HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use FINACEA Foam safely and effectively. See full prescribing information for FINACEA Foam.

FINACEA® (azelaic acid) foam, for topical use
Initial U.S. Approval: 1995

INDICATIONS AND USAGE

FINACEA Foam is indicated for the topical treatment of inflammatory papules and pustules of mild to moderate rosacea. (1)

DOSAGE AND ADMINISTRATION

- Apply a thin layer twice daily (morning and evening) to the entire facial area (cheeks, chin, forehead, and nose). (2)
- Use only very mild soaps or soapless cleansing lotion and pat dry with a soft towel before applying FINACEA Foam. (2)
- Wash hands immediately following application. (2)
- Cosmetics may be applied after the application of FINACEA Foam has dried. (2)
- Avoid use of alcoholic cleansers, tinctures and astringents, abrasives and peeling agents. (2)
- For topical use. (2)
- Not for oral, ophthalmic or intravaginal use. (2)

DOSAGE FORMS AND STRENGTHS

Foam, 15% (3)

CONTRAINDICATIONS

None. (4)

WARNINGS AND PRECAUTIONS

- *Hypopigmentation:* Isolated cases of hypopigmentation occurred after azelaic acid use. Monitor patients with dark complexion for early signs of hypopigmentation (5.1)
- *Eye and Mucous Membrane Irritation:* Azelaic acid has been reported to cause irritation of the eyes. Avoid contact with the eyes and mucous membranes. (5.2)
- *Flammability:* Contents are flammable. Instruct the patient to avoid fire, flame, and smoking during and immediately following application. (5.3)

ADVERSE REACTIONS

The most common adverse reactions (incidence ≥ 0.5% of subjects treated with FINACEA Foam) are local site pain (6.2%), pruritus (2.5%), dryness (0.7%), and erythema (0.7%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact LEO Pharma Inc. at 1-877-494-4536 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION

Revised: 12/2020

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

FINACEA Foam, 15% is indicated for topical treatment of the inflammatory papules and pustules of mild to moderate rosacea.

2 DOSAGE AND ADMINISTRATION

- Shake well before use.
- Cleanse affected area(s) using only very mild soaps or soapless cleansing lotion and pat dry with a soft towel before application of FINACEA Foam.
- Apply FINACEA Foam twice daily (morning and evening) to the entire facial area (cheeks, chin, forehead, and nose). For a single application, dispense the smallest amount of foam necessary to adequately cover the affected area(s) with a thin layer.
- Use FINACEA Foam continuously over 12 weeks.
- Wash hands immediately following application of FINACEA Foam.
- Cosmetics may be applied after the application of FINACEA Foam has dried.
- Reassess the diagnosis if no improvement is observed upon completing 12 weeks of therapy.
- Avoid the use of occlusive dressings or wrappings.
- Instruct patients to avoid use of alcoholic cleansers, tinctures and astringents, abrasives and peeling agents.
- For topical use.
- Not for oral, ophthalmic or intravaginal use.

3 DOSAGE FORMS AND STRENGTHS

Each gram of FINACEA (azelaic acid) Foam contains 0.15 g of azelaic acid (15% w/w) in a white to off-white foam.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Hypopigmentation

There have been reports of hypopigmentation after use of azelaic acid. Because azelaic acid has not been well studied in patients with dark complexion, monitor these patients for early signs of hypopigmentation.

5.2 Eye and Mucous Membranes Irritation

Azelaic acid has been reported to cause irritation of the eyes. Avoid contact with the eyes, mouth and other mucous membranes. If FINACEA Foam does come in contact with the eyes, wash the eyes with large amounts of water and consult a physician if eye irritation persists.

5.3 Flammability

The propellant in FINACEA Foam is flammable. Instruct the patient to avoid fire, flame, and smoking during and immediately following application. Do not puncture and/or incinerate the containers. Do not expose containers to heat and/or store at temperatures above 120°F (49°C).

6 ADVERSE REACTIONS

The following adverse reactions are described elsewhere in the prescribing information:

- Hypopigmentation *[see Warnings and Precautions (5.1)]*.
- Eye and Mucous Membranes Irritation *[see Warnings and Precautions (5.2)]*.

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

FINACEA Foam was evaluated for the treatment of papulopustular rosacea in two multicenter, randomized, double-blind, vehicle-controlled, 12-week clinical trials involving a total of 1362 (FINACEA Foam, 15%: 681; vehicle: 681) subjects. Overall, 95.7% of subjects were White, 73.4% were female, and the mean age was 50.6 years.

Table 1: Adverse Reactions Occurring in ≥ 0.5% of Subjects Treated with FINACEA Foam Compared with Subjects Treated with Vehicle

System/Organ Class Preferred	FINACEA Foam, 15% (N=681) n (%)	Vehicle (N=681) n (%)
General disorders and application site conditions		
Application site pain*	42 (6.2%)	10 (1.5%)
Application site pruritus	17 (2.5%)	2 (0.3%)
Application site dryness	5 (0.7%)	5 (0.7%)
Application site erythema	5 (0.7%)	6 (0.9%)

* *"Application site pain" is a term used to describe disagreeable skin sensations, including burning, stinging, paraesthesia and tenderness.*

Local Tolerability Studies

In a 21-day cumulative irritation study under occlusive conditions, mild-to-moderate irritation was observed for azelaic acid pre-foam emulsion. In a human repeat insult patch test (HRIPT) study, no sensitization potential was observed for azelaic acid pre-foam emulsion.

6.2 Postmarketing Experience

Hypersensitivity, rash and worsening of asthma have been reported from the postmarketing experience of azelaic acid-containing formulations. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Azelaic acid is minimally absorbed systemically following topical route of administration, and maternal use is not expected to result in fetal exposure to the drug *[see Clinical Pharmacology (12.3)]*.

In animal reproduction studies, embryofetal toxicity was noted when azelaic acid was administered orally during the period of organogenesis at doses 162, 19, and 65 times the maximum recommended human dose (MRHD) in rats, rabbits, and monkeys, respectively. Maternal toxicity was noted at these doses but no malformations were observed in these embryofetal developmental studies (*see Data*).

The background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

Data

Animal Data

Dermal embryofetal developmental toxicology studies have not been performed with azelaic acid, 15% foam. Oral embryofetal developmental studies were conducted with azelaic acid in rats, rabbits, and cynomolgus monkeys. Azelaic acid was administered during the period of organogenesis in all three animal species. Embryotoxicity was observed in rats, rabbits, and monkeys at oral doses of azelaic acid that generated some maternal toxicity. Embryotoxicity was observed in rats given 2500 mg/kg/day [162 times the MRHD based on body surface area (BSA) comparison], rabbits given 150 or 500 mg/kg/day (19 or 65 times the MRHD based on BSA comparison) and cynomolgus monkeys given 500 mg/kg/day (65 times the MRHD based on BSA comparison) azelaic acid. No malformations were observed in the oral embryofetal developmental studies conducted in rats, rabbits and cynomolgus monkeys.

An oral peri- and post-natal developmental study was conducted in rats. Azelaic acid was administered from gestational day 15 through day 21 postpartum up to a dose level of 2500 mg/kg/day. Embryotoxicity was observed in rats at an oral dose of 2500 mg/kg/day (162 times the MRHD based on BSA comparison) that generated some maternal toxicity. In addition, slight disturbances in the post-natal development of fetuses was noted in rats at oral doses that generated some maternal toxicity (500 and 2500 mg/kg/day; 32 and 162 times the MRHD based on BSA comparison). No effects on sexual maturation of the fetuses were noted in this study.

8.2 Lactation

Risk Summary

Azelaic acid is naturally present in human milk. When used as prescribed, azelaic acid is unlikely to be absorbed through the skin in clinically relevant amounts to cause a change in azelaic acid concentration in milk or milk production; therefore, breastfeeding is not expected to result in exposure of the infant to FINACEA Foam. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for FINACEA Foam and any potential adverse effects on the breastfed child from FINACEA Foam or from the underlying maternal condition.

8.4 Pediatric Use

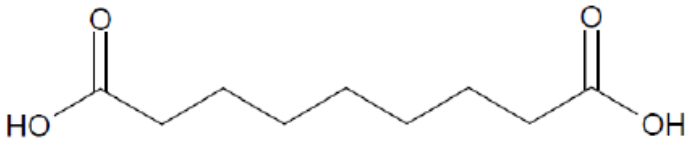
The safety and efficacy of FINACEA Foam have not been established in pediatric patients.

