

CLINICAL REVIEW

NDA #:	210566/S-003
Submission Date:	02/24/2020 (SDN 62)
Brand Name:	LEXETTE®
Generic Name:	Halobetasol propionate foam, 0.05%
Dosage Form:	Topical
Dosage Strength:	0.05%
Reviewer:	Mary Kim, M.D.
Team Leader:	Amy Weitach, D.O., M.S.
OCP Division:	Division of Inflammation and Immune Pharmacology
OND Division:	Division of Dermatology and Dentistry
Sponsor:	Mayne Pharma LLC
Submission Type:	Efficacy supplement/PREA PMR/WR
Indication Sought:	Plaque psoriasis in patients 12 years of age and older

Background

Halobetasol propionate (HBP) foam, 0.05% is a corticosteroid product, marketed under the tradename LEXETTE™. LEXETTE™ is in the super-high range of potency as compared to other topical corticosteroids, based on a vasoconstrictor assay in healthy patients. The product was approved for the treatment of plaque psoriasis in patients eighteen (18) years of age and older on May 24, 2018. The approval letter included the following postmarketing requirement (PMR) under the Pediatric Research Equity Act (PREA):

3344-1 Conduct a maximal use pharmacokinetic (PK) and HPA axis suppression study in subjects 12 years to <17 years of age with psoriasis.

The Agency issued a written request (WR) on November 29, 2017 and a revised WR was issued on June 01, 2018 to obtain needed pediatric information on halobetasol propionate (HBP) foam, 0.05%. A single multi-center study was requested to determine the pharmacokinetic properties and adrenal suppression potential of halobetasol propionate foam, 0.05% under maximal use conditions in pediatric subjects from 12 to less than 18 years of age with plaque psoriasis. The study requested included the following:

- *Patients to be Studied:*

Age group in which study will be performed:

Subjects from 12 to less than 18 years of age with greater than 10% body surface area (BSA) involvement.

Amended (June 1, 2018): Subjects from 12 to less than 18 years of age with greater than or equal to 10% body surface area (BSA) involvement.

Number of patients to be studied:

At least 20 completed and evaluable subjects. Enrollment should be approximately evenly distributed among ages and males and females and there should be sufficient number of subjects at the lowest ages.

Representation of Ethnic and Racial Minorities:

The study must take into account adequate (e.g., proportionate to disease population) representation of children of ethnic and racial minorities. If you are not able to enroll an adequate number of these patients, provide a description of your efforts to do so and an explanation for why they were unsuccessful.

- *Study endpoints:*

Pharmacokinetic Endpoints:

The pharmacokinetic (PK) endpoints for the study must include plasma levels of HBP. The PK sampling schedule should be based on available PK concentration time profile for each respective formulation in adults. PK assessment will be conducted as agreed with the Agency at the time of protocol submission and review prior to initiation of the study.

Amended (June 1, 2018) Pharmacokinetic Endpoints: The pharmacokinetic (PK) endpoints for the study shall include trough plasma levels of HBP on Day 8 and Day 15.

Safety Endpoints: Safety outcomes must include: adverse events, local skin reactions, urine pregnancy testing (as applicable), routine clinical laboratory testing, dosing compliance, and extent of exposure. The following adverse events must be actively monitored: HPA axis suppression and local skin reactions including atrophy and development of telangiectasia. HPA axis suppression is assessed via measurement of serum cortisol concentrations after stimulation of the adrenal cortex with cosyntropin (Cortrosyn® tests). HPA axis suppression is defined as a post-stimulation serum cortisol level $\leq 18 \mu\text{g/dL}$ assessed at the end of study. All adverse events must be monitored until symptom resolution or until the condition stabilizes.

Amended (June 1, 2018) Safety Endpoints: Safety outcomes must include: adverse events, local skin reactions, urine pregnancy test (as applicable), dosing compliance, and extent of exposure. The following adverse events must be actively monitored: HPA axis suppression and local skin reactions including atrophy and development of telangiectasia. HPA axis suppression is assessed via measurement of serum cortisol concentrations after stimulation of the adrenal cortex with cosyntropin (Cortrosyn® tests) on day 15. HPA axis suppression is defined as a post-stimulation serum cortisol level $< 18 \mu\text{g/dL}$ assessed at the end of study.

