Update to acne vulgaris treatment for Canadian practice

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Abstract

Objective To provide updates and apply the new 2024 American Academy of Dermatology (AAD) guidelines of care for the management of acne vulgaris (AV) to Canadian practice and summarize current evidence-based practices, treatments, and emerging trends in acne management.

Quality of evidence As per published guidelines, MEDLINE and Embase databases were searched for literature on the effectiveness and safety of available and approved treatments for AV in patients aged 9 and older in the United States. Studies meeting patient or population, intervention, comparison, and outcomes (PICO) criteria were extracted, and quality was assessed using the Cochrane Risk of Bias tool. A Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was used to classify evidence certainty as high, moderate, low, or very low, and categorize recommendations as strong or conditional. The federal Drug and Health Product Register was then searched for approved and marketed treatments currently available in Canada.

Main message Topical therapies such as benzoyl peroxide, antibiotics, and fixed-dose combinations received strong recommendations, while retinoids, clascoterone, salicylic acid, and azelaic acid received conditional recommendations. Topical minocycline is not yet available in Canada. Oral therapies such as doxycycline and isotretinoin received strong recommendations, while minocycline, combined oral contraceptives, and spironolactone received condition recommendations. Isotretinoin remains the criterion standard for treating severe acne and scarring; frequent monitoring is unnecessary for most patients receiving oral isotretinoin, and it is unlikely to be associated with neuropsychiatric disorders or inflammatory bowel disease. Intralesional corticosteroids were also strongly recommended for acne at high risk of scarring. Additional consideration must be given to pregnant individuals, people with skin of colour, and those undergoing gender-affirming therapy.

Conclusion The 2024 AAD guidelines provide a valuable framework for Canadian management of AV. Mild cases are managed with topical treatments, while moderate to severe cases often require oral medication. Antibiotic monotherapy is discouraged; combination with benzoyl peroxide may mitigate antibiotic resistance. Treatments using multiple modalities and mechanisms of action are recommended.

Editor's key points

- The American Academy of Dermatology (AAD) 2024 guidelines for the management of acne vulgaris (AV) provide a valuable framework for Canadian clinicians to optimize outcomes.
- Mild cases of AV are generally managed with topical treatments, while more severe cases often require systemic medications such as antibiotics or isotretinoin. Antibiotic monotherapy is generally discouraged; combination treatments using various mechanisms of action are recommended.
- Trifarotene, clascoterone, and a combination of clindamycin, adapalene, and benzoyl peroxide (BP) are 3 new topical treatments with excellent efficacy and safety profiles. For patients with severe acne and scarring, oral isotretinoin remains the criterion standard treatment.

Points de repère du rédacteur

- Les lignes directrices de l'American Academy of Dermatology (AAD) de 2024 sur la prise en charge de l'acné simple (AS) offrent aux cliniciens canadiens un référentiel utile pour optimiser les résultats.
- Les cas légers d'AS sont généralement pris en charge au moyen de traitements topiques, tandis que les cas les plus graves exigent souvent des médicaments systémiques, comme des antibiotiques ou de l'isotrétