

Adapalene/Benzoyl Peroxide Versus Retinoid Monotherapy for Acne Maintenance: Evidence, Relapse Prevention, And Practical Selection

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ABSTRACT

Acne vulgaris is a chronic relapsing inflammatory disease that frequently requires maintenance therapy after initial clinical improvement. Topical retinoids are widely considered the foundation of acne maintenance because they prevent microcomedone formation, normalize follicular keratinization, and reduce new lesion development. Benzoyl peroxide provides complementary antimicrobial and anti-inflammatory effects without inducing bacterial resistance. Fixed-dose adapalene/benzoyl peroxide combines these mechanisms and may offer superior relapse prevention compared with retinoid monotherapy, particularly in patients with moderate-to-severe, inflammatory, relapse-prone, or post-isotretinoin acne. Maintenance-specific evidence shows that adapalene/benzoyl peroxide reduces relapse and prolongs remission compared with vehicle, while active-treatment trials consistently demonstrate greater efficacy of the combination compared with adapalene alone. However, direct head-to-head trials comparing adapalene/benzoyl peroxide with retinoid monotherapy specifically during the maintenance phase remain limited. Therefore, current evidence supports adapalene/benzoyl peroxide as a strong maintenance option, especially in higher-risk patients, while retinoid monotherapy remains appropriate for milder, comedonal, or irritation-prone acne. This review summarizes the comparative evidence, mechanistic rationale, tolerability profile, and practical clinical selection of adapalene/benzoyl peroxide versus retinoid monotherapy in acne maintenance.

KEYWORDS: acne vulgaris; maintenance therapy; adapalene; benzoyl peroxide; topical retinoids; relapse prevention; fixed-dose combination; microcomedone.

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INTRODUCTION

Acne vulgaris is a chronic disease of the pilosebaceous unit characterized by comedones, inflammatory papules, pustules, nodules, and potential scarring. Although induction therapy can reduce active lesions, relapse is common when treatment is discontinued. For this reason, maintenance therapy is a central component of long-term acne management.

The ideal maintenance regimen should prevent new lesion formation, reduce inflammatory relapse, avoid antibiotic resistance, remain safe for long-term use, and be tolerable enough to support adherence. Topical retinoids have

traditionally served as the core maintenance therapy because they directly target microcomedone formation. Benzoyl peroxide, meanwhile, adds antimicrobial and anti-inflammatory activity and reduces reliance on antibiotics.

The fixed-dose combination of adapalene and benzoyl peroxide offers a mechanistically appealing maintenance strategy. Adapalene provides retinoid-driven normalization of follicular keratinization, while benzoyl peroxide suppresses *Cutibacterium acnes* and inflammation without promoting bacterial resistance. The key question is whether this

Adapalene/Benzoyl Peroxide Versus Retinoid Monotherapy for Acne Maintenance: Evidence, Relapse Prevention, And Practical Selection

combination is superior to retinoid monotherapy for maintenance.

Available evidence suggests that adapalene/benzoyl peroxide is likely more effective for relapse prevention in selected patients, but the confidence is moderate because direct maintenance-phase head-to-head trials against retinoid monotherapy are scarce [1–3].

METHODS

This narrative review was developed from the uploaded literature synthesis evaluating whether adapalene/benzoyl peroxide is superior to retinoid monotherapy for acne maintenance. The included evidence consisted of maintenance trials, systematic reviews, active-treatment randomized trials, fixed-dose combination studies, and comparative topical acne treatment analyses.

References are numbered according to their first appearance in the manuscript.

Rationale for Maintenance Therapy

Acne recurrence occurs because the pathogenic processes responsible for lesion formation often persist after visible improvement. These include follicular hyperkeratinization, sebum production, *C. acnes* proliferation, and inflammation.

Maintenance therapy aims to:

- Prevent microcomedone formation.

- Reduce inflammatory relapse.

- Maintain lesion clearance after induction therapy.

- Reduce need for repeated oral antibiotics.

