

From Breakouts to Bargains: Strategies for Patient-Centered, Cost-effective Acne Care

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PRACTICE POINTS

- For mild to moderate acne, fixed-dose combination adapalene–benzoyl peroxide and clindamycin–benzoyl peroxide are highly cost-effective options for most patients.
- For moderate to severe acne, doxycycline or hormonal therapy (ie, combined oral contraceptives, spironolactone) are highly cost-effective options.
- Reduction of laboratory monitoring for spironolactone and isotretinoin is an opportunity to provide higher-value care.

A range of treatment options are available for both mild to moderate and moderate to severe acne, and these options vary widely in their clinical uses, effectiveness, and costs. With the continued rise of dermatologic drug prices and increased cost-sharing due to high-deductible health plans, the importance of cost-effective treatment continues to grow. Failure to consider cost-effective, patient-centered care may lead to increased financial toxicity, reduced adherence, and ultimately worse outcomes and patient satisfaction. Combination topical products offer improved efficacy and convenience, which are associated with better adherence and outcomes. Generic fixed-dose adapalene–benzoyl peroxide (BPO) and fixed-dose clindamycin-BPO can be highly cost-effective options for patients with mild to moderate acne. Hormonal agents such as combined oral contraceptives (COCs) and spironolactone are inexpensive and likely reflect a highly cost-effective option that could reduce reliance on oral antibiotics in patients with moderate to severe acne. Doxycycline and isotretinoin

also are cost-effective options for more severe acne. Frequent laboratory monitoring for spironolactone and isotretinoin continues to be prevalent despite little evidence to support its clinical utility, and it is associated with a major cost burden to the patient and health care system. The reduction of laboratory monitoring is an opportunity to provide higher-value care.

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In the United States, acne affects 85% of adolescents and can persist into adulthood at a prevalence of 30% to 50% in adult women.^{1,2} The pathogenesis of acne is multifactorial and involves hyperkeratinization of the follicle, bacterial colonization with *Cutibacterium acnes*, and increased androgen-induced sebum production, which together lead to inflammation.^{3,4} A wide range of treatment guideline–recommended options are available, including benzoyl peroxide (BPO), topical retinoids, topical and oral antibiotics, antiandrogens, and isotretinoin.⁵ However, these options vary widely in their clinical uses, effectiveness, and costs.

Why Cost-effective Acne Care Matters

Out-of-pocket spending by patients on acne treatments can be substantial, with surveys finding that acne patients often spend hundreds to thousands of dollars per year.^{6,7} In a poll conducted in 2019 by the Kaiser Family Foundation, 3 in 10 patients said they had not taken their

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medicine as prescribed because of costs.⁸ A mixed methods study by Ryskina et al⁹ found that 65% (17/26) of participants who reported primary nonadherence—intended to fill prescriptions but were unable to do so—cited cost or coverage-related barriers as the reason. With the continued rise of dermatologic drug prices and increased prevalence of high-deductible health plans, cost-effective treatment continues to grow in importance. Failure to consider cost-effective, patient-centered care may lead to increased financial toxicity, reduced adherence, and ultimately worse outcomes and patient satisfaction. We aim to review the cost-effectiveness of current prescription therapies for acne management and highlight the most cost-effective approaches to patients with mild to moderate acne as well as moderate to severe acne.

In this review, we will take a value-oriented framework.¹⁰ Value can be defined as the cost per outcome of interest. Therefore, a treatment does not necessarily need to be inexpensive to provide high value if it delivers outstanding clinical outcomes. In addition, we will focus on incremental cost-effectiveness relative to common alternatives (eg, a retinoid could deliver high value relative to a vehicle but still provide limited value compared to other available retinoids if it is more expensive but not more efficacious). When possible, we present data from cost-effectiveness studies.^{11,12} We also use recent available price data obtained from GoodRx on August 11, 2023, to guide this discussion.¹³ However, as comparative-effectiveness and cost-effectiveness studies rarely are performed for acne medications, much of this discussion will be based on expert opinion.

Treatment Categories

Topical Retinoids—There currently are 4 topical retinoids that are approved by the US Food and Drug Administration (FDA) for the treatment of acne: tretinoin, tazarotene, trifarotene, and adapalene. These drugs are vitamin A derivatives that bind retinoic acid receptors and function as comedolytic and anti-inflammatory agents.⁵ In general, generic tretinoin and adapalene products have the lowest cost (Table).

In network meta-analyses, tretinoin and adapalene often are highly ranked topical treatment options with respect to efficacy.¹⁴ Combined with their low cost, generic tretinoin and adapalene likely are excellent initial options for topical therapy from the standpoint of cost-effectiveness.¹⁵ Adapalene may be preferred in many situations because of its better photostability and compatibility with BPO.

