CLINICAL REVIEW

Application Type	NDA
Application Number(s)	208183/S-002
Priority or Standard	Standard
Submit Date(s)	10/31/2019
Received Date(s)	10/31/2019
PDUFA Goal Date	08/31/2020
Division/Office	OII/DDD
Reviewer Name(s)	Brenda Carr, MD
Review Completion Date	07/14/2020
Established/Proper Name	halobetasol propionate, 0.05%
(Proposed) Trade Name	Ultravate
Applicant	Sun Pharmaceutical Industries, Inc.
Dosage Form(s)	lotion
Applicant Proposed Dosing Regimen(s)	Apply a thin layer to the affected skin twice daily for up to two weeks.
Applicant Proposed Indication(s)/Population(s)	topical treatment of plaque psoriasis in patients twelve (12) years of age and older
Recommendation on Regulatory Action	Approval
Recommended Indication(s)/Population(s) (if applicable)	topical treatment of plaque psoriasis in patients twelve (12) years of age and older

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Glossary

AC	advisory committee
AE	adverse event
AR	adverse reaction
BLA	biologics license application
BPCA	Best Pharmaceuticals for Children Act
BRF	Benefit Risk Framework
CBER	Center for Biologics Evaluation and Research
CDER	Center for Drug Evaluation and Research
CDRH	Center for Devices and Radiological Health
CDTL	Cross-Discipline Team Leader
CFR	Code of Federal Regulations
CMC	chemistry, manufacturing, and controls
COSTART	Coding Symbols for Thesaurus of Adverse Reaction Terms
CRF	case report form
CRO	contract research organization
CRT	clinical review template
CSR	clinical study report
CSS	Controlled Substance Staff
CST	Cosyntropin Stimulation Test
DMC	data monitoring committee
ECG	electrocardiogram
eCTD	electronic common technical document
EOS	end of study
ETASU	elements to assure safe use
FDA	Food and Drug Administration
FDAAA	Food and Drug Administration Amendments Act of 2007
FDASIA	Food and Drug Administration Safety and Innovation Act
GCP	good clinical practice
HBP	halobetasol propionate
HPA	hypothalamic-pituitary-adrenal
GRMP	good review management practice
ICH	International Council for Harmonization
IND	Investigational New Drug Application
ISE	integrated summary of effectiveness
ISS	integrated summary of safety
ITT	intent to treat

LSRs	local skin reactions
MedDRA	Medical Dictionary for Regulatory Activities
mITT	modified intent to treat
NCI-CTCAE	National Cancer Institute-Common Terminology Criteria for Adverse Event
NDA	new drug application
NME	new molecular entity
OCS	Office of Computational Science
OPQ	Office of Pharmaceutical Quality
OSE	Office of Surveillance and Epidemiology
OSI	Office of Scientific Investigation
PBRER	Periodic Benefit-Risk Evaluation Report
PD	pharmacodynamics
PI	prescribing information or package insert
PK	pharmacokinetics
PMC	postmarketing commitment
PMR	postmarketing requirement
PP	per protocol
PPI	patient package insert
PREA	Pediatric Research Equity Act
PRO	patient reported outcome
PSUR	Periodic Safety Update report
REMS	risk evaluation and mitigation strategy
SAE	serious adverse event
SAP	statistical analysis plan
SGE	special government employee
SOC	standard of care
TEAE	treatment emergent adverse event

1. Executive Summary

1.1. Product Introduction

Halobetasol propionate (HBP) lotion, 0.05% is a corticosteroid product, marketed under the tradename Ultravate. It was approved for the treatment of plaque psoriasis in adults on 11/06/2015. The approval letter included the following postmarketing requirement (PMR) under the Pediatric Research Equity Act (PREA):

> 2973-1 Conduct a safety, pharmacokinetics, and hypothalamic-pituitary-adrenal (HPA) axis suppression study of Ultravate (halobetasol propionate) lotion, 0.05% under maximal use conditions in adolescents 12 years to 16 years 11 months of age with plaque psoriasis receiving two weeks of treatment

The Applicant has submitted the final report for the study conducted to address the PREA PMR, study 177-0551-201. The data are intended to support expansion of the indication to include pediatric subjects 12 years and older. Based on the submitted data, I recommend that PMR 2973-1 be considered fulfilled.

Ultravate lotion is in the super-high range of potency as compared to other topical corticosteroids, based on a vasoconstrictor assay in healthy patients.[1]

1.2. Conclusions on the Substantial Evidence of Effectiveness

This section is not applicable.

1.3. Benefit-Risk Assessment

Effectiveness of HBP lotion for the treatment of plaque psoriasis in adolescents can be extrapolated from adults. The pathophysiology and clinical presentation are the same in both populations, and the treatment response is therefore expected to be the same. HBP lotion was well tolerated in study 177-0551-201, and the study raised no new safety concerns. The provided data support extension of the indication to include pediatric patients 12 years and older.

[1] Section 12.2 of the package insert for Ultravate lotion.

1.4. Patient Experience Data

Patient Experience Data Relevant to this Application	Checkbox Status	Section where discussed, if applicable
The patient experience data that was submitted as part of the application include:	□	
Clinical outcome assessment (COA) data, such as	□	[e.g., Sec 6.1 Study endpoints]
Patient reported outcome (PRO)	□	
Observer reported outcome (ObsRO)	X	Sec. 4.5
Clinician reported outcome (ClinRO)	X	Sec. 6.1.2
Performance outcome (PerfO)	□	
Qualitative studies (e.g., individual patient/caregiver interviews, focus group interviews, expert interviews, Delphi Panel, etc.)	□	
Patient-focused drug development or other stakeholder meeting summary reports	□	[e.g., Sec 2.1 Analysis of Condition]
Observational survey studies designed to capture patient experience data	□	
Natural history studies	□	
Patient preference studies (e.g., submitted studies or scientific publications)	□	
Other: (Please specify)	□	
Patient experience data that were not submitted in the application, but were considered in this review:	□	
Input informed from participation in meetings with patient stakeholders	□	
Patient-focused drug development or other stakeholder meeting summary reports	□	[e.g., Current Treatment Options]
Observational survey studies designed to capture patient experience data	□	
Other: (Please specify)	□	
Patient experience data was not submitted as part of this application.	□	

2. Therapeutic Context

2.1. Analysis of Condition

Psoriasis is a chronic, multisystem, inflammatory disease that classically presents as sharply-demarcated, scaly, erythematous plaques that are symmetrically-distributed. It is common, affecting approximately 2% of the general population, and the frequency is the same in males and females. Onset in childhood is reported by approximately one-third of patients,[2] and plaque psoriasis is the most common presentation in pediatric patients.[3]

2.2. Analysis of Current Treatment Options

Topical products that are approved for treatment of psoriasis in patients 12 years and older include calcipotriene and betamethasone dipropionate foam, 0.005%/0.064% (a vitamin D analog and corticosteroid combination product), and calcipotriene foam, 0.005% (a vitamin D analog). Calcipotriene foam, 0.005% is approved for treatment of plaque psoriasis on the scalp and body in pediatric patients 4 years and older.

3. Regulatory Background

3.1. U.S. Regulatory Actions and Marketing History

The halobetasol propionate moiety was initially approved on 12/17/1990 in an ointment dosage form for topical use for "the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses" (Ultravate® ointment; NDA 19968). A cream dosage form was approved for the same indication on 12/27/1990 (Ultravate® cream; NDA 19967).

3.2. Summary of Presubmission/Submission Regulatory Activity

The Applicant was granted three deferral extensions for completion of the PREA PMR study. The Applicant requested the extensions due to challenges to fully enrolling the study, despite their comprehensive recruitment efforts. The Applicant reported the challenges to enrollment as including:

- The availability of systemic treatments for the target pediatric population (e.g., etanercept).

[2] Bronckers IMGJ, Paller AS, van Geel MJ, van de Kerkhof PCM, Seyger MMB. Psoriasis in Children and Adolescents: Diagnosis, Management and Comorbidities. *Pediatr Drugs* 2015;17:373–384.
[3] Tangtatco JAA and Lara-Corrales I.Update in the management of pediatric psoriasis. *Curr Opin Pediatr* 2017;29:434–442.

- The availability of numerous other topical agents, which limited the potential target population and caretakers' willingness to allow their children to participate in the clinical study.
- The low prevalence of psoriasis in children (the Applicant reported it as ~0.2% in American children 12-17 years old).
- The requirement for ≥10% body surface area (BSA) involvement.

On 03/18/2019, the Applicant requested to terminate the study due to continued difficulty in fully enrolling the study, despite the deferral extensions. Per the PMR, 20 subjects were to have been enrolled in the study. After 2 years of recruitment, the Applicant had been able to enroll only 14 subjects. On 07/31/2019, the Agency agreed that the Applicant could terminate the study and advised the Applicant to submit a final study report in a prior approval supplement.

3.3. Foreign Regulatory Actions and Marketing History

This section is not applicable.

4. Significant Issues from Other Review Disciplines Pertinent to Clinical Conclusions on Efficacy and Safety

4.1. Office of Scientific Investigations (OSI)

OSI audit was not requested for this supplement.

4.2. Product Quality

This section is not applicable.

4.3. Clinical Microbiology

This section is not applicable.

4.4. Nonclinical Pharmacology/Toxicology

This section is not applicable.

4.5. Clinical Pharmacology

The primary objective of the required study (study 177-0551-201) was to determine the adrenal suppression potential associated with topical application of HBP Lotion, 0.05% under maximal use conditions in subjects 12 to 16 years 11 months of age with plaque psoriasis. An abnormal

hypothalamic-pituitary-adrenal (HPA) axis response was defined as a 30-minute post-stimulation serum cortisol level of ≤18 μg/dL at Day 15/end of study (EOS).

Fourteen subjects constituted the Evaluable population, and one of these subjects (7.1%) had an abnormal HPA axis response at Day 15/EOS. This subject's (Subject (b) (6)) daily average amount of test article usage was 7.3 grams, with a total test article usage of 102.2 grams. Post-Cosyntropin Stimulation Test (CST) cortisol levels for this subject had returned to normal at a follow-up visit approximately 6 months after Day 15/EOS.

Table 1. Subject(s) Who Had Adrenal Suppression at Day 15*

Subject #	Screening Post-CST Cortisol **(μg/dL)**	Day 15 Post-CST Cortisol **(μg/dL)**	Follow-Up Post-CST Cortisol **(μg/dL)**	Total Test Article Used (grams)
(b) (6)	24.4	16.2	28.2	102.2

*Source: Table 11.4-1 of the study report
CST = Cosyntropin Stimulation Test

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

Blood for pharmacokinetic (PK) analysis was drawn at Screening (pre-application, time=0), Day 8, and Day 15 (unless the lesions had cleared at Day 8), approximately 12 hours after the dose on the previous day. 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.

The Applicant reported that the morning trough concentration of halobetasol propionate in plasma was below quantification limit (lower limit of quantification [LOQ] of 0.02 ng/mL) for all subjects at all time points except for Subject (b) (6) at Day 15/EOS who was near the LOQ with a trough concentration of halobetasol propionate of 0.0282 ng/mL.

Details of the study design are provided in Sec. 6.

4.6. Devices and Companion Diagnostic Issues

This section is not applicable.

4.7. Consumer Study Review

This section is not applicable.

5. Sources of Clinical Data and Review Strategy

5.2. Table of Clinical Studies

This section is not applicable. The single study is discussed in Sec. 6.

5.3. Review Strategy

Although Study 177-0551-201 was not an efficacy trial, I discuss the study in Section 6, in accord with the format of the template.

6. Review of Relevant Individual Trials Used to Support Efficacy

6.1. An Open Label Evaluation of the Adrenal Suppression Potential and Pharmacokinetic Properties of Twice Daily Halobetasol Propionate Lotion, 0.05% in Subjects 12 to 16 Years 11 Months of Age with Plaque Psoriasis Receiving Two Weeks of Treatment (177-0551-201)

6.1.1. Study Design

Overview and Objective

The objective was to determine the adrenal suppression potential and the pharmacokinetic (PK) properties of halobetasol propionate lotion, 0.05% (Ultravate Lotion) applied twice daily in subjects aged 12 to 16 years 11 months with stable plaque psoriasis.

Inclusion criteria included the following:

- male or non-pregnant female, 12 to 16 years 11 months of age.
- clinical diagnosis of stable plaque psoriasis involving a minimum of 10% body surface area (BSA) within the Treatment Area ("Treatment Area" was defined as the entire body exclusive of the face, scalp, groin, axillae, and other intertriginous areas.)
- Investigator's Global Assessment (IGA) score of at least three (3 = moderate) at baseline

Table 2. Investigator's Global Assessment (IGA)

CLEAR (0)	
Scaling	No evidence of scaling.
Erythema	No evidence of erythema (except possible residual discoloration).
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 to very marked elevation, with hard to very hard sharp edges on virtually all or all of the plaques.