All adverse events must be monitored until symptoms resolution or until the condition stabilizes.

- *Known Drug Safety concerns and monitoring:*

HPA axis suppression is the primary systemic drug specific safety concern. Local skin reactions including atrophy and the development of telangiectasia are the primary local drug specific safety concern.

Summary of amendments to the WR issued on June 01, 2018:

- Made a change to the patients to be studied to allow for body surface area (BSA) involvement to include 10% BSA or greater.
- Changed sampling schedule for pharmacokinetic (PK) endpoints and clarified that trough level should be measured on Day 8 and Day 15.
- Changed safety outcomes to remove the requirement for routine clinical laboratory testing.

Regulatory protocol history

On February 7, 2018, the Sponsor submitted a request that the PREA protocol would satisfy the WR requirements. On May 31, 2018, the clinical review stated that, “If the PREA study, once completed, meets the time frame described and the terms specified in the Written Request, it should be adequate to form the basis of a Pediatric Exclusivity Determination.” Within the WR Amendment (06/01/2018) letter, the Agency agreed that that the proposed changes regarding body surface area, pharmacokinetic study endpoints, and safety endpoints meet the objective of the Written Request.

The PREA protocol was submitted on January 2, 2015 under IND 107302 and was reviewed and agreed upon by Dr. Milena Lolic (clinical) on April 3, 2015 and Dr. Donny Tran (clinical pharmacology) on March 4, 2015.

In Dr. Milena Lolic’s review, no safety concerns regarding the protocol were noted. Clinical pharmacology review for protocol 122-0551-209 was completed by Doanh Tran, Ph.D. on March 4, 2015 with the conclusion that design was acceptable. It was also noted that the, “Proposed protocol 122-0551-209 titled “An open label evaluation of the adrenal suppression potential and PK properties of twice daily halobetasol propionate foam 0.05% in subjects 12 to less than 18 years of age with plaque psoriasis receiving two weeks of treatment” is identical to protocol 000-0551-209 for halobetasol lotion submitted on October 8, 2014 under IND 102573 and reviewed by Jane Liedtka M.D. on January 21, 2015. Dr. Liedtka found the protocol to be acceptable.”

The protocols submitted on January 2, 2015 and October 8, 2014 are not available for review electronically.

The protocol submitted with NDA 210566 S-003 was reviewed after the submission of NDA 210566 S-003 and the reviewer concurs that the study is reasonably designed to meet the objectives of the PMR and WR.

With this submission, the applicant submitted the study report for the maximal use PK and HPA axis suppression study in subjects 12 years to less than 18 years of age (study 122-0551-209), postmarketing adverse event reports, and a labeling supplement to include the pediatrics results from study 122-0551-209 under Sections 1, 5.1, 6.2, 8.4, 12.2, and 12.3, on February 24, 2020. The applicant intends for this submission to address the PREA PMR 3344-1, meet the terms of the amended Written Request issued on June 01, 2018, and support expansion of the indication to include subjects 12 years of age and older.

Dr. Luke Oh, Clinical Pharmacology, completed a review of the maximal use PK and HPA axis suppression study 122-0551-209 and concluded the following:

“From a Clinical Pharmacology perspective, this supplement is acceptable provided the labeling comments are adequately addressed by the Applicant.”

“Clinical Pharmacology further recommends that the applicant has fulfilled PMR 3344-1 and has fulfilled the revised written request that was issued on June 01, 2018.”

Review

An Open Label, Multi-Center Evaluation of the Adrenal Suppression Potential and Pharmacokinetic Properties of Twice Daily Halobetasol Propionate Foam, 0.05% in Subjects 12 to Less Than 18 Years of Age with Plaque Psoriasis Receiving Two Weeks of Treatment (122-0551-209)

Study Design

Overview and Objective

The objective of this study was to determine the adrenal suppression potential and the pharmacokinetic (PK) properties of halobetasol propionate (HBP) foam, 0.05% applied twice daily in subjects who were 12 to less than 18 years of age with stable plaque psoriasis.