Due to the importance of the vehicle in determining retinoid tolerability, efforts have been made to use encapsulation and polymeric emulsion technology to improve tolerability. Recently, polymeric lotion formulations of tretinoin and tazarotene have become available. In a phase 2 study, tazarotene lotion 0.045% was found to have equivalent efficacy and superior tolerability to tazarotene cream 0.1%.¹⁶ Although head-to-head data

are not available, it is likely that tretinoin lotion may offer similar tolerability improvements.¹⁷ Although these formulations currently are more costly, this improved tolerability may be critical for some patients to be able to use topical retinoids, and the additional cost may be worthwhile. In addition, as these products lose market exclusivity, they may become more affordable and similarly priced to other topical retinoids. It is important to keep in mind that in clinical trials of tretinoin and adapalene, rates of dropout due to adverse events typically were 1% to 2%; therefore, because many patients can tolerate generic tretinoin and adapalene, at current prices the lotion formulations of retinoids may not be cost-effective relative to these generics.¹⁴

Trifarotene cream 0.005%, a fourth-generation topical retinoid that is highly sensitive for retinoic acid receptor γ , recently was FDA approved for the treatment of acne. Although trifarotene is efficacious for both facial and truncal acne, there is a lack of active comparator data compared to other topical retinoids.¹⁸ In a 2023 network meta-analysis, trifarotene was found to be both less efficacious and less tolerable compared to other topical retinoids.¹⁹ Thus, it is unclear if trifarotene offers any improved efficacy compared to other options, and it comes at a much higher cost (Table). In a tolerability study, trifarotene was found to be significantly more irritating than tazarotene lotion 0.045% and adapalene gel 0.3% ($P < .05$).²⁰ Therefore, trifarotene cream 0.005% is unlikely to be a cost-effective option; in fact, it may be overall inferior to other topical retinoids, given its potentially lower tolerability.

Topical Antibiotics—There are 4 commonly prescribed topical antibiotics that are approved by the FDA for the treatment of acne: clindamycin, erythromycin, dapsone, and minocycline. The American Academy of Dermatology guidelines for the treatment of acne recommend concomitant use of BPO to prevent antibiotic resistance.⁵ Clindamycin is favored over erythromycin because of increasing antibiotic resistance to erythromycin.²¹ Inexpensive generic options in multiple vehicles (eg, solution, foam, gel) make clindamycin a highly cost-effective option when antibiotic therapy is desired as part of a topical regimen (Table).

The cost-effectiveness of dapsone gel and minocycline foam relative to clindamycin are less certain. Rates of resistance to minocycline are lower than clindamycin, and minocycline foam may be a reasonable alternative in patients who have not had success with other topical antibiotics, such as clindamycin.²² However, given the absence of comparative effectiveness data to suggest minocycline is more effective than clindamycin, it is difficult to justify the substantially higher cost for the typical patient. Although dapsone gel has been suggested as an option for adult women with acne, there are no data to support that it is any more effective than other topical antibiotics in this patient population.²³ As generic dapsone prices decrease, it may become a reasonable alternative to clindamycin. In addition, the antineutrophil

Costs of Acne Treatment Options

Category	Drug	Amount	GoodRx ^a cost, \$
Topical retinoids	Tretinoin gel 0.01%	45 g	60.42
	Tretinoin gel 0.025%	45 g	60.75
	Tretinoin gel microsphere 0.04%	45 g	157.78
	Tretinoin gel microsphere 0.1%	45 g	151.85
	Tretinoin cream 0.025%	45 g	47.72
	Tretinoin cream 0.05%	45 g	59.13
	Tretinoin cream 0.1%	45 g	63.84
	Tretinoin lotion 0.05%	45 g	131.10
	Tazarotene cream 0.1%	30 g	96.04
	Tazarotene lotion 0.045%	45 g	540.21
	Trifarotene cream 0.005%	45 g	696.23
	Adapalene gel 0.1%	45 g	16.87
	Adapalene gel 0.3%	45 g	72.91
	Topical antibiotics	Clindamycin gel 1%	30 g
Clindamycin lotion 1%		60 mL	29.65
Clindamycin solution 1%		60 mL	19.94
Erythromycin gel 2%		30 g	21.87
Dapsone gel 5%		60 g	135.65
Dapsone gel 7.5%		60 g	136.03
Minocycline foam 4%		30 g	369.76
Combination topicals	Adapalene 0.1%–BPO 2.5% gel	45 g	80.70
	Adapalene 0.3%–BPO 2.5% gel	45 g	193.54
	Tretinoin 0.1%–BPO 3% cream	30 g	465.10
	Clindamycin 1.2%–BPO 5% gel	45 g	47.07
	Clindamycin 1.2%–tretinoin 0.025% gel	30 g	120.77
Topical antiandrogen	Clascoterone cream 1%	60 g	605.35
Oral antibiotics	Doxycycline hyclate 100 mg	30 capsules	29.58
	Doxycycline hyclate modified release 40 mg	30 capsules	199.30
	Minocycline 100 mg	30 capsules	25.76
	Minocycline ER 90 mg	30 tablets	127.70
	Sarecycline 100 mg	30 tablets	1048.00
Hormonal agents	Drospirenone–ethinyl estradiol	28 tablets	19.46
	Ethinyl estradiol–norgestimate	28 tablets	14.64
	Drospirenone–ethinyl estradiol–levomefolate	28 tablets	41.82
	Ethinyl estradiol–norethindrone acetate–ferrous fumarate	28 tablets	26.50
	Spirolactone 100 mg	30 tablets	17.16
Other	Isotretinoin 30 mg	30 tablets	81.27

