Statistical Analysis Plan

NCT Number: NCT06323356

Title: A Phase 3, Open-Label, Multicenter Study to Evaluate the Efficacy, Safety, and Tolerability of TAK-279 in Adult Subjects With Generalized Pustular Psoriasis or Erythrodermic Psoriasis

Study Number: TAK-279-PsO-3005

Document Version and Date: Amendment 1 / 20-AUG-2026

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STATISTICAL ANALYSIS PLAN

Study Number: *TAK-279-PsO-3005*

Study Title: *A Phase 3, Open-Label, Multicenter Study to Evaluate the Efficacy, Safety, and Tolerability of TAK-279 in Adult Subjects With Generalized Pustular Psoriasis or Erythrodermic Psoriasis*

Phase: *3*

Version: Amendment 1

Date: 20Aug2026

Prepared by:

[redacted].

Based on:

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REVISION HISTORY

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ABBREVIATIONS

AE	adverse event
AESI	adverse event of special interest
ATC	anatomic therapeutic class
BSA	body surface area
CRF	case report form
C-SSRS	Columbia-suicide severity rating scale
CSR	clinical study report
CTCAE	common terminology criteria for adverse events
DLQI	dermatology life quality index
ECG	electrocardiogram
EDC	electronic data capture
EP	erythrodermic psoriasis
FAS	full analysis set
GPP	generalized pustular psoriasis
GPPASI	generalized pustular psoriasis area and severity index
GPPGA	generalized pustular psoriasis global assessment
ICE	intercurrent event
MAV	markedly abnormal value
MedDRA	medical dictionary for regulatory activities
NAPSI	nail psoriasis severity index
PASI	psoriasis area and severity index
PASI-75	75% improvement from baseline in psoriasis area and severity index
PASI-90	90% improvement from baseline in psoriasis area and severity index
PASI-100	100% improvement from baseline in psoriasis area and severity index
PDMP	protocol deviation management plan
PGA	physician's global assessment
PHQ-8	8-tem patient health questionnaire
PK	pharmacokinetic
PKAS	PK analysis set
PPS	per-protocol set
PRO	patient-reported outcomes
PSSI	psoriasis scalp severity index
PT	preferred term (MedDRA)
PTE	pretreatment event
Q1	25th percentile
Q3	75th percentile
QD	once daily
SAE	serious adverse event
SAP	statistical analysis plan
SOC	system organ class

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sPGA	static physician's global assessment
ssPGA	scalp-specific physician's global assessment
TEAE	treatment-emergent adverse event
WOCF	worst observation carried forward

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1.0 OBJECTIVES, ENDPOINTS, AND ESTIMANDS

1.1 Objectives

1.1.1 Primary Objective

To evaluate the efficacy of TAK-279 30 mg orally administered QD for 16 weeks in subjects with GPP or EP.

1.1.2 Secondary Objective

To evaluate the efficacy of TAK-279 30 mg orally administered QD for 52 weeks in subjects with GPP or EP.

1.1.3 Safety Objective

To assess the safety and tolerability of TAK-279 30 mg orally administered QD in subjects with GPP or EP.

1.1.4 Exploratory Objectives

[redacted]

1.2 Endpoints

1.2.1 Coprimary Efficacy Endpoints

- *Static Physician's Global Assessment (sPGA) 0/1 response: Assessed as proportion of subjects achieving an sPGA of clear (0) or almost clear (1) with a ≥2-point decrease from baseline at Week 16*
- *PASI-75 response: Assessed as proportion of subjects achieving ≥75% improvement from baseline in PASI score at Week 16*

1.2.2 Secondary Efficacy Endpoints

- *sPGA 0/1 response: Proportion of subjects achieving an sPGA of clear (0) or almost clear (1) with a ≥2-point decrease from baseline at Weeks 52*
- *Durable sPGA 0/1 response: Proportion of subjects achieving an sPGA of clear (0) or almost clear (1) with a ≥2-point decrease from baseline at both the Week 16 and Week 52 visits*

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- *Enhanced sPGA response: Proportion of subjects achieving an sPGA of clear (0) at Weeks 16 and 52*
- *Simplified sPGA 0/1 response: Proportion of subjects achieving an sPGA of clear (0) or almost clear (1) at Weeks 16 and 52*
- *Simplified durable sPGA 0/1 response: Proportion of subjects achieving an sPGA of clear (0) or almost clear (1) at both the Week 16 and Week 52*
- *PASI-75 response: Proportion of subjects achieving PASI-75 at Weeks 52*
- *PASI-90 response: Proportion of subjects achieving PASI-90 at Weeks 16 and 52*
- *PASI-100 response: Proportion of subjects achieving PASI-100 at Weeks 16 and 52*
- *Durable PASI-75 response: Proportion of subjects achieving PASI-75 at both the Week 16 and Week 52 visits*
- *Durable PASI-90 response: Proportion of subjects achieving PASI-90 at both the Week 16 and Week 52 visits*
- *Scalp-specific Physician's Global Assessment (ssPGA) response: Proportion of subjects achieving an ssPGA of absence of disease (0) or very mild disease (1) with a ≥2-point decrease from baseline at Weeks 16 and 52 (for subjects with a baseline ssPGA ≥3, baseline psoriasis scalp severity index (PSSI) ≥12, and scalp surface area (SSA) involvement ≥30%)*
- *Change from baseline in ssPGA at Weeks 16 and 52*
- *Proportion of subjects achieving a PGA of the hands and/or feet of clear (0) or almost clear (1) with a ≥2-point decrease from baseline at Weeks 16 and 52 (for subjects with a baseline PGA of the hands and/or feet ≥3)*
- *Dermatology Life Quality Index (DLQI) response: Proportion of subjects with a DLQI score of 0/1 at Weeks 16 and 52 (for subjects with a baseline DLQI score ≥2)*
- *Change from baseline in DLQI at Weeks 16 and 52*
- *Change from baseline in Nail Psoriasis Severity Index (NAPSI) at Weeks 16 and 52, among subjects with nail involvement at baseline*
- *Change and percent change from baseline in BSA affected by psoriasis at Weeks 16 and 52*

1.2.3 Secondary Efficacy Endpoints for Generalized Pustular Psoriasis

- *Generalized Pustular Psoriasis Global Assessment (GPPGA) Pustulation Subscore response: Proportion of subjects achieving a GPPGA Pustulation Subscore of no visible pustules (0) at Weeks 16 and 52*

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- *GPPGA 0/1 response: Proportion of subjects achieving a GPPGA of clear (0) or almost clear (1) at Weeks 16 and 52*
- *Enhanced GPPGA response: Proportion of subjects achieving a GPPGA of clear (0) at Weeks 16 and 52*
- *Generalized Pustular Psoriasis Area and Severity Index (GPPASI)-75 response: Proportion of subjects achieving ≥75% improvement from baseline in GPPASI score at Weeks 16 and 52*
- *Change from baseline in JDA severity score at Weeks 16 and 52*

1.2.4 Safety Endpoints

- *Incidence of treatment-emergent adverse events (TEAEs)*
- *Changes in clinical laboratory parameters, vital signs, and electrocardiogram (ECG)*
- *AESIs*

1.2.5 Exploratory Endpoints

- [redacted]
- [redacted]

1.3 Estimands

Not applicable.

