3.2.P.1 Description and Composition of the Drug Product

This section contains the description and composition of the drug product for each strength. Aucta Pharmaceuticals, Inc. (Aucta) is the applicant and Pharmasol Corporation (Pharmasol) is the drug product manufacturer.

A. Description of Dosage Form

The proposed generic drug product, Clobetasol Propionate Foam is a topical solution that contains 0.05% of Clobetasol Propionate. This proposed product is designed as a generic version of the reference listed drug (RLD), OLUX™ (clobetasol propionate) Foam, 0.05% (NDA 021142 owned by Mylan Pharmaceuticals Inc.).

The bioequivalence between the proposed generic Clobetasol Propionate Foam, 0.05% and the RLD were established utilizing the In Vitro option following OGD's recommendation in Agency's Response to Control Correspondence # 15457592. The proposed generic Clobetasol Propionate Foam, 0.05% and the RLD are bioequivalent as described in the product specification draft guidance on Clobetasol Propionate Foam:

- Qualitatively and Quantitatively the same (Q1/Q2) as defined in FDA's guidance for industry ANDA Submissions – Refuse-to-Receive Standards.
- There are no inactive ingredients differ from the RLD.
- There are no ingredients proportionally more than ± 5% compared to the RLD.
- Data from the following comparative in vitro assays of test vs. reference:
    - ***Microscopic Birefringence Analysis*** on the dispensed foam after complete collapse to determine whether any crystals of undissolved clobetasol propionate form during dispensing.
    - ***Time to Break Analysis***, conducted at 30ºC, 33ºC, 35ºC, and 40ºC. Time to break is the time from dispensing to complete foam collapse (break). The testing was done on 3 different lots of the RLD and 3 lots of the test product (with each lot manufactured separately).
    - ***Weight per volume of uncollapsed foam***.

	RLD (NDA 021142) **OLUX™ (Clobetasol Propionate) Foam[1]**	**Aucta's Generic (ANDA 214612)** **Clobetasol Propionate Foam**
Name	OLUX™ (clobetasol propionate) Foam, 0.05%	Clobetasol Propionate Foam, 0.05%
Active Ingredients	Clobetasol Propionate, USP	Clobetasol Propionate, USP
Dosage Form	Aerosol, Foam	Aerosol, Foam
Strengths	0.05%	0.05%
Route of Administration	Topical	Topical
Rx	Prescription	Prescription
Inactive Ingredients [2]	Cetyl Alcohol, Citric Acid, Ethanol, Polysorbate 60, Potassium Citrate, Propylene Glycol, Purified Water, Stearyl Alcohol, Hydrocarbon (Butane/Propane) Propellant	Cetyl Alcohol, Citric Acid, Dehydrate Alcohol, Polysorbate 60, Potassium Citrate Monohydrate Granular, Propylene Glycol, Purified Water, Stearyl Alcohol, Propellant

[1] Information regarding the RLD, OLUX™ (clobetasol propionate) Foam description was obtained from FDA Drug Database, Drugs@FDA and DailyMed.

[2] Inactive Ingredients: The inactive ingredients used in the generic drug formulation are safe and well recognized for their uses in ointment dosage forms. In addition, all the excipients used in the formulation are below the allowed limits as per FDA's Inactive Ingredient Database. Please refer to Module 3.2.P.4.1 for information on each proposed excipient.

Clobetasol Propionate Foam, 0.05% is packaged in two packaging configurations:

50 g Clobetasol Propionate Foam, 0.05%:

- Can 35mm x 125mm – Aluminum, round shoulder, non-machined curl, white, unprinted, Pam internal lining
- Valve S90 – Aluminum Spherical Cup without diptube
- Actuator – White, HDPE Mars Spout Inverted, Natural PP Cap

100 g Clobetasol Propionate Foam, 0.05%:

- Can 45mm x 120mm – Aluminum, oval shoulder, non-machined curl, white, unprinted, Pam internal lining
- Valve S90 – Aluminum Spherical Cup without diptube
- Actuator – White, HDPE Mars Spout Inverted, Natural PP Cap

The physical description comparison between the reference listed drug (RLD), OLUX™ (Clobetasol Propionate) Foam, 0.05% and Aucta's generic Clobetasol Propionate Foam, 0.05% is provided in the table below:

Drug Product	Aucta's Generic Clobetasol Propionate Foam	RLD OLUX™ (Clobetasol Propionate) Foam[1]
Strength	0.05%	0.05%
Description	A white to off white colored foam when dispensed from the can	White aerosol foam

[1] Information regarding the RLD, OLUX™ (clobetasol propionate) Foam description was obtained from FDA Drug Database, Drugs@FDA.

B. Composition of Drug Product

Qualitative Composition

The qualitative composition and function of excipients are provided below:

Ingredient	Function
Clobetasol Propionate, USP	Active
Cetyl Alcohol, NF	Emulsifier, Foam Stabilizer
Stearyl Alcohol, NF	Emulsifier, Foam Stabilizer
Polysorbate 60, NF	Emulsifier
Dehydrate Alcohol, USP	Solvent
Purified Water, USP	Solvent
Propylene Glycol, USP	Solvent, Humectant
Citric Acid Anhydrous, USP	Buffering Agent
Potassium Citrate Monohydrate Granular, USP	Buffering Agent
Propellant AP-70	Propellant

Qualitative Composition

The composition of Aucta's Generic Clobetasol Propionate Foam, 0.05% is provided below.

