may be mitigated by reduced frequency of use and concurrent emollients use.[160-163] Some tretinoin formulations should be applied in the evening due to its photolabile nature and should not be applied with BP to avoid oxidation and inactivation; topical tretinoin microsphere formulations, adapalene, and tazarotene lack similar restrictions. Topical retinoids may cause photosensitivity; concurrent daily sunscreen use can reduce sunburn risks. Adapalene 0.1% gel is available over the counter while other topical retinoids are available by prescription only.

Benzoyl peroxide

BP is an over-the-counter topical antimicrobial agent that releases free oxygen radicals and is mildly comedolytic.[164,165] We recommend BP for acne treatment based on moderate certainty evidence from 8 studies (Table III and Supplementary Table XIII, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2).[63-70] Compared to vehicle at 12 weeks, a greater proportion of patients treated with BP achieved IGA success in 3 RCTs (RR, 2.70 [1.10, 6.65]).[63-65] Greater reductions in both inflammatory (mean difference [MD] in the percentage change from baseline, −22.13% [−42.53%, −1.72%]) and noninflammatory (MD, −17.05% [−22.96%, −11.14%]) lesion counts were seen in BP versus vehicle at 12 weeks in 3 RCTs.[63,66,69] BP use is limited by concentration and formulation-dependent burning sensation, stinging, dryness, erythema, pain, peeling, irritation, fabric staining and bleaching, and uncommon contact allergy. Lower BP concentrations and water-based and wash-off formulations may be better tolerated.[166,167] No *C. acnes* resistance to BP has been reported.

Topical antibiotics

Topical antibiotics (including erythromycin, clindamycin, minocycline, and dapsone) treat acne through both antibacterial and anti-inflammatory effects.[168] We recommend topical antibiotics for acne treatment based on moderate certainty evidence from 14 studies (Table III and Supplementary Table XIV, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2).[66,68,69,71,79,84-91] Compared to vehicle at 12 weeks, a greater proportion of patients treated with topical antibiotics achieved IGA success in 3 RCTs (RR, 1.49 [1.28, 1.73]).[71,86,87]

A greater reduction in inflammatory lesions was seen with topical antibiotics versus vehicle at 12 weeks in 8 RCTs (MD in the percentage change from baseline, −10.86% [−18.81%, −2.91%]),[66,69,79,84-87,91] but the difference in reduction in noninflammatory lesion counts between the groups was not statistically significant at 12 weeks in 7 RCT (−3.33% [−7.90%, 1.24%]).[66,69,79,84-87] Notably, topical antibiotic monotherapy is not recommended due to concern for antibiotic resistance. Combining topical antibiotics with BP enhances efficacy and may prevent antibiotic resistance development. Concurrent topical application of BP with either dapsone or sulfacetamide causes an orange-brown skin discoloration, which can be washed off; thus BP should be used at a different time of day than topical dapsone.[169] Glucose-6-phosphate dehydrogenase screening is not required prior to starting topical dapsone. Topical antibiotics are generally well tolerated; there have been rare case reports describing diarrhea or *Clostridium difficile*-related colitis associated with topical clindamycin use.[92,170] There is a lack of active comparator studies to suggest if any one topical antibiotic is superior to another.

Fixed-dose topical combinations

Fixed-dose topical combinations of BP, retinoids, or antibiotics facilitate treatment regimen adherence.[171] We recommend fixed-dose topical combinations of BP and topical retinoid, BP and topical antibiotic, and topical retinoid and topical antibiotic for acne treatment based on moderate certainty evidence from 7[63,64,99,109-112] 9[66,68,69,99-104], and 3[71,79,99] studies, respectively (Table III and Supplementary Tables XV-XXIII, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2). Compared to vehicle at 12 weeks, a greater proportion of patients treated with combined BP and topical retinoid achieved IGA success in 3 RCTs (RR, 2.19 [1.77, 2.72]).[63,64,109] Greater reductions in both inflammatory (MD in the percentage change from baseline, −37.34% [−72.49%, −2.18%]) and noninflammatory (MD, −20.47% [−26.31, −14.62]) lesion counts were seen in combined BP and topical antibiotic versus vehicle at 12 weeks in 4 RCTs.[66,69,99,101] Concomitant BP use is recommended with combined topical retinoid and topical antibiotic to prevent the development of antibiotic resistance. Potential adverse effect profiles of the fixed-dose combinations generally reflect those of the individual agents in summation. Some fixed-dose combination products may be less - expensive than prescribing their individual components separately.

Clascoterone

Clascoterone is a topical antiandrogen that directly binds the androgen receptor and inhibits androgen-mediated lipid and inflammatory cytokine synthesis from sebocytes.[172] We conditionally recommend clascoterone for acne treatment based on high certainty evidence from 2 studies (Table III