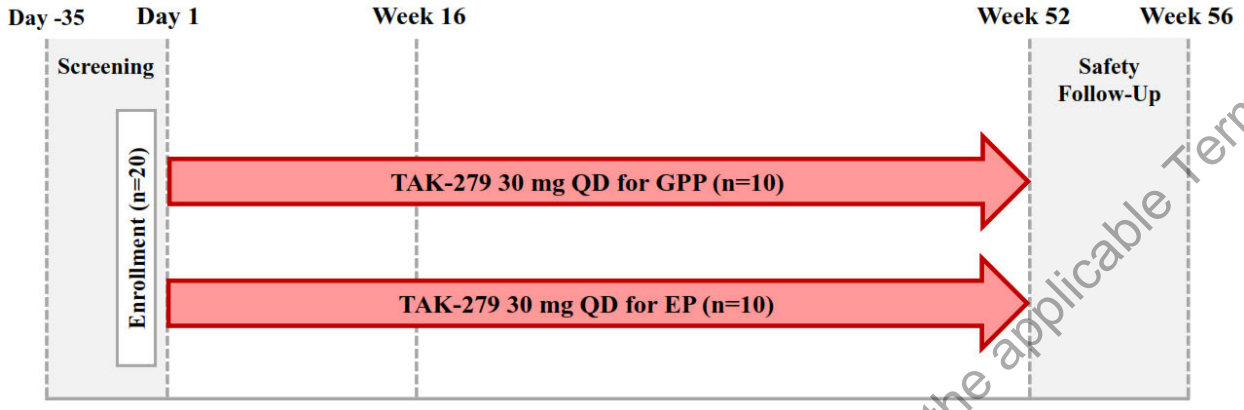
2.0 STUDY DESIGN

This is a phase 3, open-label, multicenter study to evaluate the efficacy, safety, and tolerability of TAK-279 once daily (QD) for 52 weeks in Japanese subjects with GPP or EP.

Approximately 20 male and female subjects, aged 18 years and older, with GPP or EP will be enrolled in this study. To be eligible for the study, subjects must have a diagnosis of GPP or EP prior to the screening visit. In addition, subjects will need to have the following characteristics: For GPP, total JDA severity score <14 and BSA involvement ≥10% at screening and BSA involvement ≥10% on Day 1. For EP, a history of plaque-type of psoriasis and BSA involvement ≥80% at screening and on Day 1. For both populations, eligible for phototherapy or systemic therapy.

This study will consist of 3 parts, including a screening period of up to 35 days, a treatment period of up to 52 weeks, and a safety follow-up period of 4 weeks. Thus, the maximum study duration per subject is expected to be about 61 weeks.

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GPP: Generalized Pustular Psoriasis; EP: Erythrodermic Psoriasis; QD: once daily.

Figure 2.1 Study Schema

3.0 STATISTICAL HYPOTHESES AND DECISION RULES

Not Applicable.

4.0 SAMPLE-SIZE DETERMINATION

For each disease (GPP and EP), the targeted sample size is approximately 10 subjects based on enrollment feasibility of this population in Japan, rather than statistical perspective. Consequently, the targeted sample size is approximately 20 subjects in total.

5.0 ANALYSIS SETS

5.1 All Subjects Who Signed the Informed Consent Form

All subjects who signed the informed consent form.

5.2 All Subjects Who Did Not Enter the Treatment Period

All subjects who signed the informed consent form and did not enter the treatment period.

5.3 Safety Analysis Set

All subjects who received at least 1 dose of TAK-279.

5.4 Full Analysis Set (FAS)

All subjects who received at least 1 dose of TAK-279.

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5.5 Per-protocol Set (PPS)

All subjects who received at least 1 dose of TAK-279, and did not have any important protocol deviations affecting the efficacy evaluations. All decisions to exclude subjects for PPS will be made prior to the database lock of the study. The criteria to exclude subjects for PPS may include, but not limited to, the following:

- Subjects who did not meet any eligibility criteria (i.e., any inclusion and exclusion criteria).
- Subjects with poor compliance (i.e., subjects with study drug compliance (up to Week 16) of less than 70%)
- Subjects using protocol-prohibited medications or therapies that could improve psoriasis (e.g., GPP or EP) prior to Week 16

5.6 PK Analysis Set (PKAS)

All subjects who received at least 1 dose of TAK-279 and had at least 1 measurable TAK-279 plasma concentration value after the first study treatment dose.

6.0 STATISTICAL ANALYSIS

6.1 General Considerations

The following definitions and calculation formulas will be used.

- **Treatment-emergent adverse event (TEAE)**: An adverse event whose date of onset occurs on or after the date of first dose of study drug up to 28 days after the last dose of study drug.
- **Pretreatment event (PTE)**: Any untoward medical occurrence in a clinical investigation subject who has signed informed consent to participate in a study but prior to administration of study drug. Pre-treatment events will be presented, if deemed necessary, in individual subject data listings based on all subjects who signed the informed consent form.
- **Post-treatment AE**: an AE that worsened or newly started post 28 days after the last dose of study drug (i.e., on or after 29 days after the last dose of study drug). Post-treatment AEs will be presented, if deemed necessary, in individual subject data listings based on the safety analysis set.
- **Concomitant medication**: Any concomitant medication that was continued or newly received on or after the first dose of study drug up to 28 days after the last dose of study drug will be summarized.
- **Concomitant prohibited medication prior to Week 16**: Any prohibited medication that was continued or newly received on or after the first dose of study drug up to the latest date of co-primary endpoints' evaluation will be summarized.
- **Concomitant prohibited medication prior to Week 52**: Any prohibited medication that was continued or newly received on or after the first dose of study drug up to the latest date of sPGA or PASI evaluation at Week 52 will be summarized.

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- **Concomitant prohibited procedure prior to Week 16**: Any prohibited procedure that was continued or newly received on or after the first dose of study drug up to the latest date of co-primary endpoints' evaluation will be summarized.
- **Concomitant prohibited procedure prior to Week 52**: Any prohibited procedure that was continued or newly received on or after the first dose of study drug up to the latest date of sPGA or PASI evaluation at Week 52 will be summarized.
- **Descriptive statistics**: Continuous variables will be summarized using the following descriptive summary statistics: number of subjects, mean, standard deviation, maximum, minimum, and quartiles (Q1, median, and Q3). Categorical variables will be summarized using counts and percentages.
- **Duration of exposure to study drug (days)**: Date of last dose of study drug - date of first dose of study drug + 1.
- **Duration of study after baseline (days)**: Date of last visit/contact - date of first dose of study drug + 1.
- **Study drug compliance (%)**: Number of study drugs taken / duration of exposure to study drug [days] * 100 (rounded to 1 decimal place).
- **Study drug compliance up to Week 16 (%)**: Number of study drugs taken / duration of exposure to study drug [days] * 100 (rounded to 1 decimal place). The period covered is between the day of the first dose, and the latest date of co-primary endpoints' evaluation or the day of study discontinuation, whichever occurs first.
- **Significant protocol deviation**: Deviation defined in the PDMP as “Important PD” whose Severity Classifications is “major” or “critical”.
- **Disease type**: Generalized Pustular Psoriasis (GPP) or Erythrodermic Psoriasis (EP).
- **Age (years)**: Age at informed consent will be derived as follows:
  - If the date of birth is present, then the age is derived using the date of birth in EDC.
  - If the date of birth is missing, then “Age at Informed Consent” in EDC is used.

6.1.1 Handling of Treatment Misallocations

Not Applicable.

6.1.2 Analysis Approach for Continuous Variables

For efficacy endpoints, all continuous endpoints will use the analysis method below by disease type, unless stated otherwise in the section specific to an endpoint.

- For variables other than BSA affected by psoriasis, PASI and GPPASI, descriptive statistics and two-sided 95% confidence interval of mean will be provided for observed values (baseline and post-baseline visits) and changes from baseline (each post-baseline visit’s value – baseline value). For endpoints with multiple visits, these will be provided by visit.