Ingredient	Composition (%w/w)	Weight / Bottle		Weight / Single Application[2] (mg)
		50 g	100 g	
Clobetasol Propionate, USP	0.05	0.025	0.05	1.8
Dehydrate Alcohol, USP	60.71	30.355	60.71	2185.56
Polysorbate 60, NF	0.41	0.205	0.41	14.76
Cetyl Alcohol, NF	1.14	0.57	1.14	41.04
Stearyl Alcohol, NF	0.51	0.255	0.51	18.36
Propylene Glycol, USP	2.09	1.045	2.09	75.24
Purified Water, USP	34.88	17.44	34.88	1255.68
Citric Acid Anhydrous, USP	0.08	0.04	0.08	2.88
Potassium Citrate Monohydrate Granular, USP	0.13	0.065	0.13	4.68
Propellant AP-70 [1]	5.00[1]	2.66[1]	5.29[1]	n/a[1]
Total	100.0	50	100	3600

[1] The propellant is listed as an inactive ingredient; however, it is not calculated in the composition of the formulation since it evaporates immediately upon dispense. It is only used during packaging. The components of the propellant are listed in the GRAS list, the composition specification sheet and the manufacturer document for GRAS and Residual Solvents statements are provided in 3.2.P.4.4 Propellant AP-70.

[2] The single application of Clobetasol Propionate Foam, 0.05% should not exceed 3.6 g according to the RLD label (Apply to the affected skin area 2 time each day. Do not use more than 50 g or 21 capfuls in 1 week.)

Absolute alcohol in terms of percent volume (volume/volume): 68.88%

Due to the characteristic of the drug product solution, the clobetasol propionate foam solution will congeal at 25°C. Therefore, the density was calculated at 38°C, where the clobetasol foam solution is in clear liquid form. The drug product density tested during development is 0.8774 g/ml (under 38°C). The alcohol density under 38°C is 0.773 g/ml. The dehydrate alcohol proof 200 concentration (%w/w) in the formulation is 60.71%. Based on prementioned parameters, the absolute alcohol in terms of percent volume under 38°C is 68.88 %v/v.

C. Overage / Overfill

There is no designed overage in the generic Clobetasol Propionate Foam, 0.05%

D. Elemental Iron Content

There is no color additive included in the formulation of Clobetasol Propionate Foam, 0.05%. Moreover, the maximum iron daily intake for Clobetasol Propionate Foam, 0.05% does not exceed 5 mg per day. Clobetasol Propionate Foam, 0.05% meets the requirement of 21 CFR 73.1200.

E. Maximum IID Limits

Ingredients Database (CDER IID last updated on July 28, 2020):
All the inactive ingredients used in proposed generic drug product are qualitatively same as that of RLD. The inactive ingredients in drug product comply with the limits specified by the FDA's Inactive Ingredients Database for aerosol foam through topical administration. The comparison of inactive ingredients used in proposed drug product and FDA's Inactive Ingredients Database is provided below. For topical products and other products where excipients are expressed as a percentage of the product formula, maximum potency is the highest formula percentage.

Ingredient	Composition (%w/w)	Max Daily Exposure (mg/day) [1]	IID Limit (%w/w)	Complies (Yes/No)
Dehydrate Alcohol, USP	60.71	4371.12	68.5	Yes
Polysorbate 60, NF	0.41	29.52	0.43 (Aerosol, Foam) CAS 9005678; UNII CAL22UVI4M	Yes
Cetyl Alcohol, NF	1.14	82.08	3.23 (Aerosol, Foam) CAS 36653824; UNII 936JST6JCN	Yes
Stearyl Alcohol, NF	0.51	36.72	1 (Aerosol, Foam) CAS 112925; UNII 2KR89I4H1Y	Yes
Propylene Glycol, USP	2.09	150.48	21.05 (Aerosol, Foam) CAS 57556; UNII 6DC9Q167V3	Yes
Purified Water, USP	34.88	2511.36	N/A	N/A
Citric Acid Anhydrous, USP	0.08	5.76	0.11 (Aerosol, Foam) CAS 77929; UNII XF417D3PSL	Yes
Potassium Citrate Monohydrate Granular, USP	0.13	9.36	0.17 (Aerosol, Foam) CAS 6100056; UNII EE90ONI6FF	Yes
Propellant AP-70[2] (GRAS)	5.00	N/A	N/A	N/A
Components	*max*	*max*		
Methane	*0.0075*	*0.54*	*N/A*	*N/A*
Ethane	*0.125*	*9*	*N/A*	*N/A*
Propane	*2.9895*	*215.244*	*N/A*	*N/A*
Isobutane	*1.1445*	*82.404*	*82.4 (Aerosol, Foam)* *CAS 75285; UNII BXR49TP611*	*Yes*
N-butane	*1.6155*	*116.316*	*N/A*	*N/A*
Isopentane	*0.075*	*5.4*	*N/A*	*N/A*
N-Pentane	*0.075*	*5.4*	*N/A*	*N/A*

[1] Maximum Daily Exposure (MDE) is the total amount of the excipient that would be taken in a day based on the maximum daily dose (MDD). Maximum daily dose of Clobetasol Propionate Foam, 0.05% is 7.2 g according to the RLD label. Reference FDA's July 2019 *Guidance for Industry – Using the Inactive Ingredient Database*, during the technical assessment of an ANDA, the MDE of excipients is considered for the proposed context of use only.

[2] The propellant is listed as an inactive ingredient; however, it does not have to be calculated in the composition of the formulation since it evaporates immediately upon dispense. Nonetheless, the MDE is calculated under the worst-case scenario to demonstrate that Aucta's generic product is safe. The components of the propellant are listed in the GRAS list, the composition specification sheet and the manufacturer document for GRAS and Residual Solvents statements are provided in 3.2.P.4.4 Propellant AP-70.