An international, prospective, observational cohort study to assess patient treatment satisfaction, patient-reported outcomes, effectiveness, and safety of a fixed-dose combination of Calcipotriene/Betamethasone Dipropionate PAD cream in the treatment of mild-to-moderate plaque psoriasis of the scalp in adults (PRO-SCALP)

NIS STUDY PROTOCOL
Version 1.0

STUDY PROTOCOL

Title	**An international, prospective, observational cohort study to assess patient treatment satisfaction, patient-reported outcomes, effectiveness, and safety of a fixed-dose combination of Calcipotriene/Betamethasone Dipropionate PAD cream in the treatment of mild-to-moderate plaque psoriasis of the scalp in adults (PRO-SCALP).**
Protocol identifier	M-22201-41
Date of last version of protocol	Version 1.0, 9 January, 2023
EU PAS register number	N/A
Active substances	Calcipotriene/Betamethasone Dipropionate PAD cream
Medicinal products	Wynzora®
Marketing authorisation holder	Almirall, S.A. Ronda General Mitre, 151 08022 Barcelona, Spain.
Joint PASS	No
Research question and objectives	To assess treatment satisfaction, quality of life, treatment preference, adherence and convenience, psychosocial effects of scalp psoriasis, sleep quality, and effectiveness, and safety of Calcipotriene/Betamethasone Dipropionate PAD cream in a real-world setting.
Countries of study	Germany, Spain, and the United Kingdom.
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2 List of Abbreviations

List of main abbreviations used in the study protocol

Abbreviations	*Definitions*
ADR	Adverse Drug Reaction
AE	Adverse Event
BDP	Betamethasone dipropionate
CAL	Calcipotriene
CI	Confidence Interval
CRO	Contract Research Organization
CUSP-Q	Cream Usability in Scalp Psoriasis Questionnaire
DM	Data Management
DMP	Data Management Plan
DVP	Data Validation Plan
eCRF	electronic Case Report Form
EDC	Electronic Data Capture
EOS	End of Study
ETV	Early Termination Visit
EU PAS	European Union Post-Authorization Studies
FAS	Full Analysis Set
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
ICMJE	International Committee of Medical Journal Editors
IEC	Independent Ethics Committee
MedDRA	Medical Dictionary for Regulatory Activities
MMAS-4	Morisky Medication Adherence Scale - 4 items
NIS	Non-Interventional Study
PGA	Physician’s Global Assessment
PPQ	Patient Preference Questionnaire
PRO	Patient Reported Outcomes
PSY-SCALP	Psychosocial Effects of Scalp Psoriasis Questionnaire
Q1	First Quartile
Q3	Third Quartile
Q4	Fourth Quartile

QoL	Quality of life
SAE	Serious Adverse Event
SADR	Serious Adverse Drug Reaction
SAP	Statistical Analysis Plan
SD	Standard Deviation
S-mPASI	Scalp modified Psoriasis Area and Severity Index
SmPC	Summary of Product Characteristic
SOP	Standard Operating Procedures
TSQM	Treatment Satisfaction Questionnaire Medication
UK	United Kingdom
VAS	Visual Analog Scale
WHO	World Health Organization
WI-NRS	Worst Itch Numerical Rating Scale

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4 Abstract

Title

An international, prospective, observational cohort study to assess patient treatment satisfaction, patient-reported outcomes, effectiveness, and safety of a fixed-dose combination of Calcipotriene/Betamethasone Dipropionate PAD cream in the treatment of mild-to-moderate plaque psoriasis of the scalp in adults (PRO-SCALP).

Investigators

A Site Investigator will be nominated at each investigational site. The investigator names and investigational sites will be detailed in the Clinical Study Report.

Study countries and sites

Countries: Germany, Spain, and the UK.

Study sites: Up to 60, across three countries.

Type of study

Non-interventional study (NIS).

Rationale and background

The scalp is one commonly affected region of the body in psoriasis, with a prevalence of about 40-50% and presents a significant burden to patients due to the difficult-to treat nature of this area and the difficulties in administering treatment [1-4]. Psoriasis, especially with involvement of the scalp, can lead to significant psychosocial impairment. Due to the presence of hair, poor accessibility, and unacceptable cosmetic appeal of topical therapy, patients also tend to have poor adherence and satisfaction with treatment. Effective therapeutic regimens for scalp psoriasis are essential to improving the quality of life (QoL) of patients [1].

Calcipotriene and betamethasone dipropionate (50 microgram/g CAL and 0.64 mg/g BDP, equivalent to 0.5 mg/g of betamethasone) cream (CAL/BDP cream – Wynzora® cream) is based on PAD Technology enabling development of an easy to apply, aqueous cream of CAL and BDP, despite their known pH-related instability when combined in the presence of water [5,6].

In a phase 3 clinical trial CAL/BDP PAD cream demonstrated high Physician's Global Assessment (PGA) treatment success and satisfaction, fast onset of action and a favourable safety profile in patients with scalp psoriasis [6].

This prospective observational study will evaluate treatment satisfaction, QoL, preference, adherence, convenience, psychosocial effects of scalp psoriasis and sleep quality, effectiveness, and safety of CAL/BDP PAD cream in the treatment of adult patients with mild-to-moderate scalp psoriasis in a real-world setting.

Research objectives

Primary objective:

- To assess patient satisfaction with CAL/BDP PAD cream, using the Treatment Satisfaction Questionnaire TSQM-9.

Secondary objectives:

- To assess QoL among patients treated with CAL/BDP PAD cream using the Scalpdex questionnaire.
- To assess effectiveness of CAL/BDP PAD cream, measured by Physician Global Assessment of the psoriasis on the Scalp (Scalp PGA).
- To assess effectiveness of CAL/BDP PAD cream, measured in terms of patient-reported worst level of scalp itching due to psoriasis experienced in the last week, using Worst Itch Numerical Rating Scale (WI-NRS).

Additional objectives:

- To assess effectiveness of CAL/BDP PAD cream in terms of disease severity, using Scalp modified Psoriasis Area and Severity Index (S-mPASI).
- To describe treatment convenience of CAL/BDP PAD cream in routine clinical practice using the Cream Usability in Scalp Psoriasis Questionnaire (CUSP-Q).
- To describe patient treatment preference between CAL/BDP PAD cream versus previous topical treatment used for treatment of scalp psoriasis through the Patient Preference Questionnaire (PPQ).
- To assess patient adherence to CAL/BDP PAD cream treatment according to medication adherence (Morisky Medication Adherence Scale 4 items (MMAS-4)), and patient's self-reported adherence (self-reported VAS).
- To describe the sleep quality associated with CAL/BDP PAD cream treatment in routine clinical practice through a two-item questionnaire about sleep quality according to own patient's perception.
- To describe the psychosocial effects of scalp psoriasis, using Psychosocial Effects of Scalp Psoriasis Questionnaire (PSY-SCALP).
- To assess physician satisfaction with CAL/BDP PAD cream.
- To assess safety and tolerability of CAL/BDP PAD cream in routine clinical practice up to 8 weeks of treatment.

Study design

This is an international, prospective, observational, multicentre study to assess the satisfaction of adult patients with mild-to-moderate plaque psoriasis of the scalp with a fixed-dose combination of CAL/BDP PAD cream (Wynzora®) under real-life conditions.

It is planned to include 300 patients. In this study, CAL/BDP PAD cream will be prescribed according to Summary of Product Characteristic (SmPC). Special care must be taken that the decision to prescribe the treatment will be made independently and prior to the decision to include the patient in the study, meaning that CAL/BDP PAD cream prescription to a patient will not be decided in advance by the study protocol but will be done within current clinical practice, thus the prescription of CAL/BDP PAD cream will be clearly separated from the decision to include the patient in the study. No additional diagnostic or monitoring procedures will be applied to the patients. Assessments aligned with those usually performed in the routine clinical practice are planned. A follow-up of up to

8 ± 4 weeks for each recruited patient will be performed.

Estimated Visit Schedule:

In this study, the visit schedule is not defined by the study protocol but is driven by routine clinical practice according to SmPC.

Data will be collected at study inclusion (Baseline Visit) and approximately at 8 ± 4 weeks after treatment initiation (as per clinical practice) or at the time of CAL/BDP PAD cream treatment discontinuation, whichever occurs earlier. Information regarding any unscheduled visit within the observation period due to early disease control, worsening of psoriasis or tolerability problems will be collected at the time of follow-up visit close to Week 8 ± 4 weeks (end of study (EOS) visit).

See Table 1 for more details about data collection schedule.

Study duration:

Duration of the study will be approximately 24 months, across three countries. Individual patient study observation period will be up to 8-12 weeks.

Sub-study (only in 3 selected study sites taking photographs per standard of psoriasis treatment):

All patients from sites taking photographs (approx. 30 patients from three selected sites [1 site each from Germany, Spain, and UK; approx. 10 patients per site]) will be asked to participate in the sub-study. In this subgroup, in addition to the rest of the study assessments, photographs of the scalp psoriasis-treated areas will be taken at baseline and approximately after 4 and 8 weeks of treatment start. The sub-study week-4 timepoint will be considered within an interval of approximately ± 1 weeks and the week-8 timepoint interval will correspond to the main study follow-up visit of 8 ± 4 weeks (EOS visit).

Study population

It is planned to include 300 patients with mild-to-moderate plaque psoriasis of the scalp at up to 60 sites from three countries: Germany, Spain, and the UK.

Patient recruitment:

Recruitment will be consecutive, to avoid selection bias. All patients fulfilling all selection criteria at the site during the study period will be offered to participate in the study.

Selection Criteria

Patients will be enrolled if all inclusion and none of the exclusion criteria are met, corresponding to the following criteria:

Inclusion Criteria:

1. Adult (≥18 years) male or female patients with mild-to-moderate plaque psoriasis of the scalp (defined as scalp-PGA score of 2 or 3 at baseline) with or without involvement of the trunk and limbs, and who may or may not have been previously treated (treatment-naive patients) with other anti-psoriatic therapies.
2. Patients who have been prescribed CAL/BDP PAD cream (Wynzora®) treatment to manage plaque psoriasis of the scalp according to SmPC in routine clinical practice.

3. Willingness and ability to participate in the study; patients must give their written consent to participate.

Exclusion Criteria:

1. Patients with severe plaque psoriasis, per physician global assessment.
2. Patients with erythrodermic, exfoliative or pustular psoriasis.
3. Patients previously treated with systemic drugs for psoriasis (conventional or biologic) within the last 12 weeks prior to inclusion.
4. Concomitant systemic treatment with anti-psoriatic drugs.
5. Concomitant treatment of any type for plaque psoriasis of the scalp.
6. Hypersensitivity to the active substances or to any of the excipients of CAL/BDP PAD cream (Wynzora®).
7. Patients with known disorders of calcium metabolism.
8. Patients with viral (e.g., herpes or varicella) lesions of the skin, fungal or bacterial skin infections, parasitic infections, skin manifestations in relation to tuberculosis, perioral dermatitis, atrophic skin, striae atrophicae, fragility of skin veins, ichthyosis, acne vulgaris, acne rosacea, rosacea, ulcers, and wounds.
9. Pregnant or breastfeeding women, except when the potential benefit justifies the potential risk.
10. Patients unable to comply with the requirements of the study or who in the opinion of the study physician should not participate in the study.
11. Patients for whom medical chart is inaccessible to physicians to complete baseline data collection.

Study treatment

Patients will be treated with CAL/BDP PAD cream (Wynzora®) monotherapy according to SmPC in routine clinical practice settings.

Per study inclusion/exclusion criteria, concomitant treatments for plaque psoriasis of the scalp are not allowed during the study observation period. In case of presence of plaque psoriasis in parts of the body other than the scalp, patients may be treated with relevant non-systemic treatments that the investigator considers to be the best treatment option for each included patient.

Duration of treatment

Up to 8 weeks. Treatment should be discontinued when control is achieved. If it is necessary treatment should be continued only after medical review and under regular medical supervision.

Duration of patient participation in the study (Study observation period)

Study observation period will be approximately 8 ± 4 weeks. The EOS visit will occur at approximately 8 ± 4 weeks after treatment initiation, or when the patient discontinues the treatment due to disease control, whichever occurs earlier. If a patient discontinues treatment, or if the physician decided to prolong treatment beyond 8-weeks, this data will be recorded in the eCRF. Patients who will discontinue treatment due to disease control (per clinician assessment) will not be considered as premature discontinuation of the study and will be considered as patient who completed the study.

In case of CAL/BDP PAD cream discontinuation due to reasons other than disease control before the week-8 follow-up visit or the maximum allowed treatment period as per clinical practice, whichever comes earlier, EOS visit will be completed as an Early Termination Visit (ETV), and the patients will be withdrawn from study. In case of premature study withdrawal for any other reason (not CAL/BDP PAD cream discontinuation), site investigator will make every effort to gather effectiveness and safety information associated with CAL/BDP PAD cream and complete eCRF at ETV. If it is not feasible to complete ETV, clinician will complete eCRF at the originally planned EOS visit timeframe.