Abbreviations: BPO, benzoyl peroxide; ER, extended release.

^aGoodRx costs for CVS Pharmacy in zip code 02134 (Allston, Massachusetts) accessed on August 11, 2023.¹³

properties of dapsone may be useful in other acneform and inflammatory eruptions, such as scalp folliculitis and folliculitis decalvans.²⁴

Combination Topicals—Current combination topical products include antibiotic and BPO, antibiotic and retinoid, and retinoid and BPO. Use of combination agents is recommended to reduce the risk for resistance and to enhance effectiveness. Combination products offer improved convenience, which is associated with better adherence and outcomes.²⁵ Generic fixed-dose adapalene-BPO can be a highly cost-effective option that can sometimes be less expensive than the individual component products (Table). Similarly, fixed-dose clindamycin-BPO also is likely to be highly cost-effective. A network meta-analysis found fixed-dose adapalene-BPO to be the most efficacious topical treatment, though it also was found to be the most irritating—more so than fixed-dose clindamycin-BPO, which may have similar efficacy.^{14,26,27} Generic fixed-dose tretinoin-clindamycin offers improved convenience and adherence compared to the individual components, but it is more expensive, and its cost-effectiveness may be influenced by the importance of convenience for the patient.²⁵ An encapsulated, fixed-dose tretinoin 0.1%–BPO 3% cream is FDA approved for acne, but the cost is high and there is a lack of comparative effectiveness data demonstrating advantages over generic fixed-dose adapalene-BPO products.

Topical Antiandrogen—Clascoterone was introduced in 2020 as the first FDA-approved topical medication to target the hormonal pathogenesis of acne, inhibiting the androgen receptors in the sebaceous gland.²⁸ Because it is rapidly metabolized to cortexolone and does not have systemic antiandrogen effects, clascoterone can be used in both men and women with acne. In clinical trials, it had minimal side effects, including no evidence of irritability, which is an advantage over topical retinoids and BPO.²⁹ In addition, a phase 2 study found that clascoterone may have similar to superior efficacy to tretinoin cream 0.05%.³⁰ Although clascoterone has several strengths, including its efficacy, tolerability, and unique mechanism of action, its cost-effectiveness is limited due to its high cost (Table) and the need for twice-daily application, which reduces convenience. Clascoterone likely is best reserved for patients with a strong hormonal pathogenesis of their acne or difficulty tolerating other topicals, or as an additional therapy to complement other topicals.

Oral Antibiotics—Oral antibiotics are the most commonly prescribed systemic treatments for acne, particularly tetracyclines such as doxycycline, minocycline, and sarecycline.^{31–34} Doxycycline and minocycline are considered first-line oral antibiotic therapy in the United States and are inexpensive and easily accessible.⁵ Doxycycline generally is recommended over minocycline given lack of evidence of superior efficacy of minocycline and concerns about severe adverse cutaneous reactions and drug-induced lupus with minocycline.³⁵

In recent years, there has been growing concern of the development of antibiotic resistance.⁵ Sarecycline is a narrow-spectrum tetracycline that was FDA approved for acne in 2018. In vitro studies demonstrate sarecycline maintains high efficacy against *C. acnes* with less activity against other bacteria, particularly gram-negative enterobes.³⁶ The selectivity of sarecycline may lessen alterations of the gut microbiome seen with other oral antibiotics and reduce gastrointestinal tract side effects. Although comparative effectiveness studies are lacking, sarecycline was efficacious in phase 3 trials with few side effects compared with placebo.³⁷ However, at this time, given the absence of comparative effectiveness data and its high cost (Table), sarecycline likely is best reserved for patients with comorbidities (eg, gastrointestinal disease), those requiring long-term antibiotic therapy, or those with acne that has failed to respond to other oral antibiotics.

