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New treatments for acne vulgaris over the past decade

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Introduction

Acne vulgaris is a prevalent, chronic inflammatory condition of the pilosebaceous units, commonly affecting adolescents and young adults, though it can persist or develop later in life. Conventional treatments such as retinoids, benzoyl peroxide, antibiotics, and hormonal therapies remain staples in managing acne vulgaris **(Figure 1)**. Advances in the past decade have introduced novel treatments for acne vulgaris that may be more effective and tolerable for select populations.

Novel topical therapies

Topical retinoids:

Topical retinoids remain a first-line treatment for managing acne vulgaris. Two newer topical retinoid formulations used to treat acne vulgaris are trifarotene 50 mcg/g cream and tazarotene 0.045% lotion.

Trifarotene was approved in 2019 by Health Canada for the topical treatment of acne vulgaris of the face and/or trunk in patients 12 years of age and older.[1] Unlike other topical retinoids, trifarotene is a 4th generation topical retinoid that specifically targets the retinoic acid receptor (RAR) gamma, which is the most common RAR isoform, making it more selective than other retinoids. It also has the most clinical data on safety and efficacy in treating truncal acne.[2] Adverse events are similar to those of other topical retinoids associated with cutaneous irritation that improves with continued therapy.

Tazarotene is a potent topical retinoid that remains highly effective in targeting inflammatory lesions of acne vulgaris. Although tazarotene lotion at doses of 0.05% and 0.1% were approved to treat acne vulgaris, these formulations resulted in more significant side effects given their high potency and are no longer routinely available in Canada to treat acne. Tazarotene 0.045% lotion was approved in 2021 by Health Canada for the topical treatment of acne vulgaris in patients 10 years of age and older.[3] Unlike previous formulations, tazarotene 0.045% lotion is formulated with a polymeric emulsification system that helps to

reduce dryness of the skin through its hydrating and moisturizing properties.[4]

Topical clascoterone:

Clascoterone 1% cream was approved by Health Canada in 2023 to treat acne vulgaris in patients 12 years of age and older.[5] It is the first topical hormonal therapy approved by Health Canada for acne vulgaris. It is an androgen receptor inhibitor that may reduce sebaceous gland activity. Patients treated with clascoterone applied topically twice daily for 12 weeks in two randomized control trials (RCTs) achieved higher investigator global assessment (IGA) scores compared to those using the vehicle. In addition, they experienced few local side effects, similar to those using the vehicle.[6] Unlike other hormonal therapies used to treat acne vulgaris, clascoterone is safe for use in both men and women. The most common side effects were local skin reactions, such as erythema, scaling and pruritus, but these reactions were reported at similar rates in patients taking the vehicle alternative. Systemic symptoms such as hypothalamic-pituitary-adrenal (HPA) axis suppression and hyperkalemia were not reported with prescription strength therapy.

Topical clindamycin/adapalene/benzoyl peroxide triple-combination:

The latest topical therapy approved by Health Canada to treat acne vulgaris in individuals 12 years of age and older is a gel containing clindamycin phosphate 1.2%, adapalene 0.15%, and benzoyl peroxide 3.1%.[7] This is the first triple-combination therapy approved by Health Canada, offering three mechanisms of action, including antibiotic, retinoid, and antibacterial. It is applied once daily to the affected areas, which may allow for better compliance than alternative topical regimens that require twice-daily application of multiple products. In two clinical trials, the triple-combination therapy was found to be significantly more effective at reducing both inflammatory and non-inflammatory lesions by week 12 compared to the vehicle. The most frequent side effects were mild local reactions, similar to those observed with other topical therapies used for acne vulgaris.

Topical minocycline:

While not approved by Health Canada, topical minocycline 4% foam is a topical antibiotic that received approval in the United States in 2019 from the Food and Drug Administration (FDA) to treat non-nodular lesions of acne vulgaris in patients 9 years of age and older.[8] Two clinical trials revealed significant reductions in IGA in patients treated with topical minocycline over 12 weeks, with continued improvement over 52 weeks. The most common side effect reported in these clinical trials was headache. Further, systemic absorption is low, and serious adverse reactions associated with oral minocycline were not observed in clinical studies.

9 y.o.
- Adapalene 0.1% & BPO gel 2.5%[15]

10 y.o.
- Tazarotene 0.045% lotion (*age 10-12: face only*) without other oxidizing agents[3]

12 y.o.
- Adapalene 0.1% or 0.3% gel[16]
- Adapalene 0.3% & benzoyl peroxide 2.5% gel[15]
- Benzoyl peroxide 3% or 5% & clindamycin 1% gel[17]
- Clascoterone 1% cream or solution[18]
- Clindamyin 1.2% & tretinoin 0.025% gel[19]
- Clindamycin 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%[7]
- Dapsone 5% gel[20]
- Tretinoin 0.01%/0.025% gel or 0.01%/0.025%/0.05%/0.1% cream[21]
- Trifarotene 50 mcg/g cream (*facial or truncal acne*)[1]
- PO cyproterone acetate & ethinyl estradiol (*after menarche*)[22]
- PO isotretinoin (micronized, non-micronized)[14]

14 y.o.
- PO drospirenone & ethinyl estradiol[23]
- PO levonorgestrel & ethinyl estradiol[24]

15 y.o.
- PO norgestimate & ethinyl estradiol[25]

Figure 1. Health Canada-approved pharmacologic therapies for acne vulgaris based on age of approval; *courtesy of Nikolas MacLellan, MD, FRCPC, DABD*

Novel oral therapies

Sarecycline:

Although not available in Canada, sarecycline is a tetracycline-class oral antibiotic approved by the FDA in 2018 to treat acne vulgaris in individuals 9 years of age and older.[9] Unlike other tetracycline-based antibiotics, sarecycline has a narrow spectrum of action and demonstrates a lower propensity for inducing antimicrobial resistance and gut microbiome alterations while still achieving a similar therapeutic efficacy to other antibiotics for treating acne.[10] While the most common adverse event reported was nausea, it seems to be associated with fewer instances of diarrhea, fungal overgrowth, and vaginal candidiasis compared to alternate tetracycline antibiotics.

Micronized isotretinoin:

Oral isotretinoin remains the gold standard for treating severe acne vulgaris. However, some oral formulations are poorly absorbed when taken with a low-fat diet, which may result in lower efficacy in selected patients. A new micronized formulation of isotretinoin was approved by Health Canada in 2023 to treat severe nodular and/or inflammatory acne, acne conglobata, and recalcitrant acne in patients 12 years of age and older.[11] The micronized formulation provides enhanced bioavailability that results in a comparable rate of absorption and extent of drug exposure under both fasting and fed conditions. This may be a more effective treatment option for younger patients who are on a diet or undergoing intermittent fasting and are unable to achieve the target cumulative dose of at least 120 mg/kg.[12] The side effect profiles are similar between micronized and non-micronized isotretinoin. It is recommended to start micronized isotretinoin at a dose of 0.4-0.8 mg/kg body weight daily, increasing to 1.6 mg/kg per day for a 15- to 20-week duration.

Novel physical therapies

1726-nm laser:

Physical therapies have played a role in managing acne vulgaris for decades. These include photodynamic therapy, visible light therapy, and other surgical methods such as the injection of intralesional triamcinolone acetonide or comedone extraction. In 2023, Health Canada approved a new diode laser with a 1726 nm wavelength to treat acne vulgaris due to its high selectivity for sebaceous glands.[13] It is postulated to be the first treatment since isotretinoin that significantly reduces sebaceous gland activity while being more tolerable than isotretinoin. The treatment is delivered in 3 sessions every 3 weeks. A prospective, open-label, single-arm institutional review study that included 104 participants demonstrated that the treatment is safe and effective across all skin types, as observed at 4, 12, and 26 weeks. The study showed a significant, durable reduction in acne lesions in up to 87.3% of participants 6 months post-treatment. Some patients experienced an initial transient eruption in the first 2 to 21 days post treatment (similar to the eruption that occurs after isotretinoin), and some patients experienced temporary perilesional erythema; however, there were no reports of residual erythema, edema, blistering, crusting, or dyspigmentation.

Conclusion

The treatment of acne vulgaris has evolved significantly in recent years, with new therapies offering patients more personalized and targeted options. Health Canada has approved several new treatments for the pharmacologic management of acne, including trifarotene, tazarotene 0.045% lotion, clascoterone, clindamycin/adapalene/benzoyl peroxide triple combination therapy, micronized isotretinoin, and the 1726-nm laser. These treatments offer effective options with improved safety profiles. Additionally, laser and light therapies, along with newer therapies approved by the FDA such as topical minocycline foam and oral sarecycline, offer innovative ways to tackle acne with less systemic involvement and enhanced patient outcomes. As research continues, it is likely that even more effective and safer treatments will emerge, offering renewed hope for patients with acne vulgaris who have long struggled with the psychological and physical impacts of this condition.

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