Inclusion criteria included the following:

- Subject was male or non-pregnant female and was 12 to less than 18 years of age (i.e., at least 12 years old, but not yet reached their 18th birthday at the time of enrollment).
- Subject provided written informed assent and was accompanied by the parent or legal guardian at the time of assent/consent signing. The parent or legal guardian provided informed consent for the subject. If a subject became 18 years of age during the study, the subject must have provided written informed consent at the next study visit to continue study participation
- Subject had a clinical diagnosis of stable plaque psoriasis involving a minimum of 10% BSA⁷ (excluding the face, scalp, groin, axillae and other intertriginous areas).
- Subject had an IGA score of at least 3 (3 = moderate) at the Baseline Visit.
- Subject was willing and able to apply the test article as directed, comply with study instructions, and commit to all follow-up visits for the duration of the study.
- Females must have had a negative urine pregnancy test (UPT)⁸ at the Screening (Part B) and Baseline Visits and agreed to use an effective form of birth control^{9,10} for the duration of the study.

⁷ For this evaluation 1% BSA was approximately equivalent to the area of the subject's closed hand (palm and fingers held together).

⁸ UPTs must have had a minimum sensitivity of 25 mIU β -HCG/mL.

⁹ Effective forms of birth control included a) hormonal contraceptives (e.g., oral, transdermal, injectable, implantable, or vaginal ring) (see next footnote), b) intrauterine device for at least 1 week prior to test article application, c) barrier methods (condom and spermicidal or diaphragm/cervical cap and spermicidal), d) monogamous relationship with a partner who was sterile (e.g., vasectomy performed at least 6 months prior to study entry), or e) total abstinence for subjects who were not sexually active. Subjects who became sexually active or began to have relations with a partner who was not sterile during the study must have agreed to use an effective form of birth control for the duration of the study.

¹⁰ Females taking hormonal therapy must have been on treatment prior to study entry, continued per label, and must not have changed their dosing regimen during the study; treatment must have been for (1) oral: at least 1 complete cycle (e.g., 4 to 8 weeks); (2) transdermal, injectable (e.g., Depo-Provera), implantable or vaginal ring (e.g., NuvaRing): at least 1 week.

Subjects had a Cosyntropin Stimulation Test (CST) to assess their HPA axis response at Visit 1/Screening initiated between 7 and 9 AM. Enrollment into the treatment phase of the study was timed such that the Screening CST was performed a minimum of 20 days before Visit 2/Baseline. At Visit 2/Baseline, eligible subjects with normal adrenal function were eligible to participate in the study. Subjects had blood drawn at Visit 1/Screening for baseline drug concentration in plasma. On Day 8, all subjects, regardless of lesion clearance, had blood drawn for assessment of trough drug concentration in

plasma. At the Day 15 visit, subjects who had continued to treat lesions through Day 14 had a final PK blood sample collected approximately 12 hours (\pm 30 minutes) after their Day 14 evening application and just prior to the initiation of the CST.

Subjects were instructed to apply HBP Foam, 0.05% twice daily to all psoriasis plaques identified at Visit 2/Baseline for the assigned treatment period or until the investigator verified the subject's psoriasis had cleared.

The maximum total dose of test article to be applied weekly was approximately 50 grams for up to a 2-week treatment period.

Subjects returned to the clinic on Day 8 for the following evaluations/procedures: IGA score, percent BSA affected, adverse events (AEs) and local skin reactions (LSRs) and blood draw for PK. Subjects who had completely cleared their treated lesions (IGA score of 0 in Treatment Area) discontinued dosing of test article, had a CST performed, and completed end-of-study (EOS) procedures on approximately Day 8. Subjects who had not cleared by Day 8 continued twice daily (approximately every 12 hours) application of the test article until Day 15 and returned to the clinic for collection of information on IGA score, percent BSA affected, AEs, LSRs, and a final trough PK blood sample prior, and EOS CST. Subjects with adrenal suppression (defined as post-CST cortisol level $<$ 18 $\mu\text{g/dL}$) on Day 15 were to have been scheduled for post-treatment follow-up visits approximately every four weeks for CST until the adrenal response returned to normal.