Subjects had a screening Cosyntropin Stimulation Test (CST) and screening PK for drug concentration. Subjects with a normal response to CST (post-stimulation serum cortisol > 18 μg/dL) and who continued to meet all enrollment criteria were enrolled in the study. Subjects applied the first dose in the clinic and were instructed to apply test article twice daily to

psoriatic plaques until Day 15. The maximum total dose of test article to be applied weekly was approximately 50 grams.

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 AEs, LSRs, and a final trough PK blood sample prior, and EOS CST. Subjects with adrenal suppression (defined as post-CST cortisol level < 18 μg/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.

Trial Design

This was an open-label, multinational trial.

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 ≤18 μg/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 and LSRs associated with topical application of corticosteroids (telangiectasia, skin atrophy, burning/stinging and folliculitis).

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

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.

Protocol Amendments

The upper age limit for the study was changed from "less than 18 years" to "16 years 11 months" based on an FDA recommendation following review of the protocol.

6.1.2. Study Results

Compliance with Good Clinical Practices

The Applicant attested that the study was conducted in accordance with principles of the Declaration of Helsinki, with the current Good Clinical Practice guidelines and with other applicable regulations.

Financial Disclosure

The Applicant certified that they had not entered into any financial arrangement with any clinical investigators.

Patient Disposition

A total of 19 subjects were screened: 16 subjects were enrolled into the study, and 3 subjects were screen failures. The reason for the 3 screen failures was failure to meet randomization criteria (exclusion criterion #17: subjects had a screening CST with a post 30-minute stimulation cortisol level of ≤ 18 µg/dL).

All 16 enrolled subjects completed the study. However, 2 (Subjects (b) (6) and (b) (6)) were excluded from the Evaluable population because the EOS CST was completed 6 days after their last application of test article. Thus, the Evaluable population consisted of 14 subjects. All 16 subjects were included in the Safety population.

Protocol Violations/Deviations

Protocol deviations included test article deviation (13), lab testing deviation (10), informed consent (10), visit out of window (2), and assessment deviation (1).

Demographic Characteristics

There were 6 females (37.5%) and 10 males (62.5%) enrolled into the study. All subjects were White and Hispanic or Latino (16/16, 100.0%). The average age of enrolled subjects was 14.1 years (range: 12.5 years to 16.9 years).

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

One subject reported other medical conditions: asthma, allergic rhinitis, warts, nonalcoholic steatohepatitis, and obesity. One subject reported a prior medication: fluocinonide for scalp, elbow, and knee psoriasis). This product was discontinued prior to the screening CST (the CST was done after an appropriate washout period).

Of the 14 Evaluable subjects, 12 (85.7%) had moderate (Grade 3) disease, and 2 (14.2%) had severe (Grade 4) disease at Baseline. The mean percent affected BSA at Baseline for the Evaluable population was 11.5% with a range of 10% to 14% and the mean percent BSA to be treated was 11.1% with a range of 10% to 14%.

No subjects had atrophy or folliculitis at Baseline, and 4 subjects (25%) had telangiectasia.

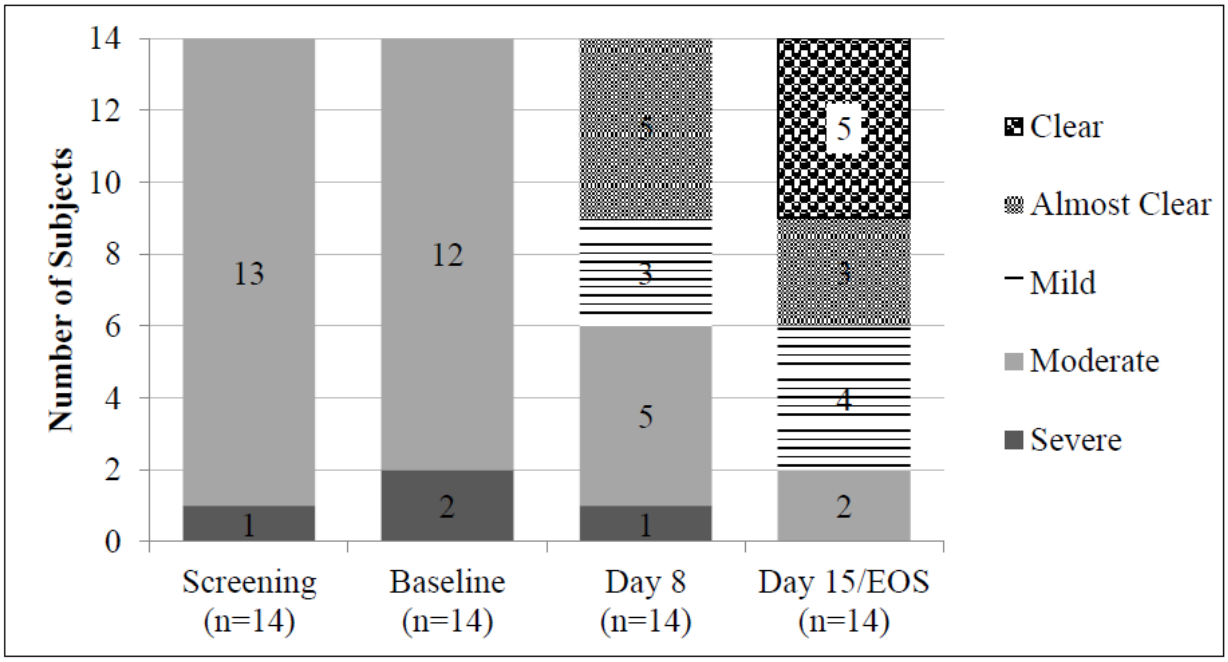
Treatment Compliance, Concomitant Medications, and Rescue Medication Use