- Prevent scarring and post-inflammatory hyperpigmentation.

- Improve long-term quality of life.

- Maintain disease control with a simple and tolerable regimen.

Without maintenance therapy, patients may experience gradual return of comedones followed by inflammatory lesions. Therefore, the maintenance agent should ideally prevent early subclinical acne activity rather than only treat visible lesions.

Topical Retinoid Monotherapy

Topical retinoids, including adapalene, tretinoin, tazarotene, and trifarotene, are widely used in acne maintenance.

Mechanism of Action

Retinoids act by:

- Normalizing follicular keratinization.

- Preventing microcomedone formation.

- Reducing comedonal lesions.

- Decreasing inflammatory signaling.

- Enhancing penetration of other topical agents.

- Preventing new acne lesions over time.

This makes retinoids particularly well suited for long-term control because microcomedones represent the precursor lesion of acne.

Evidence for Maintenance

Retinoid monotherapy is effective for maintaining response after induction therapy. In a 24-week maintenance study, adapalene monotherapy reduced lesion counts, whereas the control group worsened substantially [4].

A systematic review of acne maintenance therapy also found that adapalene monotherapy was superior to vehicle for maintaining improvement in inflammatory and noninflammatory lesions, although broader global outcomes were not consistently significant across all trials [3].

Strengths

- Strong mechanistic basis for relapse prevention.

- Useful in comedonal and mixed acne.

- Non-antibiotic and safe for long-term use.

- Central role in maintenance after antibiotics or isotretinoin.

- Usually appropriate for mild-to-moderate acne.

Limitations

- Slower visible response than antimicrobial therapy.

- Irritation, peeling, dryness, erythema, or burning may reduce adherence.

- Less direct antimicrobial effect than benzoyl peroxide.

- Generally avoided during pregnancy.

Retinoid monotherapy remains an appropriate maintenance strategy for patients with milder acne, predominantly comedonal relapse, sensitive skin, or poor tolerance of combination therapy.

Benzoyl Peroxide as a Complementary Maintenance Agent

Benzoyl peroxide is not a retinoid, but it is highly relevant to maintenance because it provides antimicrobial and anti-inflammatory effects without inducing bacterial resistance.

Its benefits include:

- Rapid reduction of *C. acnes*.

- Reduction in inflammatory lesions.

- Prevention of antibiotic resistance when used with antibiotics.

- Non-antibiotic mechanism.

- Utility in inflammatory or truncal acne.

However, benzoyl peroxide alone does not target microcomedone formation as directly as retinoids. Therefore, it is generally considered an adjunct rather than the main long-term maintenance agent when compared with topical retinoids.

Adapalene/Benzoyl Peroxide Combination

The fixed-dose combination of adapalene and benzoyl peroxide combines two complementary mechanisms:

- Adapalene: anticomedogenic, comedolytic, anti-inflammatory.

- Benzoyl peroxide: antimicrobial, anti-inflammatory, resistance-sparing.

This combination targets both early lesion formation and inflammatory relapse. It is therefore especially attractive for patients who have mixed comedonal-inflammatory acne, moderate-to-severe baseline disease, or repeated relapses after discontinuing therapy.

Adapalene/Benzoyl Peroxide Versus Retinoid Monotherapy for Acne Maintenance: Evidence, Relapse Prevention, And Practical Selection

Maintenance-Specific Evidence

The most important maintenance-specific evidence supports adapalene/benzoyl peroxide over vehicle rather than directly over retinoid monotherapy.

Poulin et al. evaluated adapalene/benzoyl peroxide as maintenance therapy after successful induction treatment in severe acne. The combination delayed relapse and improved maintenance success compared with vehicle, with 25% relapse occurring at 175 days versus 56 days and lesion-maintenance success of approximately 78% versus 46% at 24 weeks [1].

Bettoli et al. reported a 12-month post-isotretinoin maintenance cohort using adapalene 0.1%/benzoyl peroxide 2.5%, with a relapse rate of only 2.94%, supporting the combination as a useful option after isotretinoin-induced remission [5].

Kruglova and Gryazeva reported low relapse rates during 6 months of adapalene/benzoyl peroxide maintenance, with relapse in 2.9% of moderate cases and 5.8% of severe cases [6]. Together, these studies support the use of adapalene/benzoyl peroxide for relapse prevention, especially in relapse-prone patients. However, they do not fully answer whether the combination is definitively superior to retinoid monotherapy in a direct maintenance-phase comparison.

Evidence From Active-Treatment Trials

Although maintenance-specific direct comparisons are limited, active-treatment trials consistently favor adapalene/benzoyl peroxide over adapalene alone.

Large randomized trials demonstrated that fixed-dose adapalene/benzoyl peroxide provides greater lesion reduction than its individual components or vehicle in active acne treatment [2,7]. This supports the biologic plausibility that the combination may also provide stronger maintenance control, particularly when inflammatory relapse is a concern.

Systematic reviews and meta-analyses of topical acne treatments also tend to rank fixed-dose combinations above single-agent topical therapy for mild-to-moderate acne [8,9].

The limitation is that active-treatment superiority does not automatically prove maintenance superiority. Maintenance therapy occurs after disease control, when tolerability, adherence, and relapse prevention may matter more than rapid lesion reduction.

Is Adapalene/Benzoyl Peroxide Better Than Retinoid Monotherapy?

The most balanced answer is: probably yes for relapse-prone or inflammatory acne, but not definitively for every patient.

The evidence favors adapalene/benzoyl peroxide because:

It combines anticomedogenic and antimicrobial mechanisms.

It prevents relapse versus vehicle in maintenance trials.

It performs better than adapalene alone in active-treatment trials.

It has strong mechanistic rationale for mixed comedonal-inflammatory acne.

It helps reduce antibiotic reliance.

However, the confidence is moderate because:

Direct maintenance-phase trials against retinoid monotherapy are scarce.

Retinoid monotherapy is already effective.

Combination therapy may cause more irritation.

Some patients do not require the added antimicrobial component.

Long-term adherence may be better with a simpler or less irritating regimen.

Therefore, adapalene/benzoyl peroxide is best viewed as a stronger maintenance option for selected patients rather than a universal replacement for retinoid monotherapy.

Tolerability and Adherence

Tolerability is the main tradeoff with combination therapy. Both adapalene and benzoyl peroxide can cause local irritation, and combining them may increase dryness, erythema, scaling, burning, or stinging.

Potential adverse effects include:

Dryness

Peeling

Erythema

Burning or stinging

Irritant dermatitis

Bleaching of fabrics from benzoyl peroxide

Adapalene is generally among the better-tolerated topical retinoids, but irritation remains clinically relevant [10].

Adherence can be improved by:

Starting every other night.

Using a pea-sized amount for the whole face.

Applying moisturizer.

Avoiding harsh cleansers or scrubs.

Using sunscreen.

Reducing frequency temporarily during irritation.

Choosing monotherapy if combination therapy is not tolerated.

The best maintenance regimen is the one the patient can use consistently.

Patient Selection

Patients Who May Benefit More From Adapalene/Benzoyl Peroxide

The combination is particularly useful for:

Moderate-to-severe acne after induction therapy.

Patients with frequent relapse.

Patients after oral isotretinoin.

Mixed comedonal-inflammatory acne.

Papulopustular acne with persistent inflammatory tendency.

Patients recently treated with oral antibiotics.

Patients in whom antibiotic-sparing therapy is a priority.

Adapalene/Benzoyl Peroxide Versus Retinoid Monotherapy for Acne Maintenance: Evidence, Relapse Prevention, And Practical Selection

Truncal acne when benzoyl peroxide is practical.

Patients Who May Be Better Served by Retinoid Monotherapy

Retinoid monotherapy may be preferable for:

Mild comedonal acne.

Patients with sensitive or easily irritated skin.

Patients with minimal inflammatory relapse.

Patients unable to tolerate benzoyl peroxide.

Patients concerned about fabric bleaching.

Patients needing a simpler long-term regimen.

Situations where retinoids are appropriate but benzoyl peroxide is unnecessary.

Patients Who Should Avoid Retinoid-Based Maintenance

Topical retinoids are generally avoided during pregnancy or when actively trying to conceive. In such cases, pregnancy-compatible alternatives should be selected.

Practical Regimens

Retinoid Monotherapy Maintenance

A typical approach may include:

Adapalene or another topical retinoid applied at night.

Gentle cleanser and moisturizer.

Sunscreen during the day.

Gradual frequency increase as tolerated.

Adapalene/Benzoyl Peroxide Maintenance

A typical approach may include:

Fixed-dose adapalene 0.1%/benzoyl peroxide 2.5% once daily or several nights per week.

Moisturizer to reduce irritation.

Frequency adjustment based on tolerance.

Avoidance of additional irritating products.

Step-Down Strategy

For patients who clear on combination therapy but develop irritation, a step-down approach may be used:

Continue adapalene/BPO several times weekly.

Use retinoid monotherapy on alternate nights.

Reserve benzoyl peroxide for inflammatory flares or morning use.

Maintain retinoid as the long-term foundation.

Proposed Maintenance Algorithm

Assess baseline acne severity and relapse risk.

Use retinoid monotherapy for mild, mainly comedonal, or low-relapse-risk acne.

Use adapalene/BPO for moderate-to-severe, inflammatory, or relapse-prone acne.

Use adapalene/BPO after isotretinoin when relapse risk is clinically meaningful.

Use adapalene/BPO after oral antibiotics to reduce recurrence and avoid antibiotic repetition.

Adjust frequency for tolerability.

Step down to retinoid monotherapy if irritation limits adherence.

Avoid topical antibiotic maintenance monotherapy.

Reassess every 8–12 weeks initially, then extend follow-up if stable.

Continue maintenance long term in patients with recurrent acne.

DISCUSSION

The available evidence supports adapalene/benzoyl peroxide as a highly effective maintenance option, especially for relapse-prone acne. Its advantage is mechanistically logical: adapalene prevents microcomedone formation, while benzoyl peroxide suppresses bacterial and inflammatory components without antibiotic resistance.

However, the claim that adapalene/benzoyl peroxide is superior to retinoid monotherapy must be stated carefully. Maintenance-specific trials show superiority over vehicle, and active-treatment trials show superiority over adapalene alone, but direct maintenance-phase comparisons against retinoid monotherapy are limited. Therefore, the evidence leans in favor of the combination, but the conclusion is not absolute.

In practice, the choice should be individualized. A patient with mild comedonal acne may do well with retinoid monotherapy and may not need benzoyl peroxide. A patient with severe acne after isotretinoin, repeated inflammatory relapse, or prior antibiotic exposure may benefit from adapalene/benzoyl peroxide. Tolerability often determines long-term success.

Thus, the best interpretation is that adapalene/benzoyl peroxide is generally a stronger maintenance regimen, but retinoid monotherapy remains an appropriate lower-irritation option for selected patients.

CONCLUSION

Adapalene/benzoyl peroxide appears to provide stronger acne maintenance than retinoid monotherapy in relapse-prone, inflammatory, moderate-to-severe, or post-isotretinoin acne. Maintenance-specific evidence shows that adapalene/benzoyl peroxide reduces relapse and prolongs remission compared with vehicle, while active-treatment trials consistently show greater efficacy of the combination compared with adapalene alone. However, direct head-to-head maintenance trials against retinoid monotherapy remain limited. Therefore, the combination should be favored when relapse prevention is a priority and tolerability is acceptable, whereas retinoid monotherapy remains suitable for mild, comedonal, sensitive-skin, or lower-risk maintenance.

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Adapalene/Benzoyl Peroxide Versus Retinoid Monotherapy for Acne Maintenance: Evidence, Relapse Prevention, And Practical Selection

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