

and Supplementary Table XXIV, available via Mendeley at <https://data.mendeley.com/datasets/z2bmdwwdf9/2>) and based on work group discussions related to treatment access and cost.

Compared to vehicle at 12 weeks, a greater proportion of patients treated with clascoterone achieved IGA success in 2 RCTs (RR, 2.08 [1.39, 3.11]).⁹³ Despite high certainty of benefits over risks based on clinical trial evidence, the work group voted on a conditional recommendation due to concerns about the high current cost of clascoterone treatment that may impact equitable acne treatment access. This conditional recommendation may be revised in the future pending changes in treatment cost and access.

Salicylic acid

Salicylic acid is a topical comedolytic agent that is available over the counter, with concentration ranging in 0.5% to 2%. We conditionally recommend salicylic acid for acne treatment based on moderate certainty evidence from 1 RCT, showing a 25% greater reduction in inflammatory lesions, 11% greater reduction in open comedones, and no difference in closed comedones with 0.5% salicylic acid use compared to vehicle at 12 weeks (Table III and Supplementary Table XXV, available via Mendeley at <https://data.mendeley.com/datasets/z2bmdwwdf9/2>).⁹⁵ Chemical peels using salicylic acid 10% to 30% are separately discussed in the physical modalities section.

Azelaic acid

Azelaic acid is a topical comedolytic, antibacterial, and anti-inflammatory agent, which may be particularly helpful for patients with sensitive skin or darker skin types due to its lightening effect on dyspigmentation.^{96,97,173} We conditionally recommend topical azelaic acid for acne treatment based on moderate certainty evidence from 3 RCTs (Table III and Supplementary Table XXVI, available via Mendeley at <https://data.mendeley.com/datasets/z2bmdwwdf9/2>).⁹⁶⁻⁹⁸ In 1 RCT of 92 patients, 28% more patients receiving azelaic acid 20% cream twice daily achieved 50% to 100% reduction in total lesion count compared to vehicle at 3 months.⁹⁷

Considerations in topical therapies

In patients who are pregnant, the risk of fetal harm from topical azelaic acid, BP, erythromycin, and clindamycin are not expected based on limited expected systemic absorption.^{174,175} Salicylic acid can be used in pregnancy if the area of exposure and duration of therapy is limited; use for large areas or

under occlusion are not recommended due to the potential for systemic absorption.¹⁷⁴ There are no data on the safety of topical dapsone and clascoterone during pregnancy or lactation. Tazarotene is contraindicated in pregnancy based on animal reproduction studies, retinoid pharmacology, and the potential for systemic absorption. No human studies have established causal relationships between the use of topical retinoids with birth defects; nevertheless, topical therapies other than topical retinoids are preferred during pregnancy. Topical minocycline is not recommended during pregnancy or lactation.

Salicylic acid is available over the counter. Fixed-dose combination BP 2.5%/adapalene 1% gel, tretinoin 0.1%/BP 3% cream, tretinoin 0.05% lotion, trifarotene 0.005% cream, dapsone 5% gel, and minocycline 4% foam are FDA-approved for ages 9 years and above, and most other topical retinoids, antibiotics, clascoterone, and azelaic acid are approved for age 12 years and above.

Available evidence is insufficient to develop a recommendation on the use of topical glycolic acid, sulfur, sodium sulfacetamide, and resorcinol for acne treatment or to make recommendations that compare topical BP, retinoids, antibiotics, and their combinations directly against each other (Supplementary Tables XXVII-XXXV, available via Mendeley at <https://data.mendeley.com/datasets/z2bmdwwdf9/2>).

SYSTEMIC ANTIBIOTICS

Systemic antibiotics have been used extensively to treat acne, typically moderate to severe acne. Oral tetracycline-class antibiotics, including doxycycline, minocycline, and sarecycline, are commonly used. Tetracycline-class antibiotics exhibit antibiotic properties by binding the 16S ribosomal RNA of the bacterial ribosome 30S subunit to inhibit protein synthesis, as well as anti-inflammatory properties by inhibiting neutrophil chemotaxis and matrix metalloproteinases and down-regulating inflammatory cytokines.¹⁷⁶ Notably, tetracycline-class antibiotics are contraindicated in pregnancy, lactation, and childhood below age 9 years during tooth development, since repeated exposure may cause permanent teeth enamel hypoplasia or discoloration.

Limiting the use of systemic antibiotics when possible is recommended as a good practice statement to reduce the development of antibiotic resistance and other antibiotic-associated complications. In 2021, dermatologists prescribed more oral antibiotics per clinician than all other specialties, with the majority of antibiotics used for acne treatment.^{177,178}