Study Endpoints

The primary objective of this study was to assess safety. Safety endpoints were:

- HPA axis response to cosyntropin.

- HPA axis responses to stimulation by cosyntropin were dichotomized to "normal" and "abnormal." An abnormal HPA axis response was defined as a 30-minute post-stimulation serum cortisol level that is \leq 18 $\mu\text{g/dL}$ at the end of study.

- Trough HBP concentrations in plasma on Day 8 and Day 15 were calculated and summarized.

- Other safety endpoints included: AEs, LSRs associated with topical application of corticosteroids (telangiectasia, skin atrophy, burning/stinging and folliculitis), clinical laboratory tests, urine pregnancy tests (UPTs), and extent of exposure.

This was not an efficacy study; however, the Applicant assessed the IGA and percent BSA treated and affected with disease.

Table 1. Investigator's Global Assessment (IGA)

CLEAR (0)	
Scaling	No evidence of scaling.
Erythema	No erythema (hyperpigmentation may be present).
Plaque elevation	No evidence of plaque elevation above normal skin level.
ALMOST CLEAR (1)	
Scaling	No more than limited amount of very fine scales partially covers some of the plaques.
Erythema	No more than faint red coloration.
Plaque elevation	No more than very slight elevation above normal skin level, easier felt than seen.
MILD (2)	
Scaling	No more than mainly fine scales; some plaques are partially covered.
Erythema	No more than light red coloration.
Plaque Elevation	No more than a slight but definite elevation above normal skin level, typically with edges that are indistinct or sloped, on some of the plaques.
MODERATE (3)	
Scaling	No more than somewhat coarser scales predominate; most plaques are partially covered.
Erythema	No more than moderate red coloration.
Plaque Elevation	No more than a moderate elevation with rounded or sloped edges on most of the plaques.
SEVERE (4)	
Scaling	Coarse, thick tenacious scales predominate; virtually all or all plaques are covered; rough surface.
Erythema	Dusky to deep red coloration.
Plaque elevation	Marked elevation, with hard sharp edges on virtually all or all of the plaques.

Statistical Analysis Plan

Frequency counts and percentages were reported for categorical data. Sample size, mean, standard deviation (SD), median, minimum and maximum were reported for the continuous variables.

The proportion of subjects manifesting laboratory-based evidence of adrenal suppression at EOS were presented along with 95% confidence intervals for the Evaluable and Safety

populations. The observed serum cortisol levels (pre-and post-cosyntropin stimulation) and the changes in serum cortisol levels after stimulation at Screening, EOS, and, if any, at follow-up visits were also summarized. Descriptive statistics for the daily dose of test article were tabulated separately for suppressed and non-suppressed subjects.

Study Results

Patient Disposition

A total of 34 subjects were screened: 24 subjects were enrolled into the study, and 10 subjects were screen failures. Reasons for screen failures included meeting exclusion criterion #17 (9 subjects had a screening CST with a post 30-minute stimulation cortisol level of $\leq 18 \mu\text{g/dL}$), and 1 subject met exclusion criterion #1 (spontaneously improving or rapidly deteriorating plaque psoriasis) and failed to meet inclusion criterion #3 (had a clinical diagnosis of stable plaque psoriasis involving a minimum of 10% BSA excluding the face, scalp, groin, axillae and other intertriginous areas).

All enrolled subjects completed the study. However, 1 (Subject (b) (6)) was excluded from the Evaluable and PK populations due to the use of a prohibited medication (i.e., Squamax Emulsion which contained urea and salicylic acid). Thus, the Evaluable and PK population consisted of 23 subjects. All 24 subjects were included in the Safety population.

Protocol Violations/Deviations

Protocol deviations included test article deviation (2), lab testing deviation (9), visit out of window (2), assessment deviation (1), and other: photos were not taken at visit 4 with the canfield camera due to flash malfunction (2).

Demographic Characteristics

There were 11 females (45.8%) and 13 males (54.2%) enrolled into the study. All subjects were White and the majority were not of Hispanic or Latino origin (18/24, 75.0%) with the remaining being of Hispanic or Latino origin (6/24, 25.0%). The mean age of the 24 subjects was 14.7 years (standard deviation: 1.76 years, median 14.6 years, range: 12.1 to 17.7 years). Within the lowest age range, i.e. between 12 years to less than 14 years, there were 10 evaluable subjects.

Other Baseline Characteristics (e.g., disease characteristics, important concomitant drugs)

There were 6 subjects with at least 1 other medical condition documented in their medical history in addition to the condition required for entry into the study (i.e., stable plaque psoriasis). Other medical conditions included eczema left arm cubital fossa, gastritis,

allergic rhinitis, bronchial asthma, grass pollen allergy (atopy), gastroesophageal reflux disease, food intolerance, and increased alanine aminotransferase and increased aspartate aminotransferase.

There were 5 subjects (5/24, 20.8%) with any concomitant medication. The most common concomitant medications were antihistamines for systemic use (3, 12.5%), adrenergics (2, 8.3%), plain corticosteroids (2, 8.3%), and drugs for peptic ulcer and gastro-oesophageal reflux disease (2, 8.3%).

Of the 24 enrolled subjects, 22 (91.7%) had moderate (Grade 3) disease, and 2 (8.3%) had severe (Grade 4) disease at Baseline. The mean percent affected BSA at Baseline for the enrolled population was 15.1% with a range of 11% to 23% and the mean percent BSA to be treated was 14.5% with a range of 10% to 20%.

No subjects had burning/stinging or folliculitis at Baseline. Six subjects had mild and/or moderate skin atrophy at Baseline, 5 subjects had moderate telangiectasia at Baseline, and 1 subject had severe telangiectasia at Baseline.

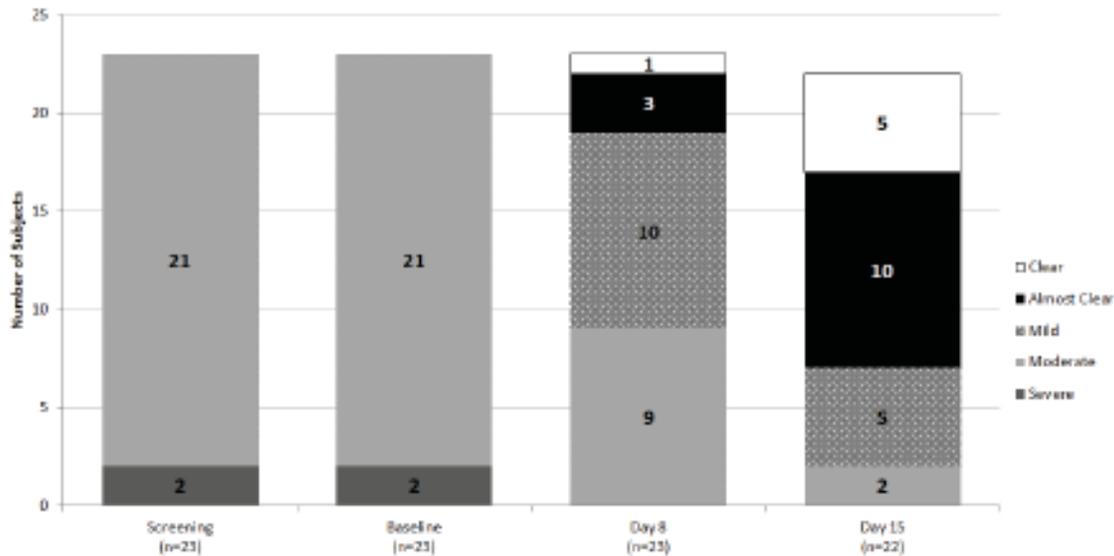
Treatment Compliance, Concomitant Medications, and Rescue Medication Use

Compliant subjects were defined as those who applied at least 80% and no more than 120% of the expected number of applications. The reported mean number of days dosed was 14.1 days with a range of 9 days to 17 days in both the Evaluable and PK populations. The average total number of applications was 28.3 with a range of 18 to 34 for both the Evaluable and PK populations. The average percent of expected doses applied was 100.6 with a range of 92.9 to 107.1 for both the Evaluable and PK populations.

Efficacy Results

The study was not intended to assess efficacy. The IGA and percent BSA treated and affected with disease were only assessed to document any changes in those parameters.

Figure 1. Investigator's Global Assessment at Each Study Visit (Evaluable Population)*



*Source: Figure 11.4.1-1 of the study report

Review of the Safety Database

Overall Exposure

The Safety population included all 24 subjects enrolled in the study, all of whom were dispensed test article and applied it at least once. Subjects were instructed to apply a thin, uniform layer of the test article to the designated Treatment Area every 12 hours for up to 2 weeks. For all populations, the average daily amount of test article used was 6.1 grams (range: 1.3 grams to 8.6 grams). The mean total amount of test article used was 85.2 grams in the Safety population and 85.3 grams in the Evaluable/PK population with a range of 20.1 grams to 124.4 grams for all populations.

Routine Clinical Tests

HPA axis testing procedures are discussed in the Clinical Pharmacology review on study 122-0551-209. The only other specified clinical evaluation was “local skin reactions.”

Safety Results

Clinical Pharmacology

Refer to Dr. Luke Oh’s, Clinical Pharmacology review on study 122-0551-209.

The primary objective of the study (study 122-0551-209) was to determine the adrenal suppression potential and the pharmacokinetic (PK) properties of HBP foam, 0.05% applied twice daily in subjects 12 to less than 18 years of age with stable plaque psoriasis.

An abnormal hypothalamic-pituitary-adrenal (HPA) axis response to a 0.25 milligram dose of cosyntropin was defined as a 30-minute post-stimulation serum cortisol level of ≤ 18 $\mu\text{g/dL}$ at Day 15/end of study (EOS).

Twenty-three subjects constituted the Evaluable population, and six of these subjects (26.1%) showed evidence of HPA axis suppression at Day 15/EOS (subjects (b) (6)). Three of the 6 subjects who showed evidence of HPA axis suppression at Day 15/EOS had quantifiable plasma concentrations at day 15/EOS (subjects (b) (6)). A total of nine subjects had measurable HBP plasma concentrations on Day 15/EOS. All six subjects who showed evidence of HPA axis suppression at Day 15/EOS had a follow up Cosyntropin Stimulation Test (CST) done at least 4 weeks after the last dose on Day 15 and the cortisol levels returned to normal. None of the subjects who showed evidence of HPA axis suppression at Day 15/EOS demonstrated any clinical signs or symptoms of adrenal suppression.

A secondary study objective was to determine the trough plasma concentrations associated with topical application of HBP foam, 0.05% in the same target population.

Blood for pharmacokinetic (PK) analysis was drawn at Screening (pre-application, time=0), pre-dose on Day 8, and on Day 15 (unless the lesions had cleared at Day 8), approximately 12 hours post-evening dose on the previous day (i.e. Day 14). All eligible subjects had blood drawn at Screening for baseline drug concentration in plasma. On Day 8, all subjects, regardless of lesion clearance, had blood drawn for assessment of trough drug concentration in plasma. At the Day 15 visit, subjects who had continued to treat lesions had a final PK blood sample collected approximately 12 hours after their Day 14 evening application and just prior to the initiation of the CST.

At Screening, all morning trough concentration of halobetasol propionate in plasma were below the quantifiable limit (BQL < 20.0 pg/mL).

On Day 8, 14 of the 23 subjects had morning trough plasma concentrations of HBP were BQL. In the remaining 9 subjects, the average plasma HBP concentration was 154.6 pg/mL with a range of 23 pg/mL to 975 pg/mL.

On Day 15/EOS, 13 of the 23 subjects had morning trough plasma concentrations of HBP were BQL. (For subject (b) (6), PK blood sample was missing as blood was drawn less than 12 hours from the previous dose). In the remaining 9 subjects, the average plasma concentration was 59.9 pg/mL with a range of 21 pg/mL to 299 pg/mL.