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- For BSA affected by psoriasis, PASI and GPPASI, descriptive statistics and two-sided 95% confidence interval of mean will be provided for observed values, changes from baseline and percent changes from baseline ([each post-baseline visit's value - baseline value] / [baseline value] x 100) by visit.

6.1.3 Analysis Approach for Binary Variables

For efficacy endpoints, all binary endpoints will use the analysis method below unless stated otherwise in the section specific to an endpoint.

- Frequency distribution will be provided with proportion and the two-sided 95% confidence interval by disease type. The confidence interval will be calculated using Clopper-Pearson method. For endpoint with multiple visits, these will be provided by visit.
  For endpoints related to sPGA and PASI considering the strategy for addressing intercurrent events in section 9.3 except analyses for durable responses and subgroup analyses, frequency distributions of the reason for nonresponse will be also provided by disease type. When calculating percentages for the reasons for nonresponse, the total number of subjects who are nonresponders will be used as the denominator.

6.1.4 Analysis Approach for Time-to-Event Variables

- Not applicable.

6.2 Disposition of Subjects

6.2.1 Study Information

Analysis Set:	All Subjects Who Signed the Informed Consent Form
Analysis Endpoint(s) :	Date First Subject Signed Informed Consent Form
	Date of Last Subject's Last Visit/Contact
	MedDRA Dictionary Version
	WHO Drug Dictionary Version
	SAS Version Used for Creating the Datasets
Analytical Method(s) :	(1) Study Information
	Study information shown in the analysis endpoints section will be provided.

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6.2.2 Screen Failures

Analysis Set:	All Subjects Who Did Not Enter the Treatment Period	
Analysis Endpoint(s) :	Age (years)	
	Sex	[Male, Female]
Analytical Method(s) :	(1) Screen Failures	
	Frequency distributions for categorical endpoints and descriptive statistics for continuous endpoints will be provided.	

6.2.3 Subject Eligibility

Analysis Set:	All Subjects Who Signed the Informed Consent Form	
Analysis Endpoint(s) :	Eligibility Status	[Eligible for Entrance into the Treatment Period, Not Eligible for Entrance into the Treatment Period]
	Primary Reason for Subject Not Being Eligible	[Adverse Event, Lost to Follow-up, Met Eligibility Criteria But Not Needed, Pregnancy, Screen Failure (Did Not Meet Eligibility Criteria), Study Terminated by Sponsor, Withdrawal by Subject, Other]
Analytical Method(s) :	(1) Eligibility for Entrance into the Treatment Period	
	Frequency distributions will be provided. When calculating percentages for the primary reasons for subject not being eligible, the total number of ineligible subjects will be used as the denominator.	

6.2.4 Number of Subjects Who Entered the Treatment Period by Site

Analysis Set:	Safety Analysis Set	
Analysis Endpoint(s) :	Status of Entrance into the Treatment Period	[Entered]
Stratum:	Site	[Site numbers will be used as categories]
Analytical Method(s) :	(1) Number of Subjects Enrolled by Site	
	Frequency distribution will be provided for each stratum by disease type.	

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6.2.5 Disposition of Subjects

Analysis Set:	Safety Analysis Set	
Analysis Endpoint(s) :	Study Drug Completion Status	[Completed Study Drug, Prematurely Discontinued Study Drug]
	Reason for Discontinuation of Study Drug	[Adverse Event, Death, Protocol Deviation, Lost to Follow-up, Withdrawal by Subject, Study Terminated by Sponsor, Pregnancy, Lack of Efficacy, Other]
	Study Completion Status	[Completed Study, Prematurely Discontinued Study]
	Reason for Discontinuation of Study	[Adverse Event, Death, Protocol Deviation, Lost to Follow-up, Withdrawal by Subject, Study Terminated by Sponsor, Pregnancy, Lack of Efficacy, Other]
Analytical Method(s) :	(1) Disposition of Subjects Frequency distributions will be provided by disease type. When calculating percentages for the reasons for discontinuation, the total number of subjects who prematurely discontinued will be used as the denominator.	

6.2.6 Protocol Deviations and Analysis Sets

6.2.6.1 Significant Protocol Deviations

Analysis Set:	Safety Analysis Set	
Analysis Endpoint(s) :	Significant Protocol Deviation	[Informed Consent and Process, Inclusion Criteria, Exclusion Criteria, Concomitant Medication, Laboratory Assessment, Study Procedures (not safety and efficacy related), Safety, Visit Schedule, IP Conditions, IP Preparation, IP Study Administration, Subject IP Compliance, Efficacy, Subject Discontinuation, Administrative, Clinician-Reported Outcomes, Patient-Reported Outcomes, PK/PD, Other Criteria]

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Analytical Method(s) :	(1) Protocol Deviations Frequency distribution will be provided for each deviation category by disease type. A subject who has several deviations will be counted once in each appropriate category. A subject who has several deviations that can be classified into the same category will be counted only once.	

6.2.6.2 Analysis Sets

Analysis Set:	Safety Analysis Set	
Analysis Endpoint(s) :	Handling of Subjects	[Categories are based on the specifications in section 5.0 Analysis Sets]
	Analysis Sets:	
	Safety Analysis Set	[Included]
	Full Analysis Set	[Included]
	Per-protocol Set	[Included]
	PK Analysis Set	[Included]
Analytical Method(s) :	(1) Subjects Excluded from Analysis Sets (2) Analysis Sets Frequency distributions will be provided by disease type. For (1), a subject who has several reasons for exclusion will be counted once in each appropriate category. A subject who has several reasons for exclusion that can be classified into the same category will be counted only once.	

6.3 Demographic and Other Baseline Characteristics

6.3.1 Demographics and Baseline Characteristics

Analysis Set:	Safety Analysis Set	
Analysis Endpoint(s) :	Age (years)	[Min<= - <=64, 65<=- <=Max]
	Sex	[Male, Female]
	Height (cm)	
	Weight (kg)	

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BMI (kg/m^2)	
Smoking Classification	[Never, Former, Current]
Alcohol Classification	[Never, Former, Current]
Duration of Disease (years)	[Min<= - <10, 10<= - <=Max]
Prior Treatment with Biologics	[Yes, No]
Prior Systemic Treatment Use	[Yes, No]
Prior Phototherapy Use	[Yes, No]
History of Psoriatic Arthritis	[Yes, No]
Active Scalp Psoriasis at Day 1	[Yes, No]
Active Nail Psoriasis at Day 1	[Yes, No]
Active Hands/Feet Psoriasis at Day 1	[Yes, No]
PASI at Baseline	[Min<= - <20, 20<= - <=Max]
BSA at Baseline	[Min<= - <20, 20<= - <=Max]
	[Min<= - <90, 90<= - <=Max]
sPGA at Baseline	[Min<= - <=2, 3, 4]
ssPGA at Baseline	[0, 1, 2, 3, 4]
PGA of the Hands and/or Feet at Baseline	[0, 1, 2, 3, 4]
DLQI at Baseline	[Min<= - <2, 2<= - <=Max]
GPPGA at Baseline	[0, 1, 2, 3, 4]
GPPASI at Baseline	[Min<= - <20, 20<= - <=Max]
JDA Severity Score at Baseline	[Min<= - <7, 7<= - <11, 11<= - <14, 14<= - <=Max]
NAPSI at Baseline	

Analytical Method(s) : (1) Demographics and Baseline Characteristics

Frequency distributions for categorical endpoints and descriptive statistics for continuous endpoints will be provided by disease type.