Variables

- Demographics and baseline clinical disease characteristics:
  - Age, gender, race/ethnicity, smoking status, alcohol intake, height/weight, amount of hair on the scalp.
  - Medical history, incl. concomitant medications (for psoriasis and comorbidities).
- Physician's assessments:
  - Scalp-PGA at baseline, week 4 (only in sites taking photographs) and EOS visit.
  - S-mPASI at baseline, week 4 (only in sites taking photographs) and EOS visit.
  - Physician satisfaction with CAL/BDP PAD cream at EOS visit.
- Patient's questionnaires (to be completed at *EOS visit* [or when disease control is achieved, if earlier], and at baseline when indicated [*]):
  - TSQM-9 (9 items), WI-NRS (1 item)*, Scalpdex questionnaire (23 items)*.
  - PPQ (5 items, related to topical treatments).
  - MMAS-4 (4 items), Self-Reported VAS for treatment adherence (1 item).
  - CUSP-Q (9 items), Sleep quality questionnaire (2 items)*, PSY-SCALP (11 items)*.
- Safety and tolerability parameters: physical examination, and documentation of (S)AEs, (S)ADRs, maternal/paternal pregnancy exposure and other special situations (definition of special situation provided in Section 10).

Data sources

The study is based on primary data collection directly from healthcare professionals (Investigators) and patients. Investigators will collect data using electronic Case Report Form (eCRFs) that are specifically designed for this study. Patients will be separately asked to complete the study questionnaires in electronic format using a mobile App. Completion of eCRF for individual patients by the investigator will signify the electronic approval of respective patients at their study site.

Study size

A total of 300 study-eligible adult patients with mild-to-moderate plaque psoriasis of the scalp will be included. No formal sample size calculation was performed. According to feasibility considerations, assuming 20% of patients with missing data for the primary analysis due to data unavailability, or dropout, we estimate the achievable precision of the primary endpoint on 240 patients.

Data analysis

There will be two analysis populations in this study:

- Safety population: all patients for whom it is known that they had at least one CAL/BDP PAD cream application during the study observation period.
- Full Analysis Set (FAS): all those patients in the safety population that had at least one post-baseline assessment for primary endpoint.

No formal statistical hypotheses will be established. Categorical variables will be summarised with number (n) and percentages (%) of cases. For continuous variables, the number of non-missing observations (n), mean, standard error (SE) of the mean, standard deviation (SD), 95% confidence interval (CI) of the mean, median, first (Q1) and third (Q3) quartiles, minimum (min) and maximum (max) will be calculated. When applicable, these summaries will be provided by visit. Additionally, for changes from baseline, 95% confidence interval (CI) for the mean value will be calculated.

All safety outcomes will be assessed on the Safety population. The primary, secondary and additional endpoints (except safety assessments) will be assessed on the FAS population. An intermediate analysis of the primary objective, secondary and selected additional objectives (as will be outlined in SAP) will be performed once the first 150 patients have completed the study. A more detailed description of the statistical methods will be provided in the statistical analysis plan (SAP). The SAP will include the shell tables to be used for the data analyses.

Primary Endpoint:

- Absolute TSQM-9 effectiveness, convenience, and global satisfaction domain scores at end of study observation period.

Secondary Endpoints:

- Absolute symptoms, emotions, and functioning scores of the Scalpdex questionnaire at end of study observation period.
- Proportion of patients achieving scalp-PGA treatment success* at week 4 (if applicable) and at end of study observation period.
- Absolute scalp WI-NRS score at Baseline and at end of study observation period.

*Scalp-PGA treatment success is defined as a scalp-PGA score of 0 (clear) or 1 (almost clear) and with a minimum 2 points improvement from baseline, on the scalp.

Additional Endpoints:

- Change from baseline in the absolute symptoms, emotions, and functioning scores of the Scalpdex questionnaire at end of study observation period.
- Absolute PPQ score at end of study observation period.
- Proportion of patients achieving scores of 2 (agree) or 3 (strongly agree) for each item of the PPQ at end of study observation period.
- Absolute scalp PGA score at all visits and change from baseline in the absolute scalp PGA score at week 4 (if applicable) and at end of study observation period.

- Time to scalp-PGA treatment success*.
- Proportion of patients achieving scalp PGA treatment score of 0 [clear] or 1 [almost clear] at week 4 (if applicable) and at end of study observation period.
- Absolute S-mPASI score at all visits and change from baseline in the absolute S-mPASI score at week 4 (if applicable) and at end of study observation period.
- Proportion of patients with a reduction of at least 75% in S-mPASI score from baseline to week 4 (if applicable) and at end of study observation period (S-mPASI 75).
- Change from baseline in the absolute scalp WI-NRS score at end of study observation period.
- Proportion of patients achieving a scalp WI-NRS score of <3 at end of study observation period, in those patients with a minimum scalp WI-NRS score of 3 at baseline.
- Proportion of patients obtaining a minimum 4-point improvement in scalp WI-NRS at end of study observation period, in those patients with a minimum scalp WI-NRS score of 4 at baseline.
- Absolute CUSP-Q scores (overall and for each item) at end of study observation period.
- Absolute MMAS-4 score at end of study observation period.
- Proportions of patients scoring 0 (high adherence), 1-2 (intermediate adherence), and 3-4 (low adherence) in the MMAS-4 at end of study observation period.
- Absolute self-reported VAS for treatment adherence score at end of study observation period.
- Proportion of patients with sleep affected due to scalp psoriasis ≥3 days per week at baseline and at end of study observation period.
- Proportion of patients sleeping well (defined as: “very well” and “rather well”) at baseline and at end of study observation period.
- Absolute PSY-SCALP scores (overall and for each item) at baseline and at end of study observation period.
- Frequency of responses to individual items of the PSY-SCALP Questionnaire, at baseline and at end of study observation period.
- Change from baseline in PSY-SCALP score, according to questions 2 and 3 of the PSY-SCALP questionnaire (collected at baseline) and corresponding questions 5 and 6 (collected at end of study observation period), at end of study observation period.
- Absolute physician satisfaction scores for effectiveness, convenience, and global satisfaction domains at end of study observation period.
- Incidence of SAEs, SADRs, maternal/paternal pregnancy exposure and other special situations during study observation period.

**Scalp-PGA treatment success is defined as a scalp-PGA score of 0 (clear) or 1 (almost clear) and with a minimum 2 points improvement from baseline, on the scalp.*

5 Amendments and Updates

Not applicable

6 Rationale and Background

Psoriasis is a chronic inflammatory, immune-mediated skin disease, which affects 2-4% of the population in Europe [7-8] and has a substantial impact on patients' quality of life (QoL) in different degree of severity, including physical, psychologic, social, sexual, and occupational elements [9-10]. Psoriasis is triggered probably by environmental factors in genetically predisposed individuals and sustained by a dysfunctional immune system [11]. Psoriasis vulgaris, also known as plaque psoriasis, is the most common form of the disease, affecting around 80-90% of patients diagnosed and it is characterised by well-defined, sharply demarcated, erythematous plaques [12].

The scalp is one commonly affected region of the body in psoriasis, with a prevalence of about 40-50% and presents a significant burden to patients due to the difficult-to treat nature of this area and the difficulties in administering treatment [1-4]. Scalp psoriasis is characterized by thickened red plaques with silver-white scale, contained within the hairline or extending to the forehead, ears, and back neck [13]. Importantly, scalp psoriasis presents a significant moderate-to-high burden to patients due to the scalp difficult-to treat nature and treatment administration difficulties [1,14]. In addition, psoriasis, especially with scalp involvement, can lead to significant psychosocial impairment and lower QoL related to the highly visible site of the lesions despite limited skin involvement [15,16]. Due to the presence of hair, poor accessibility, and unacceptable cosmetic appeal of topical therapy, patients with scalp psoriasis tend to have poor treatment satisfaction and adherence [17,18]. Therefore, effective therapeutic regimens for scalp psoriasis are essential in order to improve QoL and treatment satisfaction of patients.

Different scales and scores are used to assess psoriasis severity. The Physician's Global Assessment (PGA), sometimes referred to as the Investigator's Global Assessment (IGA), has been the measure used most frequently after the Psoriasis Area and Severity Index (PASI) [19]. The PGA/IGA is a simple instrument of 5-point ordinal scale used to assess the severity of disease over the body: global, scalp, palmoplantar and nails, ranging from 0 (clear; no symptoms) to 4 (severe) for global, scalp and palmoplantar assessment, being psoriasis of mild severity when PGA = 2 and of moderate severity when PGA = 3 [20].

Psoriasis treatment is still based on controlling the symptoms [10]. Topical therapy is the first-line treatment for patients with mild-to-moderate psoriasis [12,21]. Several classes of topical therapy exist in a variety of formulations and modalities (i.e., creams, ointments, gels and foams) including retinoids, vitamin D derivatives, topical corticosteroids, calcineurin inhibitors, dithranol, tar-based preparations, and combination therapies [22]. However, in patients who do not achieve a good disease control, topical therapies can be combined with phototherapy or systemic conventional or biologic therapies when topical treatment alone is not treating adequately psoriasis [23].

Calcipotriene and betamethasone dipropionate (50 microgram/g CAL and 0.64 mg/g BDP, equivalent to 0.5 mg/g of betamethasone) cream (CAL/BDP PAD cream – Wynzora® cream) is based on PAD Technology enabling development of an easy to apply, aqueous cream of CAL and BDP, despite their known pH-related instability when combined in the presence of water [5,6]. The CAL/BDP combination is recommended as first-line treatment of mild-to-moderate plaque psoriasis by many European, Canadian, and American guidelines and associations of dermatology [24-27]. In a phase 3 clinical trial CAL/BDP PAD cream demonstrated high PGA treatment success and satisfaction, fast onset of action and a favourable safety profile in patients with scalp psoriasis [6]. CAL/BDP combination has been shown to be superior to their single constituents alone and it also

permits a once-daily application, leading to an increased treatment adherence [28].

RATIONALE:

As stated above, the scalp is one of the most commonly affected region of the body in psoriasis presenting a significant burden to patients due to the difficult-to treat nature of this area and the difficulties in administering treatment and leading to significant psychosocial impairment. Due to the presence of hair, poor accessibility, and unacceptable cosmetic appeal of topical therapy, patients also tend to have poor adherence and satisfaction with treatment. Effective therapeutic regimens for scalp psoriasis are essential to improve QoL of patients [1].

In order to properly evaluate the effect of CAL/BDP PAD cream (Wynzora®) in the clinical practice in this short-term study (8 weeks), the patient will be asked not to have received systemic treatment for psoriasis before starting CAL/BDP PAD cream for a period of time that will depend on the pharmacokinetic and pharmacodynamic properties of the previous systemic treatments for psoriasis.

Previous data on other topical therapies or CAL/BDP combinations have shown improvements on treatment satisfaction and convenience. Clobetasol 0.05% lotion treatment demonstrated high user convenience and treatment satisfaction rate in patients with scalp psoriasis [29]. CAL/BDP foam has shown a high level of satisfaction with effectiveness and convenience in plaque psoriasis patients, including scalp psoriasis, and in those who had received previous treatments, it has been reported higher preference for CAL/BDP foam compared to previous topical treatments [30].

In phase 3 trials, the CAL/BDP PAD cream has shown high PGA treatment success and satisfaction, a good efficacy, and a favourable safety profile in patients with scalp psoriasis [2] and allows once-daily application, leading to an increased treatment adherence [23] but no data of this new formulation is available in a real-world setting.

Thus, the present observational, non-interventional study (NIS) proposes to evaluate treatment satisfaction of CAL/BDP PAD cream in the treatment of adult patients with mild-to-moderate scalp psoriasis in a real-world setting. In addition, the present study is planned to investigate QoL, preference, adherence, treatment convenience, sleep quality and psychosocial effects on this profile of patients treated with CAL/BDP PAD cream. At last, this study will also assess the CAL/BDP PAD cream effectiveness, safety, and tolerability in a real-world setting.

7 Research Question and Objectives

To assess treatment satisfaction, QoL, preference, adherence, convenience, sleep quality, psychosocial effects of scalp psoriasis, effectiveness, and safety of CAL/BDP PAD cream in a real-world setting.

7.1 Primary Objective

- To assess patient satisfaction with CAL/BDP PAD cream, using the Treatment Satisfaction Questionnaire TSQM-9.

7.2 Secondary Objectives

- To assess QoL among patients treated with CAL/BDP PAD cream using the Scalpdex questionnaire.
- To assess effectiveness of CAL/BDP PAD cream, measured by Physician Global Assessment of the psoriasis on the Scalp (Scalp PGA).
- To assess effectiveness of CAL/BDP PAD cream, measured in terms of patient-reported worst level of scalp itching due to psoriasis experienced in the last week, using Worst Itch Numerical Rating Scale (WI-NRS).

7.3 Additional Objectives

- To assess effectiveness of CAL/BDP PAD cream in terms of disease severity, using Scalp modified Psoriasis Area and Severity Index (S-mPASI).
- To describe treatment convenience of CAL/BDP PAD cream in routine clinical practice using the Cream Usability in Scalp Psoriasis Questionnaire (CUSP-Q).
- To describe patient treatment preference between CAL/BDP PAD cream versus previous topical treatment used for treatment of scalp psoriasis through the Patient Preference Questionnaire (PPQ).
- To assess patient adherence to CAL/BDP PAD cream treatment according to medication adherence (Morisky Medication Adherence Scale 4 items (MMAS-4)), and patient's self-reported adherence (self-reported VAS).
- To describe the sleep quality associated with CAL/BDP PAD cream treatment in routine clinical practice through a two-item questionnaire about sleep quality according to own patient's perception.
- To describe the psychosocial effects of scalp psoriasis, using Psychosocial Effects of Scalp Psoriasis Questionnaire (PSY-SCALP).
- To assess physician satisfaction with CAL/BDP PAD cream.
- To assess safety and tolerability of CAL/BDP PAD cream in routine clinical practice up to 8 weeks of treatment.