Reviewer comments: *In the pediatric study, 6 out of 23 (26.1%) of subjects showed HPA axis suppression. There is no set precedent in previous studies for class I topical corticosteroids that defines an approval cut-off based on the percentage of pediatric subjects demonstrating HPA axis suppression. Some class I topical corticosteroids products approved for 2 weeks of treatment of psoriasis or corticosteroid responsive*

dermatoses in patients 12 years and older do not have HPA axis suppression study results in labeling. Other class I topical corticosteroid products approved for 2 weeks of treatment of psoriasis or corticosteroid responsive dermatoses in patients 12 years and older have HPA axis suppression study outcomes ranging from 16% to 38%. These previous HPA axis suppression studies were conducted with varying methodologies in children and adults in other class I topical corticosteroid products, formulations and indications, results of which may not be comparable to LEXETTE foam.

As such, one might consider using the findings from the HPA axis suppression study in adults for LEXETTE to help guide recommendations. Per the label, (b) (6)

The reviewer finds that the percentage of patients 12 years and less than 18 years of age demonstrating HPA axis suppression in this study 122-0551-209 (26.1%) is comparable to the percentage of adult patients demonstrating HPA axis suppression in the adult study referenced in labeling (24%). As such, the data support extension of the indication to include patients 12 years of age and older for this product which carries a limitation of use for 2 weeks.

Treatment Emergent Adverse Events and Adverse Reactions

Reported treatment emergent AEs (TEAEs) were “ACTH stimulation test abnormal (6),” discussed above, “Gastritis (subject (b) (6)),” deemed moderate and not related by the investigator, and “Red blood cells urine positive due to mid-cycle bleeding (subject (b) (6)),” deemed not related by the investigator. None of the TEAEs required a change in test article dosing or discontinuation from the study.

There were no severe LSRs except for 1 case of severe telangiectasia at Baseline prior to test article application. Burning/stinging and folliculitis were absent for all subjects at all visits. Six subjects had LSRs of moderate severity (1 at baseline prior to test article application who improved during the study): telangiectasia and burning/stinging. By EOS, subjects had either improved or remained at baseline status for these LSRs. No subjects worsened relative to Baseline LSR status.

There were no other clinically significant relevant laboratory findings or abnormalities related to the study drug. The laboratory abnormalities noted during the study were also noted at baseline.

Vital signs were taken only at the screening and baseline visit.

There were no deaths, serious adverse events, or dropouts or discontinuations due to adverse effects.

Reviewer comment: *The clinical pharmacology team has concluded that the study conducted by the applicant sufficiently addresses both the PREA PMR and the terms of the Written Request. This reviewer concurs. It is recommended that the applicant is released from the PMR and that a WR is granted.*

Postmarketing safety

No safety concerns specific to HBP foam have been identified through postmarket experience. Potential adverse reactions from use of topical corticosteroids, as a general category, are well-known and are communicated in package inserts as class labeling. There were no safety concerns specific to HPA axis suppression identified through postmarket experience.

Labeling: The applicants proposed labeling was reviewed and the Agency has proposed additional modifications. Labeling negotiations are ongoing.

Conclusion: The effectiveness of HBP foam for the treatment of plaque psoriasis in patients 12 years to less than 18 years of age can be extrapolated from studies in adults. The pathophysiology and clinical presentation are the same in both populations, and the treatment response is therefore expected to be the same. HBP foam was well tolerated in study 122-0551-209, and the study raised no new safety concerns.

The applicant has adequately addressed the PREA PMR and met the terms of the WR.

Recommendation:

Based on the submitted data,

-Recommend that PMR 3344-1 is considered fulfilled and the applicant may be released from the PMR.

-Recommend that the terms of the revised WR issued on June 01, 2018 have been met and that the submission should be presented to the Pediatric Exclusivity (PE) Board. The submission was presented to the PE Board on May 19, 2021. The PE board has agreed that the terms of the revised WR issued on June 01, 2018 have been met.

-Recommend approval of extending the indication to patients twelve (12) years of age and older.

-Recommend approval of the labeling supplement upon reaching agreed upon labeling.

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

MARY E KIM
05/21/2021 01:54:53 PM

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05/24/2021 11:29:57 AM