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6.3.2 Medical History and Concurrent Medical Conditions

Analysis Set: Safety Analysis Set

Analysis Endpoint(s) : Medical History

Concurrent Medical Conditions

Analytical Method(s) : (1) Medical History by System Organ Class and Preferred Term

(2) Concurrent Medical Conditions by System Organ Class and Preferred Term

Frequency distributions will be provided by disease type. MedDRA dictionary will be used for coding. Summaries will be provided using SOC and PT, where SOC will be sorted alphabetically and PT will be sorted in decreasing frequency.

A subject with multiple occurrences of medical history or concurrent medical condition within a SOC will be counted only once in that SOC. A subject with multiple occurrences of medical history or concurrent medical condition within a PT will be counted only once in that PT.

6.4 Medication History and Concomitant Medications

Analysis Set: Safety Analysis Set

Analysis Endpoint(s) : Medication History

Concomitant Medications

Analytical Method(s) : (1) Medication History by ATC level 2 and Preferred Medication Name
(2) Concomitant Medication by ATC level 2 and Preferred Medication Name
(3) Concomitant Prohibited Medication Prior to Week 16 by ATC level 2 and Preferred Medication Name
(4) Concomitant Prohibited Medication Prior to Week 52 by ATC level 2 and Preferred Medication Name
(5) Concomitant Prohibited Procedure Prior to Week 16 by System Organ Class and Preferred Term
(6) Concomitant Prohibited Procedure Prior to Week 52 by System Organ Class and Preferred Term

For (1) to (4), frequency distributions will be provided by disease type. WHO Drug dictionary will be used for coding. Summaries will be provided using ATC level 2 and preferred medication names. ATC level 2 will be sorted alphabetically and Preferred Medication Name

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will be sorted in decreasing frequency based on the number of reports. A subject who has been administered several medications with the same preferred medication names will be counted only once for that preferred medication names. For ATC level 2, same manners in counting frequency.

For (5) to (6), frequency distribution will be provided by disease type. Procedures will be coded using the MedDRA and will be summarized using SOC and PT. A subject with multiple occurrences of procedure within a SOC will be counted only once in that SOC. A subject with multiple occurrences of procedure within a PT will be counted only once in that PT. Percentages will be based on the number of subjects in the safety analysis set.

6.5 Extent of Exposure and Compliance

Analysis Set:	Safety Analysis Set	
Analysis Endpoint(s) :	Duration of Exposure to Study Drug (days)	[0<= - <= 127, 128 <= - <= Max]
	Study Drug Compliance (%)	[Min<= - <80, 80 <= - < 120, 120<= - <=Max]
	Study Drug Compliance up to Week 16 (%)	[Min<= - <80, 80 <= - < 120, 120<= - <=Max]
Analytical Method(s) :	(1) Study Drug Exposure and Compliance Frequency distributions for categorical endpoints and descriptive statistics for continuous endpoints will be provided by disease type.	

6.6 Efficacy Analysis

6.6.1 Coprimary Efficacy Endpoints Analysis

6.6.1.1 Derivation of Endpoint(s)

See Section 9.3.

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6.6.1.2 Primary Analysis

Analysis Set: FAS

Analysis Endpoint(s):
- sPGA 0/1 response at Week 16
- PASI-75 response at Week 16

Analytical Method(s): See Section 6.1.3.

6.6.1.3 Supplementary Analyses

Analysis Set: PPS

Analysis Endpoint(s):
- sPGA 0/1 response at Week 16
- PASI-75 response at Week 16

Analytical Method(s): See Section 6.1.3.

6.6.2 Secondary Endpoints Analysis

Analysis Set: FAS

Analysis Endpoint(s): Continuous Endpoints:

- Change from baseline in ssPGA at Weeks 16 and 52
- Change from baseline in DLQI at Weeks 16 and 52
- Change from baseline in Nail Psoriasis Severity Index (NAPSI) at Weeks 16 and 52, among subjects with nail involvement at baseline
- Change and percent change from baseline in BSA affected by psoriasis at Weeks 16 and 52

Binary Endpoints:

- sPGA 0/1 response at Weeks 52
- Durable sPGA 0/1 response
- Enhanced sPGA response at Weeks 16 and 52
- Simplified sPGA 0/1 response at Weeks 16 and 52
- Simplified durable sPGA 0/1 response
- PASI-75 response at Weeks 52
- PASI-90 response at Weeks 16 and 52
- PASI-100 response at Weeks 16 and 52
- Durable PASI-75 response
- Durable PASI-90 response
- ssPGA response at Weeks 16 and 52

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- Proportion of Subjects Achieving a PGA of The Hands and/or Feet at Weeks 16 and 52
- Dermatology Life Quality Index (DLQI) response at Weeks 16 and 52

Analytical Method(s): See Section 6.1.2 and 6.1.3. For NAPSI, change from baseline to Week 16 (WOCF) or Week 52 (WOCF) will be analyzed.

6.6.3 Secondary Efficacy Endpoints for Generalized Pustular Psoriasis

Analysis Set: FAS with Generalized Pustular Psoriasis

Analysis Endpoint(s): Continuous Endpoints:

- Change from baseline in JDA severity score at Weeks 16 and 52

Binary Endpoints:

- GPPGA Pustulation Subscore response at Weeks 16 and 52
- GPPGA 0/1 response at Weeks 16 and 52
- Enhanced GPPGA response at Weeks 16 and 52
- Generalized Pustular Psoriasis Area and Severity Index (GPPASI)-75 response at Weeks 16 and 52

Analytical Method(s): See Section 6.1.2 and 6.1.3.

6.6.4 Other Efficacy Analysis

6.6.4.1 Continuous Endpoints

Analysis Set: FAS

Analysis Endpoint(s) :

- Total sPGA Score
- PASI Score
- ssPGA
- PGA of Hands and/or Feet
- DLQI
- NAPSI
- BSA

Visit: See section 9.2.2. For NAPSI, Week 16 (WOCF) and Week 52 (WOCF) will be excluded from the analysis visits.

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Analytical Method(s) : For each endpoint, summaries (1) and (2) will be provided.

(1) Descriptive statistics and two-sided 95% confidence interval of mean by Visit
See Section 6.1.2

(2) Mean Plots
Mean observed values and mean changes from baseline (each post-baseline visit - Baseline) will be plotted for each visit with 95% confidence interval bars.

6.6.4.2 Continuous Endpoints for Generalized Pustular Psoriasis

Analysis Set: FAS with Generalized Pustular Psoriasis

Analysis Endpoint(s) :
- GPPGA
- GPPASI
- JDA

Visit: See section 9.2.2.

Analytical Method(s) : For each endpoint, summaries (1) and (2) will be provided.

(1) Descriptive statistics and two-sided 95% confidence interval of mean by Visit
See Section 6.1.2

(2) Mean Plots
Mean observed values and mean changes from baseline (each post-baseline visit - Baseline) will be plotted for each visit with 95% confidence interval bars.

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6.6.5 Subgroup Analyses

Analysis Set:	FAS	
Analysis Endpoint(s):	• sPGA 0/1 response at Week 16 and 52	
	• PASI-75 response at Week 16 and 52	
	• Simplified sPGA 0/1 response at Week 16 and 52	
Subgroup(s):	Age	[Min<= - <=64, 65<= - <=Max]
	Sex	[Male, Female]
	Prior Treatment with Biologics	[Yes, No]
Analytical Method(s):	If sample size permits, the analyses based on Section 6.1.3 will be conducted for each subgroup.	

