NEW DRUG APPROVAL

Brand Name	Epsolay®
Generic Name	benzoyl peroxide
Drug Manufacturer	Sol Gel Technologies

New Drug Approval

FDA Approval Date: April 22, 2022

Review Designation: Standard

Review Type: New Drug Application (NDA): 214510

Dispensing Restrictions: N/A

Place in Therapy

DISEASE DESCRIPTION & EPIDEMIOLOGY

Rosacea is a common, chronic, and recurrent inflammatory skin disorder involving the central face (cheeks, nose, chin, central forehead, eyes). Although the cause of rosacea is unknown, it is believed that many different factors underlie the various clinical manifestations of the disease, and symptoms often worsen over time if left untreated.

The most common symptoms include centrofacial redness, flushing, papules, pustules, and telangiectasia. Other symptoms can be localized burning, stinging, swelling, skin thickening/tissue enlargement (also known as phymatous changes; usually occurs around the nose), or rough/dry look and feel of the affected centro facial skin. Most patients experience a few of these symptoms, but not all of them. The symptoms of rosacea overlap with many other common skin conditions and can be misdiagnosed as many other conditions, including adult acne vulgaris, photodermatitis, atopic dermatitis, seborrheic dermatitis, or contact dermatitis.

Rosacea prevalence estimates vary, but they range from 1% to 10% of populations with fair skin. The National Rosacea Society estimated that more than 16 million Americans are affected. Rosacea is present most commonly in adults of northern or eastern European descent, which suggests there may be a genetic component to this multifactorial disease. All ethnicities can develop rosacea, but prevalence data are limited in populations with darker skin. Rosacea is more common in women than men and usually onsets at 30 years of age and older. Adolescents and children are rarely affected. Rosacea commonly goes undiagnosed and untreated.

Efficacy

The safety and efficacy of Epsolay® was evaluated in two multicenter, randomized, double-blind, vehicle-controlled trials (Trial 1 [NCT03448939] and Trial 2 [NCT03564119]) in subjects with moderate-to-severe papulopustular rosacea. The trials were conducted in 733 subjects, aged 18 years and older. Subjects were treated once daily for 12 weeks with either Epsolay® or vehicle cream.

Subjects were required to have a minimum of 15 to 70 total inflammatory lesions (papules and/or pustules) and no more than 2 nodules (where a nodule was defined as a papule or pustule greater than 5 mm in diameter) and an Investigator Global Assessment (IGA) score of 3 (“moderate”) or 4 (“severe”) at baseline. Overall, 93% of subjects were Caucasian, 73% were female, and the mean age was 51 years (ranged from 18 to 85 years). At baseline, subjects had a mean inflammatory lesion count of 27.5, 89% were scored as moderate (IGA=3), and 11% scored as severe (IGA=4).

The co-primary efficacy endpoints in both trials were the proportion of subjects with treatment success at Week 12, defined as an IGA score of 0 (“clear”) or 1 (“almost clear”) with at least a two-grade reduction from baseline,

and the absolute change from baseline in inflammatory lesion counts at Week 12. The results at Week 12 are presented in table 1. Epsolay® was more effective than vehicle cream on the co-primary efficacy endpoints starting from 4 weeks of treatment in both trials, see Figure 1 through Figure 4.

Table 1: Efficacy Results of Epsolay® in Subjects with Moderate to Severe Papulopustular Rosacea at Week 12

	Trial 1 Epsolay® Vehicle (N=243) (N=118)	Trial 2 Epsolay® Vehicle (N=250) (N=122)
IGA Treatment Success*	47.4% 20.7%	49.2% 28.2%
Difference from Vehicle (99% CI)	26.7% (16.7%, 36.8%)	21.0% (10.7%, 31.3%)
Inflammatory Lesions		
Mean† Absolute Change	-17.4 -9.5	-20.3 -13.3
Difference from Vehicle (95% CI)	-7.9 (-10.0, -5.9)	-6.9 (-9.0, -4.9)
Mean† Percent Change	-68.2% -38.3%	-69.4% -46.0%
Difference from Vehicle (95% CI)	-29.9% (-k37.8%, -22.0%)	-23.4% (-30.5%, -16.3%)

* Investigator Global Assessment (IGA) success was defined as an IGA score of 0 (“clear”) or 1 (“almost clear”) with at least a two-grade reduction from baseline.
† Means presented in table are Least Square (LS) Means.

Figure 1: IGA Success Rate Over Time in Trial 1

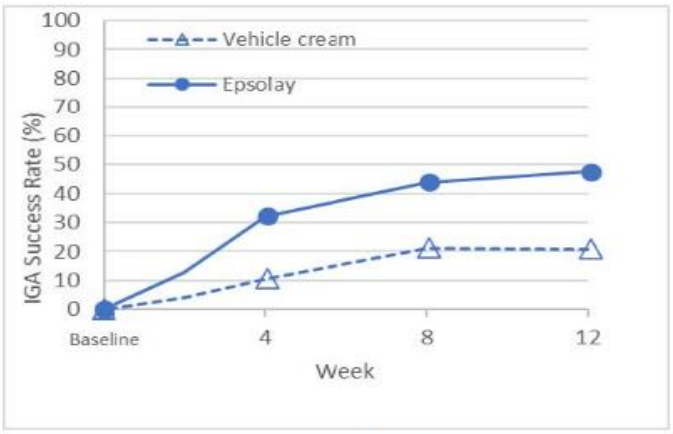


Figure 2: IGA Success Rate Over Time in Trial 2

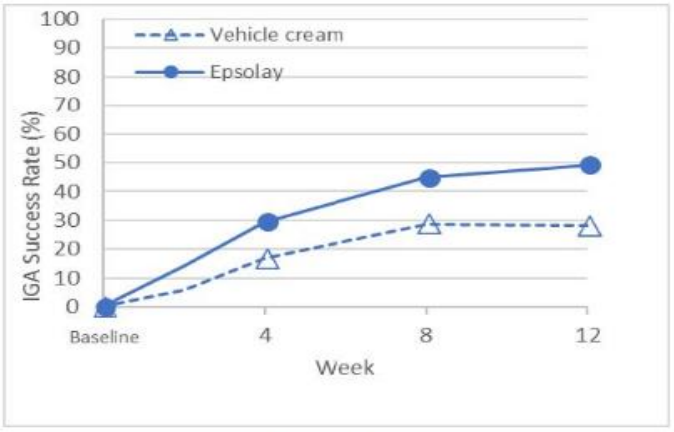


Figure 3: Mean Absolute Change in Inflammatory Lesion Counts from Baseline Over Time in Trial 1

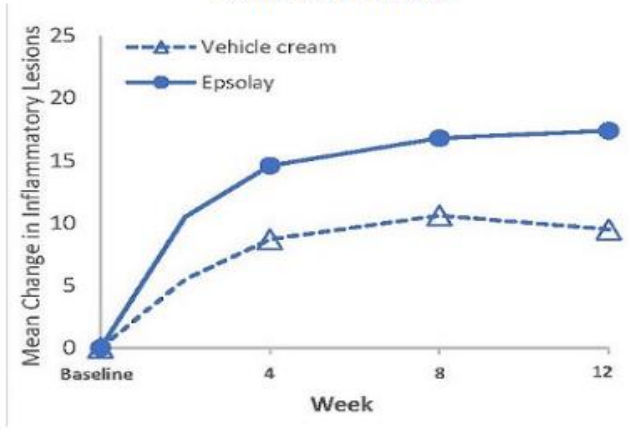
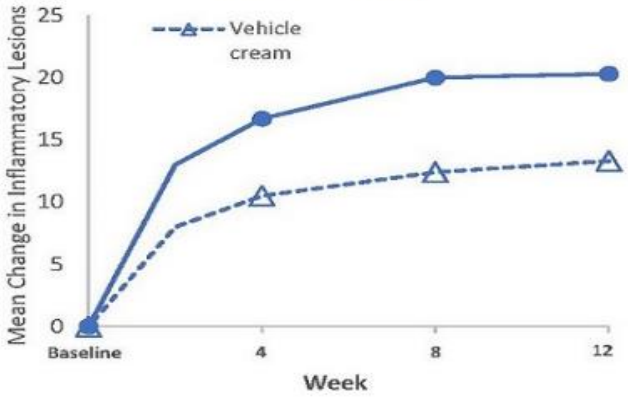


Figure 4: Mean Absolute Change in Inflammatory Lesion Counts from Baseline Over Time in Trial 2



Safety

ADVERSE EVENTS

Most common adverse reactions (incidence ≥ 1%) are application site reactions: pain, erythema, pruritis and edema.

WARNINGS & PRECAUTIONS

Hypersensitivity

Hypersensitivity reactions, including anaphylaxis, angioedema, and urticaria, have been reported with the use of benzoyl peroxide products. If a serious hypersensitivity reaction occurs, discontinue Epsolay® immediately and initiate appropriate therapy.

Skin Irritation/Contact Dermatitis

Erythema, scaling, dryness, and stinging/burning may be experienced with use of Epsolay®. Irritation and contact dermatitis may occur. Apply a moisturizer and discontinue Epsolay® if symptoms do not improve. Avoid application of Epsolay® to cuts, abrasions, eczematous or sunburned skin.

Photosensitivity

Benzoyl peroxide may increase sensitivity to sunlight. Minimize or avoid exposure to natural or artificial sunlight (tanning beds or UVA/B treatment) while using Epsolay®. Instruct the patient to implement sun protection measures (e.g., sunscreen and loose-fitting clothes) when sun exposure cannot be avoided. Discontinue Epsolay® at the first evidence of sunburn.

CONTRAINDICATIONS

Epsolay® is contraindicated in patients with a history of hypersensitivity reactions to benzoyl peroxide or any components of the formulation in Epsolay®.

Clinical Pharmacology

MECHANISMS OF ACTION

Benzoyl peroxide is an oxidizing agent with bactericidal and keratolytic effects but the precise mechanism of action in the treatment of rosacea is unknown.

Dose & Administration

ADULTS

Apply sparingly once daily; gradually increase to 2 to 3 times/day if needed. If excessive dryness or peeling occurs, reduce dose frequency or concentration. If excessive stinging or burning occurs, remove with mild soap and water; resume use the next day.

PEDIATRICS

None

GERIATRICS

Refer to adult dosing.

RENAL IMPAIRMENT

None

HEPATIC IMPAIRMENT

None

Product Availability

DOSAGE FORM(S) & STRENGTH(S)

Cream, 5%. Each gram of Epsolay® contains 50 mg of benzoyl peroxide in a white to off-white base.