8.5 Geriatric Use

Of the total number of subjects in clinical studies of FINACEA Foam, 18.8 percent were 65 and over, while 7.2 percent were 75 and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

11 DESCRIPTION

FINACEA (azelaic acid) Foam contains 15% (w/w) azelaic acid, a naturally-occurring saturated dicarboxylic acid and is suspended in an oil-in-water emulsion vehicle. It is for topical use. Chemically, azelaic acid is 1,7-heptanedicarboxylic acid. The structural formula of azelaic acid is:



Azelaic acid has a molecular formula of $C_9 H_{16} O_4$ and a molecular weight of 188.22.

The aluminum containers are filled with hydrophilic emulsion, crimped with a continuous spray valve, and pressurized with propellants consisting of propane, butane, and isobutane. Each gram of FINACEA Foam, 15% contains 0.15 g of azelaic acid. FINACEA Foam also contains benzoic acid (as a preservative), cetostearyl alcohol, dimethyl isosorbide, medium-chain triglycerides, methylcellulose, mono- and di-glycerides, polyoxyl 40 stearate, polysorbate 80, propylene glycol, purified water, sodium hydroxide (to adjust pH), and xanthan gum as inactive ingredients.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The mechanism(s) by which azelaic acid interferes with the pathogenic events in rosacea are unknown.

12.2 Pharmacodynamics

The efficacy of FINACEA Foam is being driven by local mechanisms of azelaic acid within the skin.

12.3 Pharmacokinetics

Pharmacokinetics of azelaic acid and its metabolite pimelic acid was assessed in 21 adult subjects with moderate papulopustular rosacea with a minimum of 15 and no more than 50 inflammatory lesions (papules and/or pustules). Endogenous plasma concentrations of azelaic acid (range <1-105 ng/mL) and pimelic acid (range 0.69-27 ng/mL) were measured over various time points over 2 days prior to treatment initiation. The endogenous plasma concentrations varied widely across subjects and the mean ± SD values of endogenous azelaic acid plasma concentrations ranged between 4.5 ± 2.4 ng/mL and 14.6 ± 5.6 ng/mL and pimelic acid plasma concentrations ranged between 2.2 ± 1.1 ng/mL and 3.7 ± 3.1 ng/mL.

Following topical dermal applications of a mean dose of 0.94 g of FINACEA Foam (141 mg azelaic acid) twice daily for 7 consecutive days, systemic concentrations of azelaic acid were at steady state by Day 5. On Day 7, a wide range of maximum azelaic acid (22.2 to 90.1 ng/mL) and pimelic acid (2.3-16.9 ng/mL) plasma concentrations (C_{max}) was also observed after treatment with FINACEA Foam. The mean ± SD C_{max} for azelaic acid and pimelic acid were 51.8 ± 18.5 ng/mL and 5.0 ± 3.0 ng/mL, respectively. The mean ± SD systemic exposure of azelaic acid and pimelic acid within a dosing interval (AUC_{0-12h}) were 442.0 ± 177.6 ng.h/mL and 43.4 ± 15.4 ng.h/mL, respectively.

Azelaic acid is mainly excreted unchanged in the urine, but undergoes some ß-oxidation to shorter chain dicarboxylic acids.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

In a 2-year dermal mouse carcinogenicity study, azelaic acid pre-foam emulsion was administered twice daily to CD-1 mice at topical doses of 5%, 15%, and 30% (500, 1500, and 3000 mg/kg/day azelaic acid). No drug-related tumors were noted at concentrations up to 30% azelaic acid (527 times the MRHD based on AUC comparison).

Azelaic acid was not mutagenic or clastogenic in a battery of in vitro [Ames assay, HGPRT assay in V79 cells (Chinese hamster lung cells), and chromosomal aberration assay in human lymphocytes] and in vivo (dominant lethal assay in mice and mouse micronucleus assay) genotoxicity tests.

Oral administration of azelaic acid at dose levels up to 2500 mg/kg/day (162 times the MRHD based on BSA comparison) did not affect fertility or reproductive performance in male or female rats.