6.7 Safety Analysis

6.7.1 Adverse Events

6.7.1.1 Overview of Treatment-Emergent Adverse Events

Analysis Set:	Safety Analysis Set	
Analysis Endpoint(s) :	TEAE	
Categories:	Relationship to Study Drug	[Related, Not Related]
	Intensity	[1, 2, 3, 4, 5 (based on NCI CTCAE)]
Analytical Method(s) :	The following summaries will be provided by disease type.	

(1) Overview of Treatment-Emergent Adverse Events

1) All Treatment-Emergent Adverse Events (number of events, number and percentage of subjects)
2) Relationship of Treatment-Emergent Adverse Events to study drug (number of events, number and percentage of subjects)
3) Intensity of Treatment-Emergent Adverse Events (number of events, number and percentage of subjects)
4) Treatment-Emergent Adverse Events leading to study drug discontinuation (number of events, number and percentage of subjects)
5) Serious Treatment-Emergent Adverse Events (number of events, number and percentage of subjects)

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6) Relationship of serious Treatment-Emergent Adverse Events to study drug (number of events, number and percentage of subjects)

7) Treatment-Emergent Adverse Events resulting in death (number of events, number and percentage of subjects)

TEAEs will be counted according to the rules below.

Number of subjects

- Summaries for 2) and 6)
  A subject with occurrences of TEAE in both categories (i.e., Related and Not Related) will be counted once in the Related category.
- Summary for 3)
  A subject with multiple occurrences of TEAE will be counted once for the TEAE with the maximum intensity.
- Summaries other than 2), 3), and 6)
  A subject with multiple occurrences of TEAE will be counted only once.

Number of events

For each summary, the total number of events will be calculated.

6.7.1.2 Displays of Treatment-Emergent Adverse Events

Analysis Set:	Safety Analysis Set	
Analysis Endpoint(s) :	TEAE	
Categories:	Intensity	[1, 2, 3, 4, 5 (based on NCI CTCAE)]
Analytical Method(s) :	The following summaries will be provided using frequency distribution by disease type.	

TEAEs will be coded using the MedDRA and will be summarized using SOC and PT.

SOC will be sorted alphabetically and PT will be sorted in decreasing frequency for tables provided by SOC and PT. SOC and PT will be sorted in decreasing frequency for tables provided by System Organ Class only or PT only.

(1) Treatment-Emergent Adverse Events by System Organ Class and Preferred Term

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(2) Treatment-Emergent Adverse Events by Preferred Term

(3) Drug-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term

(4) Intensity of Treatment-Emergent Adverse Events by System Organ Class and Preferred Term

(5) Intensity of Drug-Related Treatment-Emergent Adverse Events by System Organ Class, and Preferred Term

(6) Treatment-Emergent Adverse Events Leading to Study Drug Discontinuation by System Organ Class and Preferred Term

(7) Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term

(8) Treatment-Emergent Adverse Events of Special Interest by System Organ Class and Preferred Term

(9) Drug-Related Treatment-Emergent Adverse Events of Special Interest by System Organ Class and Preferred Term

The frequency distribution will be provided according to the rules below.

Number of subjects

- Summary tables other than (4) and (5)
  A subject with multiple occurrences of TEAE within a SOC will be counted only once in that SOC. A subject with multiple occurrences of TEAE within a PT will be counted only once in that PT. Percentages will be based on the number of subjects in the safety analysis set.
- Summary tables for (4) and (5)
  A subject with multiple occurrences of TEAE within a SOC or a PT will be counted only once for the TEAE with the maximum intensity. Percentages will be based on the number of subjects in the safety analysis set.

6.7.2 Other Safety Analysis

6.7.2.1 Laboratory Tests other than Urinalysis

Analysis Set: Safety Analysis Set

Analysis Endpoint(s) : See Section 9.4.

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Visit: See section 9.2.2.

Analytical Method(s) : For each endpoint, summaries (1) to (3) will be provided.

(1) Summary of Laboratory Test Results and Change from Baseline by Visit
Descriptive statistics for observed values and changes from baseline (each post-baseline visit - Baseline) will be provided by disease type for each visit.

(2) Case Plots
Plots over time for each subject will be presented.

(3) Summary of Shifts of Laboratory Test Results
Shift tables showing the number of subjects in each category at baseline and each post-baseline visit will be provided by disease type.
For each laboratory test, the laboratory values will be classified as "Low", "Normal" or "High" relative to the normal reference range provided by the central laboratory. The shift tables will be based on these classifications.

(4) Number and Percentage of Subjects with Markedly Abnormal Values of Laboratory Parameters
Frequency distributions of markedly abnormal values (MAVs) will be provided for selected parameters. Further details are given in Appendix.

6.7.2.2 Urinalysis

Analysis Set: Safety Analysis Set

Analysis Endpoint(s) : See Section 9.4.

Visit: See section 9.2.2.

Analytical Method(s) : For each continuous endpoint, summaries (1), (2) and (4) will be provided.

For each categorical endpoint, summaries (3) and (4) will be provided.

(1) Summary of Urine Laboratory Test Results and Change from Baseline by Visit
Descriptive statistics for observed values and changes from baseline (each post-baseline visit - Baseline) will be provided by disease type for each visit.

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(2) Case Plots
Plots over time for each subject will be presented.

(3) Number of Subjects in Categories of Urine Laboratory Test Results
Shift tables showing the number of subjects in each category at baseline and each post-baseline visit will be provided by disease type.

(4) Summary of Shifts of Urine Laboratory Test Results
Shift tables showing the number of subjects in each category at baseline and each post-baseline visit will be provided by disease type.
For each urine laboratory test, the laboratory values will be classified as "Low", "Normal" or "High" relative to the normal reference range provided by the central laboratory. The shift tables will be based on these classifications.

6.7.2.3 Vital Signs and Weight

Analysis Set:	Safety Analysis Set	
Analysis Endpoint(s) :	Body Temperature	Respiratory Rate
	Systolic Blood Pressure	Diastolic Blood Pressure
	Pulse	Weight
	BMI	
Visit:	See section 9.2.2.	

Analytical Method(s) : For each endpoint, summaries (1) and (2) will be provided.

(1) Summary of Vital Signs and Weight, and Change from Baseline by Visit
Descriptive statistics for observed values and changes from baseline (each post-baseline visit - Baseline) will be provided by disease type for each visit.

(2) Case Plots
Plots over time for each subject will be presented.

(3) Number and Percentage of Subjects with Markedly Abnormal Values of Laboratory Parameters
Frequency distributions of markedly abnormal values (MAVs) will be provided for selected parameters. Further details are given in Appendix.

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6.7.2.4 ECGs

Analysis Set:	Safety Analysis Set	
Analysis Endpoint(s) :	Heart Rate	
	RR Interval	
	PR Interval	
	QRS Interval	
	QT Interval	
	QTcF Interval	
	Interpretation	[Within Normal Limits, Abnormal, Not Clinically Significant, Abnormal, Clinically Significant, Not Evaluable]
Visit:	See section 9.2.2.	
Analytical Method(s) :	For each endpoint other than 12-lead ECG interpretations, summaries (1) and (2) will be provided.	
	For ECG interpretation, summary (3) will be provided.	

(1) Summary of ECG Parameters and Change from Baseline by Visit
Descriptive statistics for observed values and changes from baseline (each post-baseline visit - Baseline) will be provided by disease type for each visit.

(2) Case Plots
Plots over time for each subject will be presented.

(3) Summary of Shift of ECG Interpretation
Shift table showing the number of subjects in each category at baseline and each post-baseline visit will be provided by disease type.

(4) Number and Percentage of Subjects with Markedly Abnormal Values of ECG Parameters
Frequency distributions of markedly abnormal values (MAVs) will be provided for selected parameters. Further details are given in Appendix.