8 Research Methods

8.1 Study Design

This is an international, prospective, observational, multicentre study to assess the satisfaction of adult patients with mild-to-moderate plaque psoriasis of the scalp with a fixed-dose combination of CAL/BDP PAD cream under real-life conditions (PRO-SCALP). The main objective of this study is to assess the patient satisfaction with CAL/BDP PAD cream in a real-life setting.

It is planned to include 300 patients with mild-to-moderate plaque psoriasis of the scalp at up to 60 study sites in three countries: Germany, Spain, and the United Kingdom (UK). Sites will be hospitals or outpatient offices where patients with mild-to-moderate plaque psoriasis of the scalp are usually managed. The participating physicians will be dermatologists or general practitioners with extended roles (specialised in dermatology).

In this study, CAL/BDP PAD cream will be prescribed according to Summary of Product Characteristics (SmPC). Special care must be taken that the decision to prescribe the treatment will be made independently and prior to the decision to include the patient in the study, meaning that CAL/BDP PAD cream prescription to a patient will not be decided in advance by the study protocol but will be done within current clinical practice, thus the prescription of CAL/BDP PAD cream will be clearly separated from the decision to include the patient in the study. No additional diagnostic or monitoring procedures will be applied to the patients. No different assessments than those usually performed in the routine clinical practice are planned. It is planned to carry out a follow-up of up to 8-12 weeks for each patient included in the study.

Data collection will begin when the clinician consents and recruits study eligible patients at respective sites. The data collection will be conducted by the site investigator or collaborators. Each patient will be followed for approximately 8 $\pm$ 4 weeks (2 planned study visits: baseline visit, and end of study visit (EOS visit; at 8 $\pm$ 4 weeks), or until the time of CAL/BDP PAD cream treatment discontinuation, whichever occurs earlier. Individual patient study observation period will thus be up to 8-12 weeks.

The study is sponsored by Almirall S.A. and managed by Avant Health, LLC, a Contract Research Organization (CRO) working on behalf of Almirall. No patient-identifying information will be transferred to the Sponsor nor the study CRO.

Sub-study

All patients from sites taking photographs (30 patients from three selected sites [1 site each from Germany, Spain, and UK; 10 patients per site]) will be asked to participate in the sub-study. In this subgroup, in addition to the rest of the study assessments, photographs of the scalp psoriasis-treated areas will be taken at baseline and approximately after 4 and 8 weeks of treatment start. The sub-study week-4 timepoint will be considered within an interval of approximately ± 1 weeks and the week-8 timepoint interval will correspond to the main study follow-up visit of 8 ± 4 weeks (EOS visit).

Patient recruitment

Recruitment will be consecutive in each study site, to avoid selection bias. All patients fulfilling all selection criteria at the study site during the study period will be offered to participate in the study.

After patient identification and confirmation that they are eligible for the study per selection criteria,

the patient's informed consent will be obtained, according to local ethics requirements.

8.2 Setting

The present study is designed to collect data from 300 patients treated with CAL/BDP PAD cream (Wynzora®) according to SmPC in routine clinical practice. During the treatment period, it is planned to collect data at approximately 4 weeks (only in sites taking photographs, as part of sub-study) and 8 ± 4 weeks after starting CAL/BDP PAD cream treatment, following routine clinical practice. The decision of investigator of starting CAL/BDP PAD cream treatment must be independent of the inclusion of the patient in the present study. No different assessments and monitoring procedures than those usually performed in the routine clinical practice are planned.

8.2.1 Selection Criteria

Patients will be enrolled if all inclusion and none of the exclusion criteria are met, corresponding to the following criteria:

8.2.1.1 Inclusion Criteria

1. Adult (≥18 years) male or female patients with mild-to-moderate plaque psoriasis of the scalp (defined as PGA score of 2 or 3 at baseline) with or without involvement of the trunk and limbs, and who may or may not have been previously treated (treatment-naive patients) with other anti-psoriatic therapies.
2. Patients who have been prescribed CAL/BDP PAD cream (Wynzora®) treatment according to SmPC in routine clinical practice.
3. Willingness and ability to participate in the study; patients must give their written consent to participate.

8.2.1.2 Exclusion Criteria

1. Patients with severe plaque psoriasis, per physician global assessment.
2. Patients with erythrodermic, exfoliative or pustular psoriasis.
3. Patients previously treated with systemic drugs for psoriasis (conventional or biologic) within the last 12 weeks prior to inclusion.
4. Concomitant systemic treatment with anti-psoriatic drugs.
5. Concomitant treatment of any type for plaque psoriasis of the scalp.
6. Hypersensitivity to the active substances or to any of the excipients of CAL/BDP PAD cream (Wynzora®).
7. Patients with known disorders of calcium metabolism.
8. Patients with viral (e.g., herpes or varicella) lesions of the skin, fungal or bacterial skin infections, parasitic infections, skin manifestations in relation to tuberculosis, perioral dermatitis, atrophic skin, striae atrophicae, fragility of skin veins, ichthyosis, acne vulgaris, acne rosacea, rosacea, ulcers, and wounds.
9. Pregnant or breastfeeding women, except when the potential benefit justifies the potential risk.
10. Patients unable to comply with the requirements of the study or who in the opinion of the

study physician should not participate in the study.

11. Patients for whom medical chart is inaccessible to physicians to complete baseline data collection.

8.2.2 Description of Treatment

CAL/BDP PAD cream (Wynzora®) will be administrated as monotherapy according to SmPC and as per routine clinical practice.

CAL/BDP PAD cream should be applied to affected areas of the scalp once daily. The recommended treatment period is up to 8 weeks. Treatment should be discontinued when control is achieved. If it is necessary to continue or restart treatment after this period, treatment should be continued only after medical review and under regular medical supervision.

When using calcipotriol containing medicinal products, the maximum daily dose should not exceed 15 g. The body surface area treated with calcipotriol containing medicinal products should not exceed 30%. Patients have to rub in the cream thoroughly in a thin layer. CAL/BDP PAD cream should not be applied directly to the face or eyes. In order to achieve optimal effect, it is not recommended to take a shower or bath, immediately after application of CAL/BDP PAD cream. It is recommended to allow 8 hours between the application and showering to avoid washing it off.

Per study inclusion/exclusion criteria, concomitant treatments for plaque psoriasis of the scalp are not allowed during the study observation period. In case of presence of plaque psoriasis in parts of the body other than the scalp, patients may be treated with relevant non-systemic treatments that the investigator considers to be the best treatment option for each included patient.

8.2.3 Description of Follow-up

CAL/BDP PAD cream (Wynzora®) treatment will be administered up to 8 weeks. Treatment should be discontinued when control is achieved. If it is necessary, treatment should be continued only after medical review and under regular medical supervision.

The end of the study follow-up will occur at the end of the study observation period, approximately 8 ± 4 weeks after treatment initiation, or when the patient discontinues the treatment, whichever occurs earlier. If a patient discontinues treatment, or if the physician decided to prolong treatment beyond 8-weeks, this data will be recorded in the eCRF.

8.2.4 Premature Discontinuation Criteria

Patients may withdraw their consent and discontinue their participation in this NIS at any time at their own request and without giving reasons, with no effect on their medical care or access to treatment.

If the study physician decides to withdraw the patient from the study, he/she will be asked to document the date and reason for the decision. Some potential reasons may encompass (not exclusively) patient experiencing (S)AE, (s)ADR. maternal/paternal pregnancy exposure, lack of drug effectiveness, or patient lost to follow-up. Reasons for premature study withdrawal/discontinuation will be documented in the eCRF.

Patients who will discontinue treatment due to disease control (per clinician assessment) prior to 8-week treatment course will not be considered as premature discontinuation of the study and will be considered as patient who completed the study.

If possible, patients who discontinue CAL/BDP PAD cream treatment and withdraw from the study prior to the end of the study observation period, and not due to disease control achievement, the EOS visit will be treated as an Early Termination Visit (ETV) and conducted as soon as possible after the treatment was discontinued. If it is not feasible to complete ETV sooner, clinician will complete eCRF at the originally planned EOS visit timeframe. All the assessments planned for the ETV (Section 8.4.1.2) should be completed, giving the date and primary reason for study withdrawal. In case of premature study withdrawal for any reason other than CAL/BDP PAD cream discontinuation, site investigator will make every effort to gather effectiveness and safety information associated with CAL/BDP PAD cream and complete eCRF at ETV. Patients who prematurely discontinue the treatment or withdraw his/her consent will not be replaced in the study.

In the case of premature treatment/study discontinuation due to an AE, the investigator should manage patient's condition per best clinical judgment, as part of usual care. Investigator should make every effort to collect and report information concerning the AE (e.g., causality, event duration and outcome), as requested in eCRF at EOS visit/ETV.

8.2.5 Premature Study Termination

This study may be suspended or prematurely terminated if there is sufficient reasonable cause. Written notification documenting the reason for study suspension or termination will be provided by the suspending or terminating party. If the study is prematurely terminated or suspended, the principal Investigator (and/or the CRO) will promptly inform the Independent Ethics Committees (IECs) and will provide the reason(s) for suspension or termination. For instance, a circumstance that may warrant termination is the determination of unexpected, significant, or unacceptable risk to patients.

8.3 Variables

8.3.1 Assessments

8.3.1.1 Demographics and Baseline Clinical Disease Characteristics

Demographics and baseline characteristics consist of those parameters that are assessed only at baseline: socio-demographics (e.g., age, gender, smoking status, alcohol intake), patient characteristics (e.g., routine physical examination: height/weight measurements, as available), medical history, and treatment history.

Medical History

For the documentation of the medical history, previous (documented at any juncture in the past) and concomitant (current) comorbidities at the time of baseline visit will be documented.

Psoriasis disease information gathered will include date of diagnosis of plaque psoriasis (first diagnosis) and localized areas at first diagnoses, date of involvement of the scalp (first diagnosis of scalp psoriasis) and baseline scalp psoriasis severity (according to scalp-PGA and s-mPASI at baseline, as discussed in section 9.3.1.2).

Relevant comorbidities (prior (ever) and current) will specifically assess:

1. Cardiac disorders: atrial fibrillation, cardiomyopathy, coronary artery disease
2. Gastrointestinal disorders: inflammatory bowel disease, Crohn's disease
3. Hepatobiliary disorders: non-alcoholic fatty liver disease
4. Metabolism and nutrition disorders: obesity, abdominal obesity, diabetes mellitus, dyslipidaemia, insulin resistance, metabolic syndrome
5. Musculoskeletal and connective tissue disorders: psoriatic arthritis
6. Nervous system disorders: cerebrovascular disease, ischemic stroke
7. Psychiatric disorders: anxiety disorder, depression
8. Respiratory, thoracic, and mediastinal disorders: pulmonary embolism
9. Renal and urinary disorders: chronic kidney disease, renal failure/insufficiency
10. Vascular disorders: deep vein thrombosis, hypertension, peripheral arterial disease
11. Other disorders, specify

Prior psoriasis medications

- Prior therapy for scalp and skin plaque psoriasis (topical, phototherapy, biologic, or non-biologic systemic treatment) most recently used prior to baseline visit will be collected, including, start and finish date, dose, reason of discontinuation.
- In case of therapies used to treat plaque psoriasis of the scalp alone, information related all topical treatments used within the past 12 months of baseline visit will be collected.

Concomitant medications

- Concomitant medication for plaque psoriasis in parts of the body other than the scalp (if any) and general medication for comorbidities currently used at baseline visit will be collected, including, start and finish date, dose, and frequency (if applicable/available).

Study medication

- CAL/BDP PAD cream start date, and number of tubes of medication used during the study.

8.3.1.2 Physicians' assessments

Scalp Modified Psoriasis Area and Severity Index (S-mPASI)

The S-mPASI scale is a modification of the original PASI used for assessing and grading the severity of scalp psoriatic lesions and their response to therapy [31,32]. S-mPASI should be documented at all visits.

The severity of the scalp psoriasis is calculated by scoring the signs of the disease (erythema, induration and scaling) on the scalp, each ranging from 0 = none to 4 = very severe, multiplied by an

area score for the extent of the disease (percentage of scalp involved with psoriasis), multiplied by a constant factor, 0.1, resulting in a range of 0 to 7.2.

The scale for estimating the area of involvement for scalp involved with psoriasis is:

0 = No scalp involvement

1 = <10% scalp involvement

2 = 10-29% scalp involvement

3 = 30-49% scalp involvement

4 = 50-69% scalp involvement

5 = 70-89% scalp involvement

6 = 90-100% scalp involvement

For more details, please refer to Appendix I, Section 13.1.

Scalp Physician's Global Assessment (Scalp-PGA)

The scalp PGA describes the severity of scalp psoriasis using 5 categories [33]. Scalp PGA should be documented at all visits.

The PGA of scalp psoriasis will be made on a 5-point scale, ranging from 0 to 4 as follows:

0 = none (clear)

1 = almost clear

2 = mild

3 = moderate

4 = severe

For more details, please refer to Appendix II, Section 0.