Compliant subjects were defined as those who applied at least 80% and no more than 120% of the expected number of applications. The reported average dosing compliance was "100.5%" with a reported range of "89.3% to 114.3%" in the Evaluable and PK populations. The mean number of days dosed was 14.3 days with a range of 14 days to 16 days in the Evaluable and PK populations. The mean total number of applications was 28.1 with a range of 25 to 32 for 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 12.1.1-1 of the study report

Data Quality and Integrity

No issues were identified with the data quality or integrity.

Efficacy Results – Secondary and other relevant endpoints

This section is not applicable.

Dose/Dose Response

This section is not applicable.

Durability of Response

This section is not applicable.

Persistence of Effect

This section is not applicable.

Additional Analyses Conducted on the Individual Trial

This section is not applicable.

7. Integrated Review of Effectiveness

7.1. Assessment of Efficacy Across Trials

This section is not applicable.

7.2. Additional Efficacy Considerations

7.2.1. Considerations on Benefit in the Postmarket Setting

No differences are anticipated, regarding how the product was studied and how the product may be used, to affect recommendations on a regulatory action or labeling.

7.2.2. Other Relevant Benefits

This section is not applicable.

7.3. Integrated Assessment of Effectiveness

This section is not applicable.

8. Review of Safety

8.1. Safety Review Approach

The safety data from study 177-0551-201 were reviewed.

8.2. Review of the Safety Database

8.2.1. Overall Exposure

The Safety population included all 16 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. In the Safety population, the average daily amount of test article used was 7.2 grams (range: 2.9 grams to 10.4 grams). The mean total amount of test article used was 102.3 grams (range: 39.9 grams to 145.8 grams).

8.2.2. Relevant characteristics of the safety population:

See Sec. 6.1.2.

8.2.3. Adequacy of the safety database:

The safety database was adequate.

8.3. Adequacy of Applicant's Clinical Safety Assessments

8.3.1. Issues Regarding Data Integrity and Submission Quality

No issues were identified with the data integrity or submission quality.

8.3.2. Categorization of Adverse Events

The categorization of AEs was acceptable.

8.3.3. Routine Clinical Tests

HPA axis testing procedures are discussed in Sec. 4.5 and 6.1.1. The only other specified clinical evaluation was "local skin reactions."

8.4. Safety Results

8.4.1. Deaths

There were no deaths.

8.4.2. Serious Adverse Events

There were no serious adverse events.

8.4.3. Dropouts and/or Discontinuations Due to Adverse Effects

There were no dropouts or discontinuations due to adverse effects.

8.4.4. Significant Adverse Events

See discussion of HPA axis testing results in Sec. 4.5.

8.4.5. Treatment Emergent Adverse Events and Adverse Reactions

The only reported treatment emergent AE was "ACTH stimulation test abnormal," and this subject is discussed in Sec. 4.5.

There were no severe LSRs. Two subjects experienced LSRs of moderate severity: telangiectasia and burning/stinging. By EOS, subjects had either improved or returned to baseline status for these LSRs. No subjects worsened relative to Baseline status.