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6.7.2.5 PHQ-8

Analysis Set:	Safety Analysis Set
Analysis Endpoint(s) :	Total Scores of PHQ-8
Visit:	See section 9.2.2.
Analytical Method(s) :	The following summaries will be provided. (1) Summary of Total Scores of PHQ-8 and Change from Baseline by Visit Descriptive statistics for observed values and changes from baseline (each post-baseline visit - Baseline) will be provided by disease type for each visit.

6.7.2.6 C-SSRS

Analysis Set:	Safety Analysis Set
Analysis Endpoint(s) :	C-SSRS
Visit:	See section 9.2.2.
Analytical Method(s) :	The following summaries will be provided. (1) Summary of C-SSRS by Visit Frequency distributions will be provided by disease type.

6.8 Pharmacokinetic, Pharmacodynamic, and Biomarker Analyses

6.8.1 Pharmacokinetic Analysis

Analysis Set:	PKAS
Analysis Endpoint(s) :	TAK-279 Plasma Concentration Value
Visit:	See section 9.2.2.
Analytical Method(s) :	The following summaries will be provided. (1) Summary of Plasma Concentrations by Visit Descriptive statistics, Geometric Mean, Geometric CV%, and CV% will be provided by disease type by visit.

6.8.2 Pharmacodynamic Analysis

Not Applicable.

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6.8.3 Biomarker Analysis

[redacted]

6.9 Patient Reported Outcomes (PROs) and Health Care Utilization Endpoints Analysis

6.9.1 PRO Analysis

See Section 6.6.

6.9.2 Health Care Utilization Analysis

Not Applicable.

6.10 Other Analyses

Not Applicable.

6.11 Interim Analyses

There is no interim analysis planned in this study.

6.12 Data Monitoring Committee

Not Applicable.

7.0 REFERENCES

Not Applicable.

8.0 CHANGES TO PROTOCOL PLANNED ANALYSES

There was no change to the protocol planned analyses.

9.0 APPENDIX

9.1 Changes From the Previous Version of the SAP

From the SAP version 1.0, the major updates except minor updates such as error correction were as follows:

SAP Section	Change	Rationale for Change
Section 1 and Section 2	Clarified description	To reflect protocol amendment.
Section 5.5 Per-protocol Set	Clarified definition of criteria	Clarification
Section 6.1 General Considerations	Clarified derivation of age	To treat age derivation since some subjects have date of birth as missing.

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SAP Section	Change	Rationale for Change
Section 1 and Section 2	Clarified description	To reflect protocol amendment.
Section 5.5 Per-protocol Set	Clarified definition of criteria	Clarification
Section 6.1 General Considerations Section 6.1.3 Analysis Approach for Binary Variables	Added summary of reason for nonresponse	To support the understanding on efficacy results aligned with estimand framework.
Section 6.2.6.2 Analysis Sets	Clarified category of Analysis Sets	To derive analysis set flags without external file (e.g., subject evaluability list).
Section 6.3.1 Demographics and Baseline Characteristics	Added JDA Severity Score	To support the understanding on demographics.
Section 6.1 General Considerations Section 6.4 Medication History and Concomitant Medications	Added details of summary of Medication History and Concomitant Medications	To clarify the summary of Medication History and Concomitant Medications.
Section 6.7.2.2 Urinalysis	Clarified details of urinalysis	To reflect actual transferred items.
Section 6.7.2.3 Vital Signs and, Weight	Clarified details of vital signs analysis	To clarify the summary of vital signs.
Section 6.7.2.6 C-SSRS Section 9.2.2.1 Endpoints other than PK Samples Table 9.7 C-SSRS	Added summary of C-SSRS by visit over time with visit windows	To support the understanding on signs of suicidal ideation and behavior.
Section 6.8.1 Pharmacokinetic Analysis	Added Geometric Mean, Geometric CV%, and CV% for summary	To support the understanding on plasma concentration behavior.
Section 9.3.1.3 Strategy for Addressing Intercurrent Events	Clarified details of handling ICEs	Clarification

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9.2 Data Handling Conventions

9.2.1 Definition of Study Days

The following definitions and calculation formulas will be used.

- Study Day: The day before the first dose of the study drug will be defined as Study Day -1 and the day of the first dose will be defined as Study Day 1. If the date of the observation is on the same date or after the day of the first dose, Study Day will be calculated relative to Study Day 1. Otherwise, Study Day will be calculated relative to Study Day -1.
- Follow-up Day: The day after the last dose of the study drug will be defined as Follow-up Day 1.

9.2.2 Definition of Visit Windows

When calculating Study Day relative to a reference date (ie, date of first dose of study drug [Day 1]), if the date of the observation is on the same date or after the reference date, it will be calculated as: date of observation - reference date + 1; otherwise, it will be calculated as: date of observation - reference date. Hence, reference day is always Day 1 and there is no Day 0.

When calculating Follow-up Day relative to a reference date (ie, date of last dose of study drug [Follow-up Day 0]), it will be calculated as: date of observation - reference date. Hence, reference day is always Follow-up Day 0.

All evaluable data (ie, non-missing data) will be handled according to the following rules.

9.2.2.1 Endpoints other than PK Samples

For each visit, observation obtained in the corresponding time interval will be used. If more than one observation lies within the same visit window, the observation with the closest Study Day to the scheduled Study Day will be used. If there are two observations equidistant to the scheduled Study Day, the later observation will be used.

Data entered as Week 56 in the EDC/CRF will be treated as Week 56, regardless of the date of data collection (i.e., Study Day or Follow-up Day), unless the data is included in Time Interval of Visit other than Week 56.

For C-SSRS, time intervals are not provided for Screening and Baseline (Week 0) visits since source questionnaires are different.

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Table 9.1 Body Height and Weight

Visit	Scheduled Study Day (days)		Time Interval (days)	
			Study Day	Follow-up Day
Baseline (Week 0)	Study Day:	1	-35 – 1	
Week 4	Study Day:	29	2 – 43	<29
Week 8	Study Day:	57	44 – 85	<29
Week 16	Study Day:	113	86 – 141	<29
Week 24	Study Day:	169	142 – 211	<29
Week 36	Study Day:	253	212 – 309	<29
Week 52	Study Day:	365	310 – 379	<29
Week 56	Study Day:			

Table 9.2 Vital Signs, Clinical Laboratory Tests (Hematology, Chemistry, Urinalysis [Including Urine Chemistry], FSH)

Visit	Scheduled Study Day (days)		Time Interval (days)	
			Study Day	Follow-up Day
Baseline (Week 0)	Study Day:	1	-35 – 1	
Week 1	Study Day:	8	2 – 11	<29
Week 2	Study Day:	15	12 – 22	<29
Week 4	Study Day:	29	23 – 43	<29
Week 8	Study Day:	57	44 – 71	<29
Week 12	Study Day:	85	72 – 99	<29
Week 16	Study Day:	113	100 – 127	<29
Week 20	Study Day:	141	128 – 155	<29
Week 24	Study Day:	169	156 – 183	<29
Week 28	Study Day:	197	184 – 211	<29
Week 32	Study Day:	225	212 – 239	<29
Week 36	Study Day:	253	240 – 267	<29
Week 40	Study Day:	281	268 – 295	<29
Week 44	Study Day:	309	296 – 323	<29
Week 48	Study Day:	337	324 – 351	<29
Week 52	Study Day:	365	352 – 379	<29
Week 56	Study Day:			

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Table 9.3 12-lead ECG, Fasting Lipid Panel