Physician Satisfaction with Medication

This questionnaire is intended to be completed by the physicians at the EOS visit or ETV in case of premature withdrawal.

This ad hoc satisfaction questionnaire is very similar to TSQM-9 and will be used to assess physician (Site Investigator) satisfaction with CAL/BPD PAD cream at EOS. The individual item and subscale scorings will be done similar to the original TSQM-9 questionnaire.

For more details on TSQM-9, please refer to Appendix IV, Section 0.

8.3.1.3 Patient-reported outcomes

Patients will complete their survey with the following PRO items using a mobile App and in local language.

WI-NRS

It is a self-administered scale to assess patients' worst level of itching on the scalp (in the last week). The scale has a single-item that describes the worst level of itching on the scalp due to psoriasis in the last week on an 11-point scale anchored at 0 (no itching) and 10 (worst itching imaginable) [34]. An WI-NRS <3 points represent mild pruritus [35].

WI-NRS should be completed by the patient at baseline and at the end of study observation period.

For more details, please refer to Appendix III, Section 0.

Treatment Satisfaction Questionnaire for Medication – 9 items (TSQM-9)

This questionnaire is intended to be completed by the patients at the EOS visit or ETV in case of premature withdrawal.

The TSQM-9 is a psychometrically robust and validated instrument to assess patients' satisfaction with the treatment they are receiving [36]. It is a self-administered questionnaire that measures patients' drug therapy satisfaction considering the last two or three weeks or since the last time the patient took the medication. It consists of 9 items distributed in 3 domains: effectiveness, convenience, and global satisfaction, with scores at each domain ranging from 0 to 100. Responses are measured on a Likert scale of 5 or 7 points. TSQM-9 higher scores represent higher satisfaction on that domain.

For more details, please refer to Appendix IV, Section 0.

Scalpdex questionnaire

This questionnaire is intended to be completed by the patients at baseline, and at the EOS visit or ETV in case of premature withdrawal.

Scalpdex is a scalp dermatitis-specific QoL instrument that can be used to determine which aspect of the disease most bothers the patient and to evaluate QoL as one variable of responsiveness to the therapeutic intervention [37]. It has 23 items, with possible answers scoring on a 5-point Likert-type scale ("never" = 0, "rarely" = 25, "sometimes" = 50, "often" = 75, and "all the time" = 100). The final scale scores (symptoms, emotions, and functioning) are calculated by the mean of the item scores pertaining to each scale. A lower score on symptoms, emotions, and functioning represents a better related-QoL for each scale.

For more details, please refer to Appendix V, Section 13.5.

Patient preference questionnaire (PPQ)

This questionnaire is intended to be completed by the patients at the EOS visit or ETV in case of premature withdrawal.

The PPQ is a 10-item instrument to assess patients' treatment preference [38,39]. It includes 5 items comparing with previous topical treatments and 5 items comparing with previous systemics. Each item is scored on a 4-point Likert-type scale (0 = strongly disagree, 1 = disagree, 2 = agree and 3 = strongly agree) and a supplementary option 'Does not apply to me'. Overall score ranges from 0 to 30. In this study, the 5 questions comparing with systemics will be excluded. Thus, overall score of 5-item PPQ will range from 0 to 15. The higher the score, the more preferred the current treatment

is (compared to previous topical treatment).

For more details, please refer to Appendix VI, Section 0.

Patient treatment adherence (MMAS-4 and self-reported VAS)

Patient adherence to treatment should be documented at the EOS visit or ETV in case of premature withdrawal. It will be assessed using two instruments:

Morisky Medication Adherence Scale, 4 items (MMAS-4)

The MMAS-4 is a patient self-reported, medication-taking behaviour scale in which the specific health issue (scalp psoriasis) is inserted for the “health concern”. It consists of four items with a scoring scheme of “Yes” = 1 and “No” = 0. The items are summed to give a range of scores from 0 to 4. A score of 0 indicates high adherence; a score of 1 or 2 indicates intermediate adherence; and a score of 3 or 4 indicates low adherence.

For more details, please refer to Appendix VII, Section 13.7.

Self-reported VAS for treatment adherence

Treatment adherence to CAL/BDP PAD cream will be assessed by the patients on visual analogue scale (VAS, 100 mm) where 0% represents the lowest possible adherence and 100% the highest possible adherence.

VAS for treatment adherence will be completed by the patient.

For more details, please refer to Appendix VIII, Section 13.8.

Patient treatment convenience: Cream Usability in Scalp Psoriasis Questionnaire (CUSP-Q)

The CUSP-Q is intended to be completed by the patients at EOS visit or ETV in case of premature withdrawal.

The CUSP-Q is a self-reported instrument to assess patients’ treatment convenience. It consists of ten items on an 11-point scale anchored at 0 (not at all) and 10 (very much). The items 3, 4, 5, 7, 8 are reverse scored questions.

For more details, please refer to Appendix IX, Section 13.9.

Sleep quality questionnaire

The sleep quality of patients is intended to be assessed at baseline and EOS visit or ETV in case of premature withdrawal.

It will consist of two questions to assess the sleep quality of the patients according to their own perception.

For more details, please refer to Appendix X, Section 13.10.

Psychosocial Effects of Scalp Psoriasis questionnaire (PSY-SCALP)

The PSY-SCALP is intended to be completed by the patients at baseline and EOS visit or ETV in case of premature withdrawal.

The questionnaire is a self-reported instrument to assess patients' feelings, self-esteem, hair style changes, and relationship and satisfaction with physician's care. It consists of 11 items (three questions at baseline and eight questions at EOS visit/Early Termination Visit) with possible answers "No", "A little", "Quite a lot", and "Very much". The baseline items 1 and 2, and EOS visit items 5 and 6 are reverse scored questions.

For more details, please refer to Appendix XI, Section 13.11.

8.3.1.4 Adverse Events (AE)

The Investigator will document the safety and tolerability of the CAL/BDP PAD cream as specified in section 11. Study patients' safety is the utmost priority of study clinicians/investigators.

In the case of premature treatment/study discontinuation due to safety or tolerability reasons (including lack of efficacy), the study investigator should make every effort to collect and report information concerning any observed AE, (S)AEs and (S)ADRs (e.g., causality, event duration and outcome), as requested in eCRF at all visits.

8.3.2 Endpoints

8.3.2.1 Primary Endpoint

- Absolute TSQM-9 effectiveness, convenience, and global satisfaction domain scores at end of study observation period.

8.3.2.2 Secondary Endpoints

- Absolute symptoms, emotions, and functioning scores of the Scalpdex questionnaire at end of study observation period.
- Proportion of patients achieving scalp-PGA treatment success* at week 4 (if applicable) and at end of study observation period.
- Absolute scalp WI-NRS score at Baseline and at end of study observation period.

*Scalp-PGA treatment success is defined as a scalp-PGA score of 0 (clear) or 1 (almost clear) and with a minimum 2 points improvement from baseline, on the scalp.

8.3.2.3 Additional Endpoints

- Change from baseline in the absolute symptoms, emotions, and functioning scores of the Scalpdex questionnaire at end of study observation period.
- Absolute PPQ score at end of study observation period.
- Proportion of patients achieving scores of 2 (agree) or 3 (strongly agree) for each item of the PPQ at end of study observation period.
- Absolute scalp PGA score at all visits and change from baseline in the absolute scalp PGA score at week 4 (if applicable) and at end of study observation period.
- Time to scalp-PGA treatment success*.
- Proportion of patients achieving scalp PGA treatment score of 0 [clear] or 1 [almost clear] at week 4 (if applicable) and at end of study observation period.

- Absolute S-mPASI score at all visits and change from baseline in the absolute S-mPASI score at week 4 (if applicable) and at end of study observation period.
- Proportion of patients with a reduction of at least 75% in S-mPASI score from baseline to week 4 (if applicable) and at end of study observation period (S-mPASI 75).
- Change from baseline in the absolute scalp WI-NRS score at end of study observation period.
- Proportion of patients achieving a scalp WI-NRS score of <3 at end of study observation period, in those patients with a minimum scalp WI-NRS score of 3 at baseline.
- Proportion of patients obtaining a minimum 4-point improvement in scalp WI-NRS at end of study observation period, in those patients with a minimum scalp WI-NRS score of 4 at baseline.
- Absolute CUSP-Q scores (overall and for each item) at end of study observation period.
- Absolute MMAS-4 score at end of study observation period.
- Proportions of patients scoring 0 (high adherence), 1-2 (intermediate adherence), and 3-4 (low adherence) in the MMAS-4 at end of study observation period.
- Absolute self-reported VAS for treatment adherence score at end of study observation period.
- Proportion of patients with sleep affected due to scalp psoriasis ≥3 days per week at baseline and at end of study observation period.
- Proportion of patients sleeping well (defined as: “very well” and “rather well”) at baseline and at end of study observation period.
- Absolute PSY-SCALP scores (overall and for each item) at baseline and at end of study observation period.
- Frequency of responses to individual items of the PSY-SCALP Questionnaire, at baseline and at end of study observation period.
- Change from baseline in PSY-SCALP score, according to questions 2 and 3 of the PSY-SCALP questionnaire (collected at baseline) and corresponding questions 5 and 6 (collected at end of study observation period), at end of study observation period.
- Absolute physician satisfaction scores for effectiveness, convenience, and global satisfaction domains at end of study observation period.
- Incidence of SAEs, SADRs, maternal/paternal pregnancy exposure and other special situations during study observation period.

**Scalp-PGA treatment success is defined as a scalp-PGA score of 0 (clear) or 1 (almost clear) and with a minimum 2 points improvement from baseline, on the scalp.*

8.4 Data Sources

The study is based on primary data collection directly from healthcare professionals (Investigators) and patients. Investigators will collect data using electronic Case Report Form (eCRFs) that are specifically designed for this study. At baseline visit, the Investigator will collect the patient general

information: demographics and clinical characteristics, selection criteria and informed consent. The general information will be collected by asking the patient or by inspecting his/her medical records. Also, at study visits during the study observation period, the Investigator will perform most of the effectiveness assessments: S-mPASI and Scalp PGA, in addition to gathering all safety and tolerability data.

Patients will be separately asked to complete the study questionnaires in electronic format using a mobile App. Patients will complete the Scalpdex, WI-NRS, sleep quality, and psychosocial questionnaires at Baseline visit and end of study observation period (EOS visit or ETV); patients will complete self-reported compliance (using VAS and MMAS-4), TSQM-9, PPQ, and CUSP-Q questionnaires only at end of study observation period.

Completion of eCRF for individual patients by the investigator will signify the electronic approval of respective patients at their study site. Study patient log (in all sites) and photo documentation (only for sites participating in the sub-study) will be considered as source documentation, prepared specifically for the study. All other information will be gathered directly from patient medical charts or perceptual data (PROs and clinician reported outcomes) directly reported by patients and clinicians into mobile App and eCRF, respectively.

8.4.1 Data Collection Schedule

8.4.1.1 Study Flow Chart

In this study, the visit schedule is not defined by the study protocol but is driven by routine clinical practice according to SmPC.

Data will be collected at study inclusion (Baseline visit) and approximately at 8 $\pm$ 4 weeks after treatment initiation (as per clinical practice) or at the time of CAL/BDP PAD cream treatment discontinuation, whichever occurs earlier. Information regarding any unscheduled visit within the observation period due to early disease control, worsening of psoriasis or tolerability problems will be collected at the time of follow-up visit close to Week 8.

The post-baseline study follow-up timepoint will be considered within an interval of approximately 8 ± 4 weeks and will be treated as end of study (EOS) visit. The Baseline visit which will be the date of study inclusion will have no time interval.

The flow chart in **Table 1** lists all of the assessments and indicates with an ‘X’ the visits at which they will be performed. For study sites participating in the sub-study (photographs), list of assessments for additional visit are summarised in

Table 2.

Table 1 Data Collection Schedule

Visit	Baseline	EOS visit	Early Termination Visit^
Week†	0	8 ± 4 weeks, as per routine practice**	-
Informed consent*	x		
Selection criteria	x		
Demographics/baseline characteristics[1]	x		
Routine physical examination[2]	x		
Psoriasis medical history and relevant comorbidities[3]	x		
Prior skin and scalp/plaque psoriasis medication (including topicals for scalp)	x		
Concomitant general medication	x	x	x
Physician assessments (Scalp PGA, S-mPASI)	x	x	x
Physician satisfaction with medication		x	x
Patient questionnaires			
Scalpdex, WI-NRS, Sleep quality, and Psychosocial effects,	x	x	x
TSQM-9, PPQ, MMAS-4, self-reported VAS for treatment adherence, CUSP-Q		x	x
(S) AEs/(S)ADRs[4], Special Situation reports		x	x
Reason to continue CAL/BDP PAD cream (if applicable)		x	
Reasons for premature study withdrawal			x

† Expected visit schedule based on routine clinical practice, and index date (date of first administration of CAL/BDP PAD cream).

*The cream start date should be the same day of the study inclusion date or 24-hour prior to the study inclusion date as a maximum.

**If more than one visit is conducted (post-baseline) as per clinical practice, all routine assessments will be collected in the eCRF at EOS visit.