8.4.6. Laboratory Findings

See Sec. 4.5.

8.4.7. Vital Signs

Vital signs were taken only at the baseline visit.

8.4.8. Electrocardiograms (ECGs)

ECGs were not done in the study.

8.4.9. QT

This section is not applicable.

8.4.10. Immunogenicity

This section is not applicable.

8.5. Analysis of Submission-Specific Safety Issues

See discussion of HPA axis testing in Sec. 4.5 and LSRs in Sec. 8.4.5.

8.6. Safety Analyses by Demographic Subgroups

There were only 16 subjects enrolled in the study, all of whom were White and Hispanic. The number of subjects in any subgroup is too small to permit any meaningful assessment.

8.7. Specific Safety Studies/Clinical Trials

This review pertains to a safety study.

8.8. Additional Safety Explorations

8.8.1. Human Carcinogenicity or Tumor Development

This section is not applicable.

8.8.2. Human Reproduction and Pregnancy

No pregnancies were reported in the study.

8.8.3. Pediatrics and Assessment of Effects on Growth

This review pertains to a pediatric assessment (12 years to 16 years 11 months). Per the approval letter, pediatric studies for ages 0 to 11 years 11 months were waived "because the product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this age group and is not likely to be used in a substantial number of pediatric patients in this group. Topical corticosteroid products are available for treating pediatric patients with psoriasis."

8.8.4. Overdose, Drug Abuse Potential, Withdrawal, and Rebound

Per the label, treatment with HBP beyond two weeks is not recommended, and the total dosage should not exceed 50 grams (50 ml) per week because of the potential for HPA axis suppression. There is no information suggesting addiction or abuse potential with HBP.

8.9. Safety in the Postmarket Setting

8.9.1. Safety Concerns Identified Through Postmarket Experience

No safety concerns specific to HBP lotion 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.

8.9.2. Expectations on Safety in the Postmarket Setting

Based on the available safety data, the expectation is that the postmarketing safety experience with HBP lotion for patients aged 12 years to 16 years 11 months will be similar to the experience of adults.

8.9.3. Additional Safety Issues From Other Disciplines

There were no safety issues from other disciplines.

8.10. Integrated Assessment of Safety

This section is not applicable to this review.

9. Advisory Committee Meeting and Other External Consultations

This application was not discussed at an advisory committee meeting.

10. Labeling Recommendations

10.1. Prescription Drug Labeling

The medical officer has reviewed labeling. Labeling was being finalized as this review closed.

10.2. Nonprescription Drug Labeling

This section is not applicable to this review.

11. Risk Evaluation and Mitigation Strategies (REMS)

A REMS is not necessary.

12. Postmarketing Requirements and Commitments

This section is not applicable to this review.

13. Appendices

13.1. References

See footnotes.

13.2. Financial Disclosure

Covered Clinical Study (Name and/or Number): An Open Label Evaluation of the Adrenal Suppression Potential and Pharmacokinetic Properties of Twice Daily Halobetasol Propionate Lotion, 0.05% in Subjects 12 to 16 Years 11 Months of Age with Plaque Psoriasis Receiving Two Weeks of Treatment

Was a list of clinical investigators provided:	Yes ☒	No ☐ (Request list from Applicant)
Total number of investigators identified: 5		
Number of investigators who are Sponsor employees (including both full-time and part-time employees): 0		
Number of investigators with disclosable financial interests/arrangements (Form FDA 3455): 0		
If there are investigators with disclosable financial interests/arrangements, identify the number of investigators with interests/arrangements in each category (as defined in 21 CFR 54.2(a), (b), (c) and (f)): Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: _____ Significant payments of other sorts: _____ Proprietary interest in the product tested held by investigator: _____ Significant equity interest held by investigator in S Sponsor of covered study: _____		
Is an attachment provided with details of the disclosable financial interests/arrangements:	Yes ☐	No ☐ (Request details from Applicant)
Is a description of the steps taken to minimize potential bias provided:	Yes ☐	No ☐ (Request information from Applicant)
Number of investigators with certification of due diligence (Form FDA 3454, box 3) 0		

Is an attachment provided with the reason:	Yes ☐	No ☐ (Request explanation from Applicant)

APPEARS THIS WAY ON ORIGINAL

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/

BRENDA CARR
07/30/2020 06:52:37 PM

SNEZANA TRAJKOVIC
07/31/2020 09:54:32 AM