Visit	Scheduled Study Day (days)		Time Interval (days)	
			Study Day	Follow-up Day
Baseline (Week 0)	Study Day:	1	-35 – 1	
Week 4	Study Day:	29	2 – 71	<29
Week 16	Study Day:	113	72 – 141	<29
Week 24	Study Day:	169	142 – 267	<29
Week 52	Study Day:	365	268 – 379	<29
Week 56	Study Day:			

Table 9.4 PASI, sPGA, BSA, ssPGA (for Subjects with Scalp Psoriasis at Study Day 1), GPPGA, GPPASI, JDA Severity Score, PGA of Hands and/or Feet (for Subjects with Hands and/or Feet Psoriasis at Study Day 1), DLQI Questionnaire

Visit	Scheduled Study Day (days)		Time Interval (days)	
			Study Day	Follow-up Day
Baseline (Week 0)	Study Day:	1	-35 – 1	
Week 1	Study Day:	8	2 – 11	<29
Week 2	Study Day:	15	12 – 22	<29
Week 4	Study Day:	29	23 – 43	<29
Week 8	Study Day:	57	44 – 71	<29
Week 12	Study Day:	85	72 – 99	<29
Week 16	Study Day:	113	100 – 127	<29
Week 20	Study Day:	141	128 – 155	<29
Week 24	Study Day:	169	156 – 183	<29
Week 28	Study Day:	197	184 – 211	<29
Week 32	Study Day:	225	212 – 239	<29
Week 36	Study Day:	253	240 – 267	<29
Week 40	Study Day:	281	268 – 295	<29
Week 44	Study Day:	309	296 – 323	<29
Week 48	Study Day:	337	324 – 351	<29
Week 52	Study Day:	365	352 – 393	<29

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Table 9.5 NAPSI (for Subjects with Nail Psoriasis at Study Day 1)

Visit	Scheduled Study Day (days)		Time Interval (days)	
			Study Day	Follow-up Day
Baseline (Week 0)	Study Day:	1	-35 – 1	
Week 2	Study Day:	15	2 – 22	<29
Week 4	Study Day:	29	23 – 43	<29
Week 8	Study Day:	57	44 – 71	<29
Week 12	Study Day:	85	72 – 99	<29
Week 16	Study Day:	113	100 – 127	<29
Week 20	Study Day:	141	128 – 155	<29
Week 24	Study Day:	169	156 – 183	<29
Week 28	Study Day:	197	184 – 211	<29
Week 32	Study Day:	225	212 – 239	<29
Week 36	Study Day:	253	240 – 267	<29
Week 40	Study Day:	281	268 – 295	<29
Week 44	Study Day:	309	296 – 323	<29
Week 48	Study Day:	337	324 – 351	<29
Week 52	Study Day:	365	352 – 393	<29
Week 16 (WOCF)	Study Day:	113	2 – 127	<29
Week 52 (WOCF)	Study Day:	365	2 – 393	<29

Table 9.6 PHQ-8

Visit	Scheduled Study Day (days)		Time Interval (days)	
			Study Day	Follow-up Day
Baseline (Week 0)	Study Day:	1	-35 – 1	
Week 8	Study Day:	57	2 – 85	<29
Week 16	Study Day:	113	86 – 141	<29
Week 24	Study Day:	169	142 – 225	<29
Week 40	Study Day:	281	226 – 323	<29
Week 52	Study Day:	365	324 – 379	<29
Week 56	Study Day:			

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Table 9.7 C-SSRS

Visit	Scheduled Study Day (days)		Time Interval (days)	
			Study Day	Follow-up Day
Screening	Study Day:			
Baseline (Week 0)	Study Day:			
Week 2	Study Day:	15	2 – 36	<29
Week 8	Study Day:	57	37 – 85	<29
Week 16	Study Day:	113	86 – 141	<29
Week 24	Study Day:	169	142 – 225	<29
Week 40	Study Day:	281	226 – 323	<29
Week 52	Study Day:	365	324 – 379	<29
Week 56	Study Day:			

9.2.2.2 PK Samples

Plasma concentration data will be used as entered in the EDC/CRF according to the scheduled visit.

9.3 Derivation of Endpoints

9.3.1 Coprimary Efficacy Endpoints

9.3.1.1 sPGA 0/1 Response at Week 16

- sPGA 0/1 scores will be calculated for baseline and each post-baseline visit, based on the protocol Appendix 5.
- sPGA 0/1 responder at Week 16 is defined as a subject with 0 or 1 score at Week 16 and ≤ -2-point change from baseline for Week 16. Subjects with 0 or 1 score at baseline will be excluded from the analysis.

9.3.1.2 PASI-75 Response at Week 16

- PASI scores will be calculated for baseline and each post-baseline visit, based on the protocol Appendix 4. For the PASI scores, percent changes from baseline ([each post-baseline visit's value - baseline value] / [baseline value] x 100) will be calculated for each post-baseline visit.
- PASI 75 responder at Week 16 is defined as a subject with ≤ -75% percent change from baseline for Week 16.

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9.3.1.3 Strategy for Addressing Intercurrent Events

The expected intercurrent events (ICEs) prior to Week 16 are listed below:

- *Permanent treatment discontinuation due to AEs*
- *Permanent treatment discontinuation due to lack of efficacy*
- *Permanent treatment discontinuation due to other reasons*
- *Initiation of a protocol-prohibited medication/therapy that could improve psoriasis* (e.g., GPP or EP)

A composite strategy will be implemented to address these ICEs. Specifically, nonresponder imputation will be used for coprimary efficacy endpoints for subjects who permanently discontinue treatment prior to Week 16, initiate a protocol-prohibited therapies or procedures that could improve psoriasis during the first 16 weeks of treatment, or who have otherwise missing endpoint data at the specified timepoint. For example, even though subjects have available a coprimary efficacy endpoint data at Week 16, subjects with ICE(s) whose occurrence date is before the evaluation date of the coprimary efficacy endpoint will be treated as nonresponder.

ICEs are generally counted for a particular visit if they occur before the efficacy assessments at that visit. However, permanent treatment discontinuation occurring exactly one day before a visit is counted as an ICE from the next visit onward, since efficacy assessments are scheduled before dosing at each visit.

9.3.2 Secondary Efficacy Endpoints

(1) The following endpoints will be derived the same as the coprimary efficacy endpoints, including the strategy for addressing intercurrent events prior to Week 16 or 52.

- sPGA 0/1 response at Weeks 52
- Durable sPGA 0/1 response at both the Week 16 and Week 52 visits
- Enhanced sPGA response at Weeks 16 and 52
  - ✧ Proportion of subjects achieving an sPGA of clear (0) at Weeks 16 and 52
- PASI-75 response at Weeks 52
- PASI-90 response at Weeks 16 and 52
- PASI-100 response at Weeks 16 and 52
- Durable PASI-75 response at both the Week 16 and Week 52 visits
- Durable PASI-90 response at both the Week 16 and Week 52 visits

(2) The following endpoints will be derived the same as the coprimary efficacy endpoints, including the strategy for addressing intercurrent events prior to Week 16 or 52. All FAS subjects (especially subjects with 0 or 1 score at baseline) will be included from the analysis.

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- Simplified sPGA 0/1 response at Weeks 16 and 52
- Simplified durable sPGA 0/1 response at both the Week 16 and Week 52

(3) The following endpoints will be derived, based on the protocol Appendix 7.

- Scalp-specific Physician's Global Assessment (ssPGA) response at Weeks 16 and 52
  - ✧ Proportion of subjects achieving an ssPGA of absence of disease (0) or very mild disease (1) with a ≥2-point decrease from baseline at Weeks 16 and 52. This analysis will be performed only for subjects with a baseline ssPGA ≥3, baseline psoriasis scalp severity index (PSSI) ≥12, and scalp surface area (SSA) involvement ≥30%.
- Change from baseline in ssPGA at Weeks 16 and 52

(4) The following endpoint will be derived, based on the protocol Appendix 12.