^Conducted (if feasible) as result of patient discontinuation from study for reasons other than achievement of scalp psoriasis disease control; this will be serve as the EOS visit for these patients. If this visit is not feasible to conduct earlier (closer to actual date of discontinuation), data collection will be performed the original EOS visit timeframe. Clinician assessments and patient surveys completed, if feasible.

[1] Age, gender, alcohol intake, smoking status, other demographic data, and patient clinical characteristics.

[2] Height/weight measurements, if documented per usual care.

[3] Disease information (date of diagnosis and baseline severity), comorbidities.

[4] All AE/ADR information will be reported in the eCRF. If the (S)AE/(S)ADR has not resolved or stabilized by the time the subject completed the EOS visit or at the time of Subject's premature termination from the study, the Investigator may subsequently follow-up with the Subject to check the status of SAE/SADR, prior to completing the eCRF for EOS visit/ETV, if feasible.

ADR, adverse drug reaction; AE, adverse event; BDP, betamethasone dipropionate; CAL, calcipotriene; CUSP-Q, cream usability in scalp psoriasis questionnaire; eCRF, electronic Case Report Form; EOS, End of Study; ETV, Early Termination Visit; MMAS, Morisky Medication Adherence Scale; PGA, physician's global assessment; PPQ, patient preference questionnaire; SAE, serious adverse event; SADR, serious adverse drug reaction; TSQM, treatment satisfaction questionnaire for medication; V, visit; VAS, visual analogue scale; WI-NRS: Worst Itch Numerical Rating Scale.

Table 2 Data Collection Schedule for study sites participating in the sub-study

Visit	Baseline	Additional Visit	EOS visit	Early Termination Visit^
Week†	0	4 ± 2 weeks	8 ± 4 weeks, as per routine practice**	-
Informed consent*	x			
Selection criteria	x			
Demographics/baseline characteristics[1]	x			
Physical examination[2]	x			
Psoriasis medical history and relevant comorbidities[3]	x			
Prior skin and scalp/plaque psoriasis medication (including topicals for scalp)	x			
Concomitant general medication	x		x	x
Photography	x	x	x	x
Physician's assessments (Scalp PGA, S-mPASI)	x	x	x	x
Physician satisfaction with medication			x	x
Patients' questionnaires				
Scalpdex, WI-NRS, Sleep quality, and Psychosocial effects	x		x	x
TSQM-9, PPQ, MMAS-4, self-reported VAS for treatment adherence, CUSP-Q			x	x
(S)AEs/(S)ADRs[4], special situation reports		x	x	x
Reason to continue CAL/BDP PAD cream (if applicable)			x	
Reasons for premature study withdrawal				x

† Expected visit schedule based on routine clinical practice, and index date (date of first administration of CAL/BDP PAD cream).

*The cream start date should be the same day of the study inclusion date or 24-hour prior to the study inclusion date as a maximum.

**If more than one visit is conducted (post-baseline) as per clinical practice, all routine assessments will be collected in the eCRF at EOS visit.

^Conducted (if feasible) as result of patient discontinuation from study for reasons other than achievement of scalp psoriasis disease control; this will be serve as the EOS visit for these patients. If this visit is not feasible to conduct earlier (closer to actual date of discontinuation), data collection will be performed the original EOS visit timeframe. Clinician assessments and patient surveys completed, if feasible.

[1] Age, gender, alcohol intake, smoking status, other demographic data, and patient clinical characteristics.

[2] Height/weight measurements, if documented per usual care.

[3] Disease information (date of diagnosis and baseline severity), comorbidities.

[4] All AE/ADR information will be reported in the eCRF. If the (S)AE/(S)ADR has not resolved or stabilized by the time the subject completed the EOS visit or at the time of Subject's premature termination from the study, the Investigator may subsequently follow-up with the Subject to check the status of SAE/SADR, prior to completing the eCRF for EOS visit/ETV, if feasible.

ADR: Adverse drug reaction; AE, adverse event; BDP, betamethasone dipropionate; CAL, calcipotriene; CUSP-Q, cream usability in scalp psoriasis questionnaire; eCRF, electronic Case Report Form; EOS, End of Study; ETV, Early Termination Visit; MMAS, Morisky Medication Adherence Scale; PGA, physician's global assessment; PPQ, patient preference questionnaire; SAE, serious adverse event; SADR, Serious adverse drug reaction; TSQM, treatment satisfaction questionnaire for medication; V, visit; VAS, visual analogue scale; WI-NRS: Worst Itch Numerical Rating Scale.

8.4.1.2 Study Visit Description

The patient visits to the site will occur as per normal clinical practice. Should a patient have more than one follow-up visit within the study observation period of 8 ± 4 weeks, the follow-up visit closest to the 8-week time period will be considered as EOS visit.

Visit 1 - Baseline

To be conducted at study inclusion and after CAL/BDP PAD cream prescription and treatment initiation. The data collection will encompass:

- Verification of selection criteria.
- Obtaining of written informed consent.
- Collection of medical history (relevant comorbidities, atopic dermatitis, asthma, etc), and demographic parameters.
- Routine physical examination (height/weight measurements) if part of usual care.
- Photographs of areas to be treated (only sites participating in the sub-study). CAL/BDP PAD cream start date (index date) and reason to start.
- Clinical history of plaque (skin and scalp) psoriasis.
- Prior plaque (skin and scalp) psoriasis medication (including topical therapies for scalp).
- Concomitant medications for relevant comorbidities, and for plaque psoriasis in parts of the body other than the scalp (if applicable).
- Physician's assessments (S-mPASI, scalp PGA).
- Completion of patients' questionnaires (Scalpdex, scalp WI-NRS, sleep quality, and PSY-SCALP).

Visit 2 – End of Study (EOS) visit

Study observation period will be approximately 8 ± 4 weeks. The EOS visit will occur at approximately 8 ± 4 weeks after treatment initiation, or when the patient discontinues the treatment due to disease control, whichever occurs earlier. If a patient discontinues treatment, or if the physician decided to prolong treatment beyond 8-weeks, this data will be recorded in the eCRF. Patients who will discontinue treatment due to disease control (per clinician assessment) will not be considered as premature discontinuation of the study and will be considered as patient who completed the study.

The data collection will encompass:

- Date of visit.
- Photographs of treated areas (only sites participating in the sub-study).
- Concomitant medication for comorbidities.
- Date of CAL/BDP PAD cream discontinuation/finalisation or achievement of disease control, if applicable.

- Main reason for CAL/BDP PAD cream discontinuation/finalisation, if applicable.
- Reason to continue CAL/BDP PAD cream after 8 weeks of treatment (if applicable).
- Physician assessments (S-mPASI, scalp PGA, satisfaction with medication).
- Patient questionnaires (TSMQ-9, Scalpdex, scalp WI-NRS, PPQ, MMAS-4, self-reported VAS, CUSP-Q, sleep quality, and PSY-SCALP).
- Documentation of safety and tolerability, including occurrence of (S)AEs, (S)ADRs, special situations.

Early Termination Visit (ETV)

This visit only applies to patients who discontinue treatment with CAL/BDP PAD cream (not due to achieving disease control) prior to the regular end of the observation period, i.e., prior to the maximum allowed treatment period as per clinical practice. EOS visit and ETV will be the same for patients discontinuing from the study prematurely. ETV should be performed as soon as possible after the decision for treatment discontinuation is made so that the documentation in context with this NIS will be stopped. If it is not feasible to complete ETV, clinician will complete eCRF at the originally planned EOS visit timeframe.

The data collection will encompass:

- Date of visit.
- Photographs of treated areas (only sites participating in the sub-study), if feasible.
- Concomitant medication for comorbidities.
- Main reason for CAL/BDP PAD cream discontinuation/finalisation, including premature study withdrawal, if applicable.
- Stop date for the CAL/BDP PAD cream treatment and/or study withdrawal.
- Physician assessments (S-mPASI, scalp PGA, satisfaction with medication), if feasible.
- Patient questionnaires (TSMQ-9, Scalpdex, scalp WI-NRS, PPQ, MMAS-4, self-reported VAS, CUSP-Q, sleep quality, and PSY-SCALP), if feasible.
- Documentation of safety and tolerability, including occurrence of (S)AEs, (S)ADRs, special situations, if available.

Only in study sites participating in the sub-study:

Additional Visit (to take place before End of Study (EOS) visit)

Expected to be conducted approximately 4 weeks after CAL/BDP PAD cream treatment start:

- Concomitant medication for comorbidities.
- Photographs of treated areas

- End of CAL/BDP PAD cream (and treatment end date), due to disease control achievement, if applicable.
- Physicians' assessments (S-mPASI, scalp PGA).
- Documentation of safety and tolerability: Occurrence of (S)AEs, (S)ADRs, special situations.

8.5 Study Size

A total of 300 study-eligible adult patients with mild-to-moderate plaque psoriasis of the scalp will be included. No formal sample size calculation was performed. The primary endpoint of this study is to assess the treatment satisfaction of adult patients with mild-to-moderate plaque psoriasis of the scalp treated with a CAL/BDP PAD cream. A sample size of 300 adult patients will suffice to estimate with a 95% confidence and a precision +/-2.5 units, a population mean of TSQM-9 score, which has been considered to present a standard deviation of 20 units. Assuming 20% of patients with missing data for the primary analysis due to data unavailability, or dropout, we estimate the achievable precision of the primary endpoint on 240 patients.

Recruitment will be consecutive in each study site. All patients fulfilling all selection criteria at the study site during the study period will be offered to participate in the study.

8.6 Data Management

8.6.1 Data Collection, Monitoring, Processing of Data and Archiving

Data will be collected using eCRFs (for investigators) and surveys (for patients) that are specifically designed for this study. The Investigator or person designated by him/her will record patient data in eCRFs. Only persons authorised by the Investigator and duly trained to make original eCRF entries are allowed to make corrections.

The Investigator must maintain source documents for each patient in the study. Data to be entered to eCRF will correspond only to data from source documents, besides (survey) data based on self-perceptions.

Patients will be asked to complete the surveys/questionnaires in an electronic platform (a mobile App). After physician completion of the eCRF for respective patients, each patient will be considered as electronically approved by the physician. Patient surveys/questionnaires in paper will be used only in exceptional conditions if requested by the study site.

Assessments will be conducted and recorded consistent with the table of assessments listed in Section 8.4.1.1.

During the study visit, data entered in the eCRF/electronic data capture (EDC) system will be immediately saved in the study database. The study database will be defined according to the last approved version of the corresponding CRF, questionnaires and the study protocol. The back-end EDC platform will be programmed with edit checks and will be reflected on the Data Validation Plan and the programmer-version of eDCFs with edit checks will be made part of the DMP. The EDC will

be appropriately validated by the CRO and pre-tested with dummy data prior to start of the study. The study data procedures will ensure that the incoming data from Site Investigators and patients are automatically checked for data quality and safety events.

All changes in the eCRF are tracked separately to provide an audit trail. This, among all Data Management (DM) activities, will be described in the Data Management Plan (DMP). Investigators will be oriented to eCRF completion guidelines and EDC, so that the data quality is acceptable already before monitoring data.

The study CRO will review the data entered into the eCRFs by investigational staff for completeness and accuracy and will instruct the site personnel to make any required corrections or additions. Automatic checks defined in the Data Validation Plan (DVP) will be performed within the EDC system, at the time of data entry performed by study site staff. Manual queries will also be created, if needed, after data and listings review from study CRO. Designated Investigator site staff will be required to respond to the checks and queries and confirm or correct the data. As a result of data queries, if any data corrections are required in the EDC portal, those edits will be made at the back-end by the central research staff and ratified by the CRO Program Lead for appropriateness and correctness. At the end of the study. when all data have been entered, reviewed, monitored, and edited, the principal Investigator will be notified of the completion of study data collection and data will be locked by the CRO's Data Manager to prevent further editing.

SADR, fatal AE and special situations reconciliation will be performed by the study CRO. All discrepancies should be resolved before database lock. The CRO will work with Almirall to facilitate any safety data reconciliation with Almirall study safety database.

Any additional quality assessment(s) will be carried out at the time of pre-specified study analytic timeframes, per the data management plan. Following completion of all data review activities for all patients, records within the master dataset will be locked, followed by completion of medical coding for concomitant medications and adverse events and preparation of dataset for statistical analyses. Prior or current psoriasis treatment and concomitant medications will be coded using the World Health Organization (WHO) Drug Reference List, which employs the Anatomical Therapeutic Chemical classification system. AEs/ADRs, special situations and relevant medical history (comorbidities) will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) terminology. A Quality Control check to ensure the accuracy of the data will be done by the CRO when data is cleaned prior to the database lock and analyses. Specifications of the Quality Control check will be found in the DMP. An audit trail of data modifications will be maintained in order to protect the authenticity and integrity of the study data.

8.7 Data Analysis

A detailed Statistical Analysis Plan (SAP), which will provide the technical details of the statistical analysis outlined below, will be prepared, and approved, prior to the intermediate analysis.

8.7.1 Data Set to be analysed

- Safety population will comprise all patients for whom it is known that they had at least one CAL/BDP PAD cream application during the study duration.

- The Full Analysis Set (FAS) will include all those patients in the safety population that had at least one post-baseline assessment for primary endpoint.

All safety outcomes will be assessed on the Safety population. The primary, secondary and additional endpoints will be assessed on the FAS population.