Hormonal Treatments—Hormonal treatments such as combined oral contraceptives (COCs) and spironolactone often are considered second-line options, though they may represent cost-effective and safe alternatives to oral antibiotics for women with moderate to severe acne.^{38–41} There currently are 4 COCs approved by the FDA for the treatment of moderate acne in postmenarcheal females: drospirenone-ethinyl estradiol (Yaz [Bayer HealthCare Pharmaceuticals, Inc]), ethinyl estradiol-norgestimate (Ortho Tri-Cyclen [Ortho-McNeil Pharmaceuticals, Inc]), drospirenone-ethinyl estradiol-levomefolate (Beyaz [Bayer HealthCare Pharmaceuticals, Inc]), and ethinyl estradiol-norethindrone acetate-ferrous fumarate (Estrostep Fe [Allergan USA, Inc]).⁵ Treatment with COCs has been shown to cause substantial reductions in lesion counts across all lesion types compared to placebo, and a meta-analysis of 24 randomized trials conducted by Arowojolu et al⁴² demonstrated no consistent differences in acne reduction among different COCs.^{43,44} Although oral antibiotics are associated with faster improvement than COCs, there is some evidence that they have similar efficacy at 6 months of therapy.⁴⁵ Combined oral contraceptives are inexpensive and likely reflect a highly cost-effective option (Table).

Spironolactone is an aldosterone inhibitor and androgen receptor blocker that is used off label to treat acne. It is one of the least expensive systemic medications for acne (Table). Although randomized controlled trials are lacking, several large case series support the effectiveness of spironolactone for women with acne.^{38,46} In addition, observational data suggest spironolactone may have similar effectiveness to oral antibiotics.⁴¹ Spironolactone generally is well tolerated, with the most common adverse effects being menstrual irregularities, breast tenderness, and diuresis.^{47,48} Many of these adverse effects are dose dependent and less likely with the dosing used in acne care. Additionally, menstrual irregularities can be reduced by concomitant use of a COC.⁴⁸

Although frequent potassium monitoring remains common among patients being treated with

spironolactone, there is growing evidence to suggest that potassium monitoring is of low value in young healthy women with acne.⁴⁹⁻⁵¹ Reducing this laboratory monitoring likely represents an opportunity to provide higher-value care to patients being treated with spironolactone. However, laboratory monitoring should be considered if risk factors for hyperkalemia are present (eg, older age, comorbidities, medications).⁵¹

Isotretinoin—Isotretinoin is the most efficacious treatment available for acne and has the unique property of being able to induce a remission of acne activity for many patients.⁵ Although it remains modestly expensive (Table), it may be less costly overall relative to other treatments that may need continued use over many years because it can induce a remission of acne activity. As with spironolactone, frequent laboratory monitoring remains common among patients being treated with isotretinoin. There is no evidence to support checking complete blood cell counts.⁵² Several observational studies and a Delphi consensus support reduced monitoring, such as checking lipids and alanine aminotransferase at baseline and peak dose in otherwise young healthy patients.^{53,54} A recent critically appraised topic published in the *British Journal of Dermatology* has proposed eliminating laboratory monitoring entirely.⁵⁵ Reducing laboratory monitoring for patients being treated with isotretinoin has been estimated to potentially save \$100 million to \$200 million per year in the United States.⁵²⁻⁵⁴

Other Strategies to Reduce Patient Costs

Although choosing a cost-effective treatment approach is critical to preventing financial toxicity given poor coverage for acne care and the growth of high-deductible insurance plans, some patients may still experience high treatment costs.⁵⁶ Because pharmacy costs often are inflated, potentially related to practices of pharmacy benefit managers, it often is possible to find better prices than the presented list price, either by using platforms such as GoodRx or through direct-to-patient mail-order pharmacies such as Cost Plus Drug.⁵⁷ For branded medications, some patients may be eligible for patient-assistance programs, though they typically are not available for those with public insurance such as Medicare or Medicaid. Compounding pharmacies offer another approach to reduce cost and improve convenience for patients, but because the vehicle can influence the efficacy and tolerability of some topical medications, it is possible that these compounded formulations may not perform similarly to the original FDA-approved products.

Conclusion

For mild to moderate acne, multimodal topical therapy often is required. Fixed-dose combination adapalene-BPO and clindamycin-BPO are highly cost-effective options for most patients. Lotion formulations of topical retinoids may be useful in patients with difficulty tolerating other formulations. Clascoterone is a novel topical

antiandrogen that is more expensive than other topical therapies but can complement other topical therapies and is well tolerated.

For moderate to severe acne, doxycycline or hormonal therapy (ie, COCs, spironolactone) are highly cost-effective options. Isotretinoin is recommended for severe or scarring acne. Reduced laboratory monitoring for spironolactone and isotretinoin is an opportunity to provide higher-value care.

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