- Proportion of Subjects Achieving A Physician's Global Assessment (PGA) of The Hands and/or Feet at Weeks 16 and 52
  - ✧ This endpoint is defined as a subject with clear (0) or almost clear (1) with a ≥2-point decrease from baseline at Weeks 16 and 52.
  - ✧ This analysis will be performed only for subjects with a baseline PGA of the hands and/or feet ≥3.

(5) The following endpoints will be derived, based on the protocol Appendix 16.

- Dermatology Life Quality Index (DLQI) response at Weeks 16 and 52
  - ✧ Proportion of subjects with a DLQI score of 0/1 at Weeks 16 and 52. This analysis will be performed only for subjects with a baseline DLQI score ≥2.
- Change from baseline in DLQI at Weeks 16 and 52

(6) The following endpoint will be derived, based on the protocol Appendix 13.

- Change from baseline in Nail Psoriasis Severity Index (NAPSI) at Weeks 16 and 52, among subjects with nail involvement at baseline
  - ✧ For Weeks 16, a composite strategy will be implemented to address the ICEs. Specifically, worst observation (prior to the occurrence of 1st ICE) carried forward (WOCF) will be used for this endpoint for subjects who permanently discontinue treatment prior to Week 16, initiate a protocol-prohibited therapies or procedures that could improve psoriasis during the first 16 weeks of treatment, or who have otherwise missing endpoint data at the specified timepoint. For example, even though subjects have available a NAPSI endpoint data at Week 16, subjects with ICE(s) whose occurrence date is before the evaluation date of this endpoint will be treated as worst observation (prior to the occurrence of 1st ICE).
  - ✧ For Weeks 52, a composite strategy will also be implemented to address the ICEs. Specifically, worst observation (prior to the occurrence of 1st ICE) carried forward

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(WOCF) will be used for this endpoint for subjects who permanently discontinue treatment, initiate a protocol-prohibited therapies or procedures that could improve psoriasis, or who have otherwise missing endpoint data at the specified timepoint.

(7) The following endpoint will be derived, based on the protocol Appendix 6.

- Change and percent change from baseline in BSA affected by psoriasis at Weeks 16 and 52

9.3.3 Secondary Efficacy Endpoints for Generalized Pustular Psoriasis

(1) The following endpoints will be derived, based on the protocol Appendix 9.

- Generalized Pustular Psoriasis Global Assessment (GPPGA) Pustulation Subscore response at Weeks 16 and 52
  - ✧ Proportion of subjects achieving a GPPGA Pustulation Subscore of no visible pustules (0) at Weeks 16 and 52
- GPPGA 0/1 response at Weeks 16 and 52
  - ✧ Proportion of subjects achieving a GPPGA of clear (0) or almost clear (1) at Weeks 16 and 52
- Enhanced GPPGA response at Weeks 16 and 52
  - ✧ Proportion of subjects achieving a GPPGA of clear (0) at Weeks 16 and 52

(2) The following endpoints will be derived, based on the protocol Appendix 10.

- Generalized Pustular Psoriasis Area and Severity Index (GPPASI)-75 response at Weeks 16 and 52
  - ✧ Proportion of subjects achieving ≥75% improvement from baseline in GPPASI score at Weeks 16 and 52

(3) The following endpoints will be derived, based on the protocol Appendix 11.

- Change from baseline in JDA severity score at Weeks 16 and 52

9.3.4 Other Endpoints

(1) The following endpoints will be derived, based on the protocol Appendix 17.

- Total Scores of PHQ-8

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9.4 Lists of Laboratory Tests

Table 9.8 Clinical Laboratory Tests

Laboratory testing	Tests included
Hematology	aPTT, HCT, Hgb, INR, MCH, MCHC, MCV, MPV, PLT, PT, RBC, WBC, and differentials (neutrophils, lymphocytes, monocytes, eosinophils, and basophils relative and absolute)
Chemistry	Albumin, alkaline phosphatase, ALT, AST, calcium, CPK, creatinine (enzymatic), GGT, glucose random, potassium, sodium, total bilirubin, direct bilirubin if total bilirubin >ULN, urea (BUN), uric acid
Urinalysis	Color, clarity, pH, specific gravity, bilirubin, glucose, ketones, leukocytes, nitrite, blood, protein, urobilinogen Quantitative analysis of albumin and creatinine as well as albumin:creatinine ratio Microscopic analysis (as required)
Fasting lipids	Cholesterol (total, LDL, and HDL), triglycerides (all fasting)
Others	
Hepatitis B (test once per month for the first 6 months and every 3 months thereafter)	HBV [HBsAg, anti-HBc, anti-HBs, hepatitis B virus DNA] (for subjects of the #3 and #5 types in Protocol Appendix 2 after initiation of study drug)
CRP	
Other screening tests	HCV [with reflex to HCV RNA if positive] HIV FSH levels (for female subjects only) Serum pregnancy test (beta-hCG) at screening or urine dipstick test at subsequent visits for subjects of childbearing potential Tuberculosis test (T-SPOT) Note: If required per guidelines, additional TB testing can be performed by local laboratory. TSH and reflex free T4 and T3 Calculated creatinine clearance

ALT: alanine aminotransferase; anti-HBc: antibody to hepatitis B core antigen; aPTT: activated partial thromboplastin time; AST: aspartate aminotransferase; beta-hCG: beta-human chorionic gonadotropin; BUN: blood urea nitrogen; CPK: creatine phosphokinase; CRP: C reactive protein; FSH: follicle-stimulating hormone; GGT: gamma-glutamyl transferase; HBsAg: hepatitis B surface antigens; HBV: hepatitis B virus; HCT: hematocrit; HCV: hepatitis C virus; HDL: high density lipoprotein; Hgb: hemoglobin; HIV: human immunodeficiency virus; INR: international normalized ratio; LDH: lactate dehydrogenase; LDL: low-density lipoprotein; MCH: mean corpuscular Hgb; MCHC: mean corpuscular Hgb concentration; MCV: mean corpuscular volume; MPV: mean platelet volume; PLT: platelets; PT: prothrombin time; RBC: red blood cell (count); T3: triiodothyronine; T4: thyroxine; TSH: thyroid stimulating hormone; ULN: upper limit of normal; WBC: white blood cell (count).

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9.5 Markedly Abnormal Values

Markedly Abnormal Values (MAVs) will be based on applicable Common Terminology Criteria for Adverse Events (CTCAE) grading or similar. The parameters to be analyzed for MAVs and the criteria of MAVs will be determined prior to the database lock of the study.

For each selected parameter, all evaluable data (i.e., non-missing data) obtained from Study Day 2 until Follow-up Day 28 will be classified as a Markedly Abnormal Value (MAV) or not. For each parameter and subject, classifications will be made according to the conditions (1) to (3) provided below. If there are criterion for lower and criterion for upper in one parameter, the lower and the upper criteria will be considered separately.

(1) A subject with at least one evaluable data after baseline that meets the MAV criteria will be classified as a subject with MAV.

(2) A subject who does not meet condition (1) and has at least one evaluable data after baseline that doesn't meet the MAV criteria will be considered as a subject without MAV.

(3) A subject who does not meet conditions (1) or (2) will be excluded from the analysis of MAV for that parameter.

9.6 Individual Subject Data Listings

The specification of individual subject data listings will be defined in a separate document.

9.7 Analysis Software

SAS (version 9.4)

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