8.7.2 Statistical analysis

8.7.2.1 General considerations

The analysis plan will be fully described in a written and approved statistical analysis plan (SAP). The SAP will comprise all the planned statistical analyses defined below and will be conducted once all data from all included patients has been collected. The SAP will include the shell tables to be used for the data analyses.

No formal statistical hypotheses are to be tested.

Categorical variables will be summarised with number (n) and percentages (%) of cases. For continuous variables, the number of non-missing observations (n), number of missing, mean, standard deviation (SD), standard error (SE) of the mean, 95% confidence interval (CI) of the mean, median, first (Q1) and third (Q3) quartiles, minimum (min) and maximum (max) will be calculated. When applicable, these summaries will be provided by visit. Additionally, for changes from baseline, 95% CI for the mean value will be calculated.

All results will be presented through 4 weeks (if site participated in the sub-study), and EOS visit/ETV, depending on the availability of data. Details of analysis windows for week 4 (where appropriate) and end of study will be outlined in the SAP. The statistical analysis will be performed using the Statistical Analysis System (SAS, version to be specified in the SAP).

Both intermediate and final analyses are planned:

- An intermediate analysis is planned to be performed once the first 150 patients have completed the study. The Intermediate Analysis Report will be reviewed and approved by Almirall and described in the SAP. No clinical report is planned for preliminary results (only tables and figures).

- Final analysis will be performed once all data from all patients have been collected in the database, cleaned, and database lock has occurred. Final analysis will be performed for the entire study cohort.

8.7.2.2 Analysis of the primary objective

The analysis of the primary endpoint will be based on the FAS population.

The primary endpoint (absolute TSQM-9 effectiveness, convenience, and global satisfaction domain scores at end of study observation period) will be described using descriptive statistics (see Section 8.7.2.1) for each TSQM-9 domain. In addition, absolute and relative frequencies of patients' answers and number of patients with missing data for each TSQM-9 item at end of study observation period will also be described.

The TSQM-9 domain scores (effectiveness, convenience, and global satisfaction) will be calculated as recommended by the instrument authors [40]. Details on dealing with missing data for the primary endpoint will be described in the SAP.

8.7.2.3 Analysis of secondary objectives

The analysis of the secondary endpoints will be based on the FAS population. The secondary endpoints to be presented in this analysis are summarised in Section 9.3.2.2.

All secondary endpoints will be summarised using descriptive statistics (see Section 8.7.2.1).

PRO measures Scalpdex and scalp WI-NRS, as well as clinician reported scalp-PGA success will be described as categorical and/or continuous variables for point of time, where applicable. To evaluate them, the answers will be described by each point of time they were completed according to study design. Scalp-PGA treatment success will be assessed as a scalp-PGA score of 0 (clear) or 1 (almost clear) at end of study observation and with a minimum 2 points improvement from baseline, on the scalp. Furthermore, all answers will be described by number of patients who answer in each category or domain (if applicable).

Further specification of the secondary endpoint analyses will be described in the SAP.

8.7.2.4 Analysis of additional objectives

The additional endpoints to be presented in this analysis are summarised in Section 9.3.2.3.

The analysis of the non-safety additional endpoints will be based on the FAS population; these endpoints will be summarised using descriptive statistics (see Section 8.7.2.1).

S-mPASI, S-mPASI 75, and Scalp-PGA measures will be described as categorical and/or continuous variables for point of time, where applicable. To evaluate them, the answers will be described by each point of time they were completed according to study design. Changes will be calculated as the difference between baseline and follow-up visits (4 weeks [if applicable] and end of study observation period) and will be compared using chi-square tests for categorical variables, or parametric paired t-test (or non-parametric test of Wilcoxon signed ranks) for continuous variables. Physician satisfaction measures will be analysed using methods identical to the analyses of study primary endpoint (see Section 9.7.2.2). Furthermore, all answers will be described by number of patients who answer in each category or domain (if applicable).

Questionnaires scores and individual answers (where applicable; Scalpdex, PPQ, scalp WI-NRS, MMAS-4, self-reported VAS, CUSP-Q, sleep quality, and PSY-SCALP) provided by patients will be described by each point of time they were completed according to study design. Changes in questionnaires completed at baseline and end of study observation period will be calculated as the difference between baseline visit and end of study observation period and will be compared using chi-square tests for categorical variables, or parametric paired t-test (or non-parametric test of Wilcoxon signed ranks) for continuous variables, in order to accomplish the additional objectives. Furthermore, all answers will be described by number of patients who answer in each category or domain (if applicable).

The analyses of safety outcomes/endpoints will be performed on the Safety Population. Safety outcomes include drug-related adverse events (adverse drug reactions; ADRs) and un-related adverse events (AEs).

Adverse Events

All adverse events starting on or after the administration of first dose of CAL/BDP PAD cream will be collected.

The number and percentage of patients who experienced at least one AE, ADR, SAE, SADR, AEs/ADRs leading to study discontinuation, and fatal AEs/ADRs will be summarised and tabulated by System Organ Class (SOC) term, preferred term, intensity, seriousness, outcome, causality with a suspect drug and action taken with the study drug.

In the event of one episode of an AE/ADR (continuous in time) with multiple intensities being reported by the same patient, the maximum intensity (severe > moderate > mild), the most serious causality with a suspect drug (Yes > No), the most serious seriousness criteria (Yes > No), the last action taken, and the last outcome will be chosen.

All AEs/ADRs will be listed.

8.7.2.5 Missing data

It is optimal to prevent missing data, to the extent possible, through strategies set forth in the design and conduct of a study. For the current study, we will aim to minimize missing information by:

- Collecting only critical data elements (i.e., variables aligned with the study objectives) to minimize site/participant burden.
- Including "not applicable", "unknown " on case report forms to ensure every question has a non-missing response.
- Programming EDC and patient questionnaires with automated edit checks and missing-data warnings/notifications to ensure relevant information is entered, where needed.
- Training of sites and data abstractors regarding data collection; setting reporting windows around a target timepoint.

Should missing data occur, the data will be analysed as they are recorded in study eCRFs and questionnaires. However, the amount of missing values for data elements will be reported, and we will assess the likely impact of missing data on the analysis and the pattern of the missing information. No missing data imputation is planned for study primary endpoint.

Handling of critical missing data, if any, will be discussed during the review of the data before the database lock.

8.8 Quality control

Before the first patient is recruited into the study, the study CRO will:

- Establish the adequacy of the facilities and the investigator's speciality.
- Discuss with the investigator(s) (and other personnel involved with the study) their responsibilities with regards to protocol compliance, and the responsibilities of Almirall or its representatives.

During the study, the study CRO can implement different activities to assure compliance with Almirall standards of quality. These activities could include but are not limited to:

Contacts with the Sites to:

- Provide information and support to the investigator(s).
- Confirm that the research team is complying with the protocol and that data are being accurately recorded in the eCRFs.
- Ensure that the patient ICFs are signed and stored at the investigator's site.
- Ensure that the eCRFs are completed properly and with adequate quality.

Monitoring Activities to:

- Clarify key data points and checking that patients exist in medical records.

The study CRO will conduct telephone monitoring visits according to a pre-agreed schedule and with enough frequency to perform source data verification, control protocol compliance by Investigators and report any potential deviation as soon as possible.

If there is a suspicion of a potential non-optimal level of protocol compliance by the site investigator, specific measures should be adopted to evaluate the situation, identify the issue, and implement specific action plans to correct the situation.

The Investigator must make arrangements to store the essential study documents until Almirall or the study CRO confirms in writing to the Investigator that the documents are no longer to be retained. The Investigator is responsible for archiving all relevant source documents, patient's files, and patient's identification codes for a minimum of 5 years after completion of the study for subsequent access and evaluations. All relevant source documents will be destroyed after this time if this has been previously agreed with the Sponsor unless local regulations require a longer retention period.

Almirall stores the original CRFs (in case of available paper forms), all eCRF data, and the above-mentioned essential documents for a minimum of 10 years (unless local regulations require a longer retention period), with the possibility of considering destroying them right thereafter, except for source documents pertaining to the individual site, which are kept only by the Investigator.

All information on eCRFs must be traceable to the source documents in the patient's file. Data defined before study start as not requiring a separate written record are recorded directly in the eCRF and are considered source documentation; these would relate to all PRO elements (completed only via online survey) and perceptual questions that investigators address as part of eCRFs.

Audits may be carried out by Almirall or the study CRO, during or after the study. The Investigator will permit and assist Almirall, the study CRO or responsible government agencies (as required by law) to have direct access to all source data/documents, if and when needed.

8.9 Limitations of the Research Methods

Patients should be eligible for being treated with CAL/BDP PAD cream before their inclusion in the study. All patients with mild-to-moderate scalp psoriasis should have been preselected to initiate CAL/BDP PAD cream treatment according to the SmPC and clinical practice before patient inclusion in the study.

Considering the main objective of this study, a non-interventional and prospective design is the best choice. However, this design brings some limitations. Although the study protocol proposes a structured and standardized form of collecting and analysing the data to reduce the presence of confounders, selection bias, and a significant loss of statistical power, there is a possibility for the analysis to be still biased inherent to the NIS design. For instance, limitations of the study include selection bias, missing information about the primary endpoint and loss to follow-up. To limit selection bias in the sample, all patients attending the physician's office and fulfilling the selection criteria will be invited to participate in a consecutive manner. The sites will be carefully chosen (based on their research capability and available staff) and rigorously oriented to study steps to minimize these limitations and to guarantee the availability of relevant study data.

8.10 Other Aspects

Not applicable

9 Protection of Human Patients

9.1 Regulatory and Ethical Compliance

This study is designed and should be implemented and performed in accordance with the ICH Harmonised Tripartite Guidelines for Good Clinical Practice, applicable local/regional/national legislation, applicable legislation on NIS and the ethical principles set forth in the Declaration of Helsinki. Copies of the latter and subsequent amendments can be obtained from the World Medical Association website at http://www.wma.net/en/10home/index.html.

9.2 Potential Risks and Benefits

Patients' participation in this study do not include any clinical procedure/test that there are not indicated according to routine clinical practice. Therefore, there is neither specific risk nor immediate clinical benefit related to the patient participation in the study.

9.3 Patient Information and Consent

Eligible patients can take part in the study only after providing the written informed consent approved by the IEC. Informed consent must be obtained before starting any procedure pertaining to the study (i.e., all the procedures described in the protocol).

A Patient Information Sheet and ICF, which meet regulatory requirements and are appropriate for this study, will be provided to the patient. The investigator at each site will ensure that the patient is given full and adequate information about the nature, purpose, possible risk, and benefit of the study. Patients must also be notified that they are free to withdraw consent at any time. The patients should be given the opportunity to ask questions and allowed time to consider the information provided.

The obtaining of informed consent must be recorded in the patient's source documents (e.g., patient log). The investigator must store the original signed patient ICFs. A copy of the signed patient ICF must be given to the patient.

9.4 Patient Confidentiality

All the participating study sites must confirm that they handle the patient information strictly in confidence. No personally identifiable information will be collected from patients in this study.

The process of collecting patient information will comply with the standards for protection of privacy by applicable local/regional/national requirements for patient confidentiality. All records will be kept confidential, and the patient's name or other personally identifiable information will neither be collected, nor will be disclosed/released at any time.

The Patient ICF will incorporate wording that complies with relevant data protection and privacy legislation. Pursuant to this wording, patients will authorise the collection, use and disclosure of their pseudo-anonymous health data by the investigator and by those persons at the clinic who need that information for the purposes of the study. The Patient ICF will explain that study data will be stored in a computer database, maintaining confidentiality in accordance with the local/regional/national laws for Data Protection.

The Patient ICF will also explain that in case of a data audit to meet a requirement from a government

agency and accessing study source documentation is warranted, the study CRO or relevant government agency staff may require direct access to source documents that are part of the hospital or practice records relevant to the study, but at no juncture will study patient identifiable information will be collected or disclosed.

9.5 Interference with Medical Prescription Habits

In this study CAL/BDP PAD cream is prescribed in the usual manner in accordance with the terms of the marketing authorisation i.e., CAL/BDP PAD cream SmPC. The prescription of CAL/BDP PAD cream to a patient is not decided in advance by the study protocol but falls within current clinical practice, thus the prescription of CAL/BDP PAD cream is clearly separated from the decision to include the patient in the study. No additional diagnostic or monitoring procedures will be applied to the patients. No different assessments than those usually performed in the routine clinical practice are planned.

9.6 Patient Withdrawals

Each patient may withdraw from the study at any time, and each patient can be removed from the study for any reason deemed necessary for his/her well-being. All data generated until the time of withdrawal from the study will be analysed, and the reason(s) for withdrawal will be recorded.

In the case of premature treatment discontinuation due to an adverse event, the Investigator should ensure that the patient receives a suitable therapy appropriate to his/her condition and should make every effort to collect and report further information necessary for an appropriate causality assessment (e.g., event duration and outcome, as requested per safety report form and/or eCRF). Therefore any (S)AEs, (S)ADRs will be collected from the study inclusion date to the EOS visit or ETV in case of premature withdrawal. As part of usual care, Site Investigator will follow Subjects concerning all SAEs and SADRs until adequate resolution or stabilization. If the SAE/SADR has not resolved or stabilized by the time the patient completed the final study encounter or at the time of patient's termination from the study, the Site Investigator may subsequently follow-up with the patient to check the status of patient's SAE/SADR, prior to completing the eCRF for patient's EOS visit or ETV, if feasible.