14 CLINICAL STUDIES

The efficacy and safety of FINACEA Foam was evaluated in two multicenter, randomized, double-blind, vehicle-controlled, 12-week clinical trials (Trials 1 and 2) in subjects with papulopustular rosacea, with a mean lesion count of 21.3 (range 12 to 50) inflammatory papules and pustules. A total of 1362 (active: 681; vehicle: 681) subjects aged 19 to 92 years (mean age = 50.6 years), 95.7% Caucasian, and 73.4% female participated in the trials. The following subjects were excluded: a) those with ocular rosacea, phymatous rosacea or plaque-type rosacea lesions; b) those with rosacea that requires systemic treatment; c) those who are known non-responders to azelaic acid, and d) those with a known hypersensitivity to any ingredients of the study drug. FINACEA Foam or its vehicle were to be applied twice daily for 12 weeks; no other topical or systemic medication affecting the course of rosacea and/or evaluability was to be used during the studies. Subjects were instructed to avoid any food and beverages that, by their own experience, may provoke erythema, flushing and blushing, including spicy food, hot drinks and alcoholic beverages during the study. Subjects were also instructed to avoid use of products which may cause local irritation such as soaps, alcohol-containing cleansers, tinctures and astringents, abrasives and peeling agents during the study.

The efficacy endpoints were 1) nominal change in inflammatory lesion count from baseline and 2) success defined as a score of “clear” or “minimal” with at least 2-step reduction from baseline on a 5-point Investigator’s Global Assessment (IGA). Details on IGA are specified below:

Clear	no papules and/or pustules; no erythema
Minimal	rare papules and/or pustules; faint, up to but not including mild erythema
Mild	few papules and/or pustules; mild erythema
Moderate	pronounced number of papules and/or pustules, but less than numerous papules and/or pustules; moderate erythema
Severe	numerous papules and/or pustules, occasionally with confluent areas of inflamed lesions; moderate to severe erythema

FINACEA Foam was superior to its vehicle in the treatment of rosacea in reducing the number of inflammatory papules and pustules and demonstrating success according to IGA at the end of treatment (Table 2).

Table 2: IGA Success Rate and Nominal Change in Inflammatory Lesion Count from Baseline to End of the 12-Week Treatment Period

	Trial 1		**Trial 2**	
	FINACEA Foam, 15% N=483	**Vehicle** N=478	**FINACEA Foam, 15%** N=198	**Vehicle** N=203
IGA success rate	32.1%	23.4%	43.4%	32.5%
Mean nominal change in inflammatory lesion count from baseline	-13.2	-10.3	-13.3	-9.5

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

FINACEA (azelaic acid) Foam 15% is a white to off-white emulsion supplied in a pressurized 50 g (NDC 50222-303-50) aluminum can.

Storage and Handling

Store at 25˚C (77˚F); excursions permitted between 15–30˚C (59–86˚F) [See USP Controlled Room Temperature].

Flammable. Avoid fire, flame, or smoking during and immediately following application. Contents under pressure. Do not puncture or incinerate. Do not expose to heat or store at temperatures above 120°F (49°C).

17 PATIENT COUNSELING INFORMATION

Inform patients using FINACEA Foam of the following:

Administration Instructions

- For topical use only.
- Shake well before use.
- Before applying FINACEA Foam, cleanse affected area(s) with a very mild soap or a soapless cleansing lotion and pat dry with a soft towel.
- Wash hands immediately following application of FINACEA Foam.
- Cosmetics may be applied after the application of FINACEA Foam has dried.
- Avoid the use of occlusive dressings and wrappings.
- Avoid use of alcoholic cleansers, tinctures and astringents, abrasives and peeling agents.
- If allergic reactions occur, discontinue use and consult your physician.
- Discard product 8 weeks after opening *[see Dosage and Administration (2)]*.

Hypopigmentation

- Advise patients to report abnormal changes in skin color to their healthcare provider *[see Warnings and Precautions (5.1)]*.

Eye and Mucous Membranes Irritation

- Avoid contact with the eyes, mouth and other mucous membranes. If FINACEA Foam does come in contact with the eyes, wash the eyes with large amounts of water and consult your physician if eye irritation persists *[see Warnings and Precautions (5.2)]*.

Flammability

- The propellant in FINACEA Foam is flammable. Avoid fire, flame, or smoking during and immediately following application *[see Warnings and Precautions (5.3)]*.

FINACEA is a registered trademark of LEO Pharma A/S.

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