	Windows® 2000, Windows® XP, Windows Vista®; Mac OS® X
Browsers:	• Internet Explorer (Windows Only) 8.0 or above – compatibility mode is supported only for 9.0 and above. • Windows Edge Current Version • Mozilla Firefox Current Version • Safari (Mac OS only) 6.2 or above • Google Chrome Current Version
PDF Reader:	Acrobat® or similar software may be required to view and print PDF files
Screen Resolution:	1024 x 768 Recommended
Enabled Security Settings:	Allow per session cookies
Mobile Signing:	• Apple iOS 7.0 or above • Android 4.0 or above

** These minimum requirements are subject to change. If these requirements change, we will provide you with an e-mail message at the e-mail address we have on file for you at the time the hardware and software requirements are revised.
Pre-release (e.g. beta) versions of operating systems and browsers are not supported.

Acknowledging your access and consent to receive materials electronically
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