9.7 Ethics Committees

Before starting the study, the final version of the protocol and informed consent must be reviewed and approved by a properly constituted IEC(s) in each of the countries participating in the study. A document dated and signed by the IEC to confirm that the protocol and informed consent have been approved must be obtained before starting the study. Likewise, the IEC must also approve any amendment to the protocol.

10 Management and Reporting of Adverse Events/Adverse Reactions and special situations

Due to the prospective nature of this study, all SAEs, SADRs and special situations will be monitored and collected and/or reported during the observational period. The safety reporting period will cover the entire prospective observational period (from the study inclusion date up to EOS visit or ETV). AEs/SAEs will be recorded on the appropriate forms (eCRF).

An AE is any untoward medical occurrence in a patient administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. If, according to the investigator, there is a worsening of a medical condition that was present prior to the administration of the intervention, this should also be considered a new AE and reported. Correspondingly, any medical condition present prior to the administration of the intervention that remains unchanged or improved should not be recorded as an AE at subsequent visits.

Documentation regarding the AE should be made as to the nature, date of onset, end date, intensity, severity, relationship to product, action(s) taken, and outcome of any sign or symptom observed by the physician or reported by the patient upon indirect questioning.

Special situations, namely, lack of efficacy of CAL/BDP PAD cream, maternal/paternal pregnancy exposure, lactation reports, suspected drug interactions, suspected transmission of infectious agent via medicinal product, unexpected therapeutic clinical benefit from use of CAL/BDP PAD cream, and exposure conditions such as overdose, off-label use, misuse, abuse, medication error or occupational exposure, should not be documented as an AE, however maternal/foetal complications or abnormalities will be recorded as AEs or SAEs, as appropriate.

At baseline visit, the Investigator will document patient's pre-existing conditions/disorders (if any). During the following visit, the patient will be asked again about any changes to pre-existing conditions/disorders and, incidence and type of AEs (if any observed) will be documented using eCRF. In case of abnormal laboratory results reported (during the study observation period) spontaneously by the study clinicians for a study patient, these will be collected/reported as AE/SAE on the appropriate forms (eCRF).

The Investigator shall evaluate whether the AE is classified as a SAE.

A SAE is any AE that:

- results in death.
- is life-threatening. (The term 'life-threatening' refers to an event in which the patient was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it was more severe).
- requires in-patient hospitalisation or prolongation of existing hospitalisation.
- results in persistent or significant disability/incapacity (i.e., a substantial disruption in a patient's ability to conduct normal activities of daily living).

- is a congenital anomaly/birth defect.
- is an important medical event that, while it may not result in death or be immediately life-threatening or requires / prolongs hospitalisation, may jeopardise the patient and / or may require medical or surgical intervention to prevent one of the outcomes listed above. Examples of such events are intensive treatment in an emergency room or at home for allergic bronchospasm; blood dyscrasias or convulsions that do not result in hospitalisation; or the development of drug dependency or drug abuse.

Additionally, any suspected transmission via a medicinal product of an infectious agent should be considered as a serious adverse reaction.

In-patient hospitalisation is considered to have occurred if the patient has had to stay for a night at the hospital. The criterion for prolongation of hospitalisation is also defined as an extra night at the hospital. This does not include an emergency room visit or admission to an outpatient facility. Hospitalisation for an elective or planned procedure to treat a pre-existing condition is not considered a SAE unless it results in one of the outcomes listed above (but it has to be documented as planned).

The clinical intensity of an AE is classified as:

- Mild: Awareness of event, symptoms, or signs, but easily tolerated (acceptable).
- Moderate: Sufficient discomfort and interferes with usual activity (disturbing).
- Severe: Incapacitating with inability to do normal daily living activities or significantly affects clinical status, and warrants intervention (unacceptable).

ADRs are all untoward and unintended responses to a study product related to any dose administered. All AEs judged by either the reporting Investigator or the Sponsor as having a reasonable suspected causal relationship to a study product qualify as ADRs, i.e., they are related to the study product. Each AE for which a causal relationship to CAL/BDP PAD cream (Wynzora®) cannot be excluded is classified as an ADR and must be comprehensively documented in the eCRF.

The AE Causality to drug is classified as:

- **YES**: AEs with good reasons and sufficient information (e.g. plausible time sequence, dose-response relationship, pharmacology, positive de-challenge and/or re-challenge) to assume a causal relationship with the study medication in the sense that it is plausible, conceivable or likely.
- **NO :** AEs with good reasons and sufficient information (e.g. implausible time sequence and/or attributable to concurrent disease or other drugs) to rule out a causal relationship with the study medication.

Data pertaining to (S)AEs/(S)ADRs are collected during each study visit through the patient's spontaneous description or through the Investigator's inquiry or examination of the patient.

All ADRs (serious and non-serious), (S)AEs with fatal outcome, and any special situation (lack of efficacy of CAL/BDP PAD cream, maternal/paternal pregnancy exposure, lactation reports, suspected drug interactions, suspected transmission of infectious agents, unexpected therapeutic or clinical benefit from use of the product, exposure conditions such as overdose, off-label use, misuse, abuse, medication error or occupational exposure) – even in the absence of an ADR – must

be documented on the “Safety Report Form”, or “Pregnancy form” and be reported to study CRO within 1 working day (24 hours) of knowledge of the event to:

Avant Health
Fax: +1 833.478.1478
Phone: +1 301.799.8268
E-mail: safety@avant-health.com

Study CRO will forward these reports to the Drug Safety Department of Almirall S.A. in Spain as defined in an appropriate safety agreement/safety reporting plan. Almirall takes responsibility for appropriate reporting of ADRs (serious and non-serious), (S)AEs with fatal outcomes, and special situations as applicable to regulatory authorities.

10.1 Management and reporting of pregnancies

Investigators must instruct female patients to inform them immediately if they become pregnant during the study and up to 1 month after last application of CAL/BDP PAD cream. In case of pregnancy during the participation in the study, the investigator will assess the potential benefits and risks for the female patient to continue the study treatment and decide the study discontinuation, as appropriate.

Pregnancies will be recorded on the Pregnancy form with all the available information and reported within the same timeframe and following the same routing as for ADRs. This will be done independently from the occurrence of an AE.

The investigator will make every effort to obtain all information related to the pregnancy and its final outcome, prior to completing eCRF at the end of study period for that patient. If a pregnancy results in an abnormal outcome which the investigator considers might be due to the study treatment, this will be considered as a SAE and it will be treated as an expedited report.

All pregnancies initiated during the patient’s participation in the study or up to 1 month after last application of CAL/BDP PAD cream which come to the knowledge of the investigator, will be reported to the study CRO (as part of study eCRF) during the study observation period.

11 Plans for Disseminating and Communicating Study Results

Almirall will prepare a NIS report within 12 months after completion of the last patient, i.e., the end of data collection (defined as the final date on which data is collected). Almirall is obliged to analyse and report all NIS data as described in the protocol.

In accordance with the Declaration of Helsinki, both authors and publishers have ethical obligations. In publication of the results of the NIS, the authors are obliged to preserve the accuracy of the results. Negative as well as positive results should be published or otherwise made publicly available. Almirall endeavours to publish the results of NIS and is committed to ensure that the data are reported in a responsible and coherent manner.

Study results may be published in a peer-reviewed English journal and/or presented at appropriate congresses. Almirall seeks to ensure that publications in biomedical journals follow the guidelines established by the International Committee of Medical Journal Editors (ICMJE) and published in *its Uniform Requirements of Manuscripts Submitted to Biomedical Journals*.

Neither information nor unpublished data given to/collected by an Investigator or person designated by him/her may be transmitted to a third party without written approval of Almirall; no Investigator or person designated by him/her shall publish or otherwise disclose in any form any research findings resulting from the study, or any of its parts, prior to obtaining Almirall's written consent. Likewise, Almirall will not use the Investigator's name in any publication without the prior written permission of the Investigator. The Investigator will not use Almirall's name in any publication without the prior written permission of Almirall.

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13 Appendices

13.1 Appendix I – Scalp modified Psoriasis Area and Severity Index (S-mPASI)

The S-mPASI scale is a modification of the original PASI used for assessing and grading the severity of scalp psoriatic lesions and their response to therapy. The S-mPASI produces a numeric score that ranges from 0-7.2.

The severity of the scalp psoriasis is calculated by scoring the signs of the disease (erythema, induration and scaling) on the scalp, each ranging from 0 = none to 4 = very severe, multiplied by an area score for the extent of the disease (percentage of scalp involved with psoriasis), multiplied by a constant factor, 0.1, resulting in a range of 0 to 7.2.

The scoring system for the signs of the disease is:

0 = none

1 = slight

2 = moderate

3 = severe

4 = very severe

The scale for estimating the area of involvement for scalp involved with psoriasis is:

0	=	No scalp involvement
1	=	1% to 9% scalp involvement
2	=	10% to 29% scalp involvement
3	=	30% to 49% scalp involvement
4	=	50% to 69% scalp involvement
5	=	70% to 89% scalp involvement
6	=	90% to 100% scalp involvement

The S-mPASI formula is:

$S\text{-mPASI} = 0.1(E_h + I_h + S_h) A_h$

where E = erythema, I = induration, S = Scaling, and A = area.

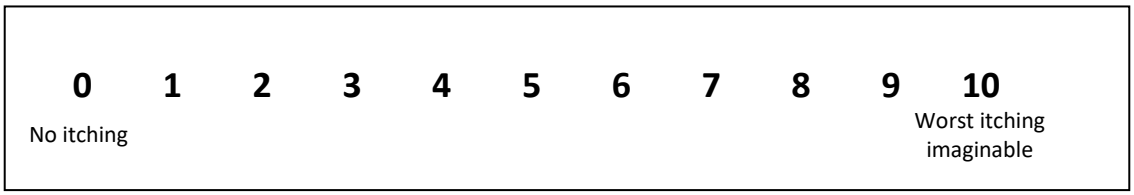
13.2 Appendix II - Scalp Physician's Global Assessment (Scalp-PGA)

Assessment of the average severity of scalp psoriasis lesions at the assessment time point according to the following categories:

0	Clear	No signs of plaque psoriasis on the scalp
1	Almost Clear	Just perceptible erythema and just perceptible scaling on the scalp
2	Mild	Light pink erythema with minimal scaling with or without pustules on the scalp
3	Moderate	Dull red, clearly distinguishable erythema with diffuse scaling, some thickening of the skin, with or without fissures, with or without pustule formation on the scalp
4	Severe	Deep, dark red erythema with obvious and diffuse scaling and thickening as well as numerous fissures with or without pustule formation on the scalp

13.3 Appendix III – Scalp Worst Itch Numeric Rating Scale (Scalp WI-NRS)

Please consider the worst level of itching on the scalp (in the last week) you experienced in the area identified for treatment with CAL/BDP PAD cream (Wynzora®). If a zero (0) means “no itching” and a ten (10) means “worst itching imaginable”, on the scale of 0-10, what is the worst level of itching due to psoriasis on the scalp you experienced in the last week? Please select the number that describes the ‘worst level’ most accurately.



13.4 Appendix IV – Treatment Satisfaction Questionnaire for Medication (TSQM-9)

Instructions: Please take some time to think about your level of satisfaction or dissatisfaction with the medication you are taking in this clinical trial. We are interested in your evaluation of the effectiveness and convenience of the medication over the last two to three weeks, or since you last used it. For each question, please select the response that most closely corresponds to your own experiences.

1. How satisfied or dissatisfied are you with the ability of the medication to prevent or treat your condition?

   ☐1 Extremely Dissatisfied
   ☐2 Very Dissatisfied
   ☐3 Dissatisfied
   ☐4 Somewhat Satisfied
   ☐5 Satisfied
   ☐6 Very Satisfied
   ☐7 Extremely Satisfied

2. How satisfied or dissatisfied are you with the way the medication relieves your symptoms?

   ☐1 Extremely Dissatisfied
   ☐2 Very Dissatisfied
   ☐3 Dissatisfied
   ☐4 Somewhat Satisfied
   ☐5 Satisfied
   ☐6 Very Satisfied
   ☐7 Extremely Satisfied

3. How satisfied or dissatisfied are you with the amount of time it takes the medication to start working?

   ☐1 Extremely Dissatisfied
   ☐2 Very Dissatisfied
   ☐3 Dissatisfied
   ☐4 Somewhat Satisfied
   ☐5 Satisfied
   ☐6 Very Satisfied
   ☐7 Extremely Satisfied

4. How easy or difficult is it to use the medication in its current form?

- ☐1 Extremely Difficult
- ☐2 Very Difficult
- ☐3 Difficult
- ☐4 Somewhat Easy
- ☐5 Easy
- ☐6 Very Easy
- ☐7 Extremely Easy

5. How easy or difficult is it to plan when you will use the medication each time?

- ☐1 Extremely Difficult
- ☐2 Very Difficult
- ☐3 Difficult
- ☐4 Somewhat Easy
- ☐5 Easy
- ☐6 Very Easy
- ☐7 Extremely Easy

6. How convenient or inconvenient is it to apply the medication as instructed?

- ☐1 Extremely Inconvenient
- ☐2 Very Inconvenient
- ☐3 Inconvenient
- ☐4 Somewhat Convenient
- ☐5 Convenient
- ☐6 Very Convenient
- ☐7 Extremely Convenient

7. Overall, how confident are you that applying this medication is a good thing for you?

- ☐1 Not at All Confident
- ☐2 A Little Confident
- ☐3 Somewhat Confident
- ☐4 Very Confident
- ☐5 Extremely Confident

8. How certain are you that the good things about your medication outweigh the bad things?

- ☐1 Not at All Certain
- ☐2 A Little Certain
- ☐3 Somewhat Certain
- ☐4 Very Certain
- ☐5 Extremely Certain

9. Taking all things into account, how satisfied or dissatisfied are you with this medication?

- ☐1 Extremely Dissatisfied
- ☐2 Very Dissatisfied
- ☐3 Dissatisfied
- ☐4 Somewhat Satisfied
- ☐5 Satisfied
- ☐6 Very Satisfied
- ☐7 Extremely Satisfied

13.5 Appendix V – Scalpdex

This questionnaire has 23 items, with possible answers “never”, “rarely”, “sometimes”, “often”, and “all the time”.

