
Acne Agents: Topical Acne and Rosacea Agents

Defense Health Agency Formulary Management Branch

Executive Summary

- The Topical Acne and Rosacea Agents Drugs have not been previously reviewed for formulary placement. Clindamycin 1% gel, cream, lotion, and solution (Cleocin T, generics), and tretinoin 0.025% and 0.05% cream (Retin-A and generics) are currently on the Basic Core Formulary (prior to implementation of the Uniform Formulary in 2005). See Table 1 for a complete listing of the drugs in the class. Refer to the August 2016 DoD P&T Committee meeting minutes for additional clinical information (<http://www.health.mil/PandT>).

Topical Acne Products

- There are currently over 35 topical products available for treatment of mild to moderate acne, several of which have generic formulations or therapeutic equivalents.
- Guidelines based on good-quality, patient-oriented evidence support use of topical benzoyl peroxide or a retinoid for mild comedonal acne and any topical combination therapy for mild to moderate inflammatory acne.
- Benzoyl peroxide used in combination with the clindamycin 1% gel or solution is a first-line choice for treatment of mild to moderate acne. Monotherapy with clindamycin is not recommended, due to the risk of bacterial resistance.
- Dapsone 7.5% gel (Aczone) was approved in February 2016 for treatment of acne in patients 12 years of age and older. Aczone 7.5% was superior to placebo, but there are no head-to-head studies with other acne products. Dapsone is also available in a 5% gel with the same trade name as the 7.5% gel (Dapsone); patent expiration for this product is expected in the fall of 2016.
- Adapalene (Differin) gel 0.1% was approved in July 2016 for over-the-counter use.
- Azelaic acid 20% cream (Azelex) is the only product with a pregnancy category B rating.
- For pediatrics, the adapalene and benzoyl peroxide (Epiduo) combination is approved for use in patients 9 years and older. Tretinoin 0.05% is safe and effective in children 10 years and older. Adapalene and clindamycin/tretinoin products are labeled for use in ages 12 years and up.
- The major adverse events for the topical acne formulations are primarily dermatological in nature, including hypopigmentation with azelaic acid, photosensitivity with retinoids, the potential to induce bacterial resistance with the topical antibiotics, and the rare potential for methemoglobinemia with dapsone 5% gel. The retinoid tazarotene (Fabior) has a limited role, due to its pregnancy category X rating.

Topical Rosacea Products

- There are currently 9 topical products available for treatment of inflammation and erythema associated with rosacea, three of which are branded products with no generically available equivalents (azelaic acid, brimonidine, and ivermectin).
- Topical brimonidine 0.33% gel (Mirvaso) is an alpha adrenergic agonist approved for treatment of persistent facial erythema of rosacea. It was superior to placebo in achieving a two-grade improvement of facial erythema. Mild, transient dermatological adverse events were reported most commonly. Brimonidine will not alter the course of disease. A recent update to the package insert warns of the risk of hypotension, bradycardia, and dizziness, particularly in patients with pre-existing cardiovascular disease.
- Topical ivermectin 1% cream (Soolantra) is indicated for the treatment of inflammatory (papulopustular) lesions of rosacea. One study demonstrated superiority of once daily topical ivermectin cream over twice daily topical metronidazole, with a comparable incidence of adverse events between the two drugs. Ivermectin is the preferred product for treating papulopustular rosacea associated with proliferation of Demodex mites
- The 2015 Cochrane review indicated that in most comparisons of the topical rosacea products with placebo, there were no statistically significant differences in number of adverse events, with most events being mild and transient.

Indications

All the topical acne agents are indicated for treatment of mild to moderate acne. The topical rosacea products are indicated for either treatment of facial erythema of rosacea or papulopustular (inflammatory) rosacea. Topical azelaic acid, ivermectin, and metronidazole are indicated for treatment of inflammatory rosacea; topical brimonidine is indicated for treatment of persistent facial erythema of rosacea. Sulfur-based products, such as sulfacetamide sodium/sulfur have multiple indications, including topical control of acne vulgaris, rosacea, and seborrheic dermatitis.

Table 1. Topical Acne and Rosacea Products Available in the United States

Active Ingredient	Brand (Manufacturer)	Strengths	Generics Available?	Patent Exp Date
adapalene	Differin (Galderma)	0.1% lotion 0.1% gel, gel w/ pump, cream 0.3% gel	NO YES NO	9/15/2026 - 03/12/2023
adapalene/ benzoyl peroxide	Epiduo (Galderma) Epiduo Forte (Galderma)	0.1% - 2.5% gel; gel w/pump 0.3% - 2.5% gel w/pump	NO NO	12/23/2022 12/23/2022
azelaic acid	Azelex (Allergan) – for acne Finacea (Intendis) – for rosacea	20% cream 15% gel 15% foam	NO NO NO	- 11/18/2018 12/08/2027
brimonidine	Mirvaso (Galderma)	0.33% gel	NO	03/25/2031
clindamycin	Clindacin PAC (Medimetriks) Clindagel Cleocin various Evoclin , generics (Prestium, generics)	0.1% gel 0.1% gel 1% gel, cream, lotion, soln 0.1% foam	NO NO YES YES	- - -
clindamycin/ benzoyl peroxide	Acanya (Valeant) Benzacilin, Duac (Valeant, generics) Neuac (Medimetriks) Onexton (Valeant)	1.2% - 2.5% gel 1% - 5%; 1.2% - 5% gel 1.2% - 5% gel combination kit 1.2% - 3.75% gel	NO YES NO NO	06/03/2029 - - 04/05/2029
clindamycin/ tretinoin	Veltin (Stiefel) Ziana ¹ (Valeant)	1.2% - 0.025% gel	NO NO ¹	- -
dapsone	Aczone (Allergan)	5% gel 7.5% gel	NO NO	9/11/2016 11/18/2033
erythromycin/ benzoyl peroxide	Benzamycin generics (Valeant, generics) Benzamycin Pak (Valeant)	3% - 5% gel 3% - 5% gel (singles)	YES NO	-
erythromycin	Ery, Erygel, generics (Valeant, generics)	2% gel	YES	-
ivermectin	Soolantra (Galderma)	1% cream	NO	04/22/2024
metronidazole	Metronidazole, generics (Galderma, generics) Noritrate (Valeant) Rosadan, generics (Medimetriks, generics)	0.75% cream, lotion; 1% gel 1% cream 0.75% cream, gel	YES NO YES	-
sulfacetamide sodium/sulfur	(Valeant, generics)	10% lotion	YES	-
tazarotene	Fabior (Stiefel)	0.1% foam	NO	02/24/2030
tretinoin	Atralin, generics (Valeant, generics) Avita (Mylan); Retin-A, generics (Valeant, generics) Tretin-X (Onset)	0.05% gel 0.01%, 0.025% gel 0.025%, 0.05%, 0.1% cream 0.0375%, 0.075% cream	YES NO NO NO	- - -
tretinoin microsphere	Retin-A Micro, generics (Valeant, generics) Retin-A Micro Pump (Valeant)	0.04%, 0.1% gel 0.04%, 0.08%, 0.1% gel	YES NO	9/21/2016 9/21/2016

¹ Ziana is indicated for use in patients 12 and up. In July 2016, a new AB-rated generic product was launched by Actavis with no utilization/pricing data yet.

Products in **bold** are still branded

References

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4. Soolantra 1% Cream (ivermectin) [prescribing information]. Fort Worth, TX: Galderma Laboratories, December 2014.
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