Item	Scale
1. My scalp psoriasis hurts	S
2. My scalp psoriasis makes me feel depressed	E
3. My scalp psoriasis itches	S
4. I am ashamed of my scalp psoriasis	E
5. I am embarrassed by my scalp psoriasis	E
6. I am frustrated by my scalp psoriasis	E
7. I am humiliated by my scalp psoriasis	E
8. My scalp psoriasis bleeds	S
9. I am annoyed by my scalp psoriasis	E
10. I am bothered by the appearance of my scalp psoriasis	E
11. My scalp psoriasis makes me feel self-conscious	E
12. I am bothered that my scalp psoriasis is incurable	E
13. My scalp psoriasis affects how to wear my hair (hairstyle, hats)	F
14. I am bothered by people’s questions about my scalp psoriasis	E
15. My scalp psoriasis affects the colour of clothes I wear	F
16. I am bothered by the persistence/reoccurrence of my scalp psoriasis	E
17. I feel stressed about my scalp psoriasis	E
18. Caring for my scalp psoriasis is inconvenient for me	F
19. I feel that my knowledge about caring for my scalp psoriasis is adequate	E
20. The cost of caring for my scalp condition bothers me	E
21. My scalp psoriasis makes my daily life difficult	F
22. My scalp psoriasis makes me feel different from others	E
23. My scalp condition makes it hard to go to the hairdresser	F

Scales: symptoms (S), emotions (E) and functioning (F). Each item scores: 0 “never”, 25 “rarely”, 50 “sometimes”, 75 “often” and 100 “all the time”.

13.6 Appendix VI -Patient Preference Questionnaire (PPQ)

1. The current treatment is more effective than the previous topical treatments:

Strongly Disagree	Disagree	Agree	Strongly Agree	Does not Apply to Me
☐	☐	☐	☐	☐

2. The current treatment is easier to use than the previous topical treatments:

Strongly Disagree	Disagree	Agree	Strongly Agree	Does not Apply to Me
☐	☐	☐	☐	☐

3. The current treatment has fewer side-effects than the previous topical treatments:

Strongly Disagree	Disagree	Agree	Strongly Agree	Does not Apply to Me
☐	☐	☐	☐	☐

4. I consider the current treatment to be more tolerable than the previous topical treatment:

Strongly Disagree	Disagree	Agree	Strongly Agree	Does not Apply to Me
☐	☐	☐	☐	☐

5. I prefer the current treatment to previous topical treatments:

Strongly Disagree	Disagree	Agree	Strongly Agree	Does not Apply to Me
☐	☐	☐	☐	☐

13.7 Appendix VII – Morisky Medication Adherence Scale (MMAS-4)

1. Do you ever forget to use your Scalp Psoriasis medicine?

   Yes ☐ No ☐

2. Do you ever have problems remembering to use you Scalp Psoriasis medication?

   Yes ☐ No ☐

3. When you feel better, do you sometimes stop using your Scalp Psoriasis medicine?

   Yes ☐ No ☐

4. Sometimes if you feel worse when you use your Scalp Psoriasis medicine, do you stop using it?

   Yes ☐ No ☐

Scoring scheme: “Yes” = 1; “No” = 0. A score of 0 indicates high adherence; a score of 1 or 2 indicates intermediate adherence; and a score of 3 or 4 indicates low adherence.

13.8 Appendix VIII – Self-reported Visual Analogic Scale (VAS) for treatment adherence

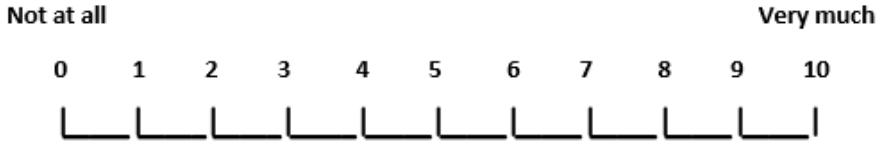
Please estimate your level of treatment adherence to CAL/BDP PAD cream (Wynzora®) by using the following sliding scale.

If a 0% means “no cream was applied” and 100% means “cream was applied once daily, for the entire treatment duration (i.e., last 8-12 weeks)”, on the scale of 0-100%, what is your adherence?

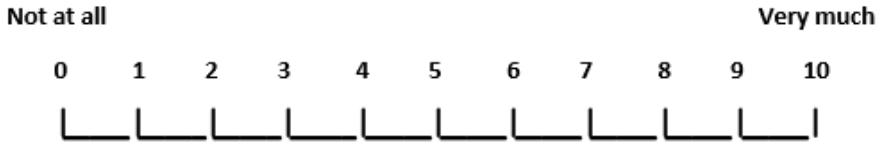
13.9 Appendix IX – Cream Usability Scalp Psoriasis Questionnaire (CUSP-Q)

Please rate the CAL/BDP PAD cream (Wynzora®) by selecting a response to each question that most closely corresponds to your own experience:

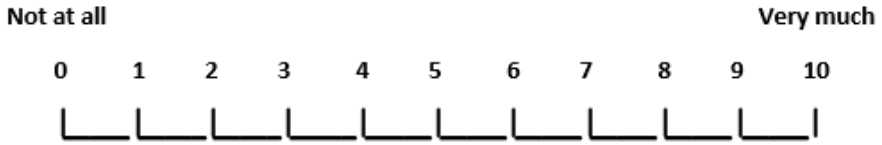
1. Was it easy to apply the cream and spread it on the scalp?



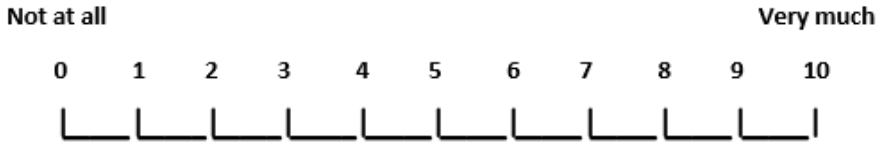
2. Was the cream absorbed quickly into the scalp?



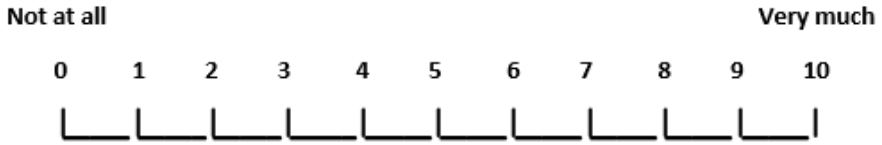
3. Once the cream was absorbed, did your scalp or hair feel sticky?



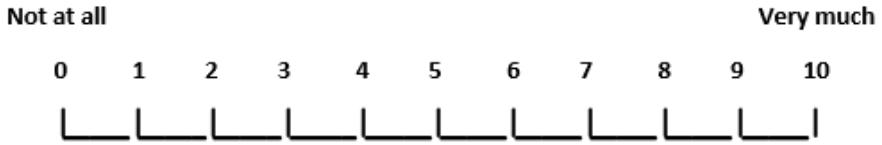
4. Did you feel any stinging or burning sensation after applying the cream?



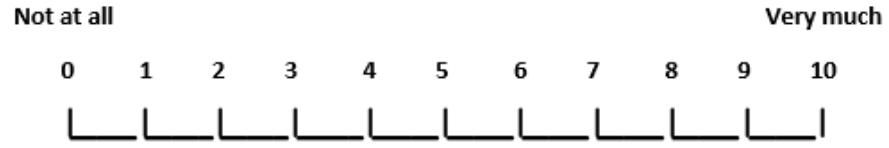
5. Did the cream leave residues on your scalp or hair?



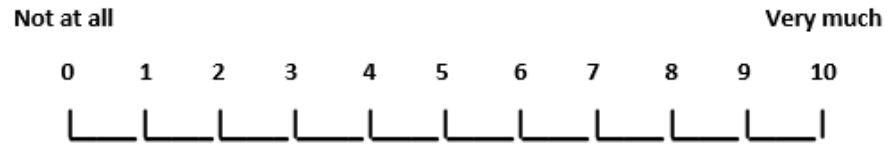
6. Was the cream easy to remove when you washed your hair?



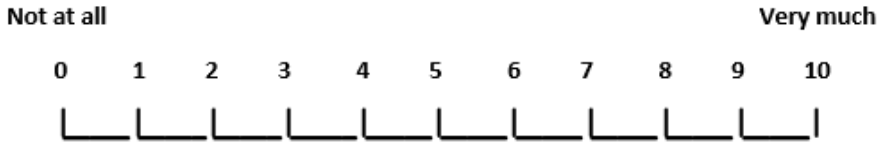
7. Was the cream on your scalp or hair noticeable to you?



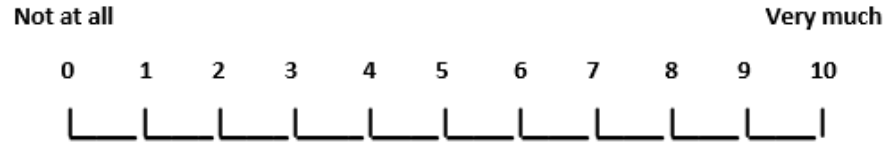
8. Was the cream on your scalp or hair noticeable to others?



9. Considering all the issues associated with the usability of the cream, how satisfied are you with the cream?



10. Would you use the cream again in the future to treat your scalp psoriasis?



13.10 Appendix X – Sleep quality questionnaire

Please rate your sleep quality during the last week by selecting a response to each question that most closely corresponds to your own experience:

1. In the last week, how many days has your scalp psoriasis affected your sleep at night?

- ☐ None
- ☐ 1 day per week
- ☐ 2 days per week
- ☐ 3 days per week
- ☐ 4 days per week
- ☐ 5 days per week
- ☐ 6 days per week
- ☐ All days of the week

2. In the last week, have you slept well at night?

- ☐ Very well
- ☐ Rather well
- ☐ Not well but not badly
- ☐ Rather badly
- ☐ Very badly

13.11 Appendix XI – Psychosocial effects questionnaire (PSY-SCALP)

Please take some time to think about the following questions in relation with your scalp psoriasis. For each question, please select a response that most closely corresponds to your own experiences.

At Baseline Visit

1. Have you ever concealed or hidden you scalp psoriasis? (i.e., needed to wear a hat, cap, or headscarf)

- ☐ 0 No
- ☐ 1 A little
- ☐ 2 Quite a lot
- ☐ 3 Very much

2. Has your psoriasis stopped you from having the hair style/colour that you would like?

- ☐ 0 No
- ☐ 1 A little
- ☐ 2 Quite a lot
- ☐ 3 Very much

3. Are you satisfied with your HCP's care of your scalp psoriasis?

- ☐ 0 No
- ☐ 1 A little
- ☐ 2 Quite a lot
- ☐ 3 Very much

At End-of Study Visit or at Early Termination Visit (if applicable)

Since using the cream:

1. Are you better able to control your scalp psoriasis?

- ☐ 0 No
- ☐ 1 A little
- ☐ 2 Quite a lot
- ☐ 3 Very much

2. Is your hair in better condition?

- ☐ 0 No
- ☐ 1 A little
- ☐ 2 Quite a lot
- ☐ 3 Very much

3. Do you feel better about your own appearance?

☐ 0 No
☐ 1 A little
☐ 2 Quite a lot
☐ 3 Very much

4. Has your self-esteem improved?

☐ 0 No
☐ 1 A little
☐ 2 Quite a lot
☐ 3 Very much

5. Have you concealed or hidden you scalp psoriasis (i.e., needed to wear a hat, cap, or headscarf)

☐ 0 No
☐ 1 A little
☐ 2 Quite a lot
☐ 3 Very much

6. Has your psoriasis stopped you from having the hair style/colour that you would like?

☐ 0 No
☐ 1 A little
☐ 2 Quite a lot
☐ 3 Very much

7. Are you satisfied with your HCP's care of your scalp psoriasis?

☐ 0 No
☐ 1 A little
☐ 2 Quite a lot
☐ 3 Very much

8. Will you need to access your HCP ***less*** often about your scalp psoriasis?

☐ 0 No
☐ 1 A little
☐ 2 Quite a lot
☐ 3 Very much

13.12 APPENDIX XII: Signature Page

The signature below constitutes the approval of this protocol and the attachments, and provides the necessary assurances that this study will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to relevant legal and regulatory requirements.

Study Investigator

PPD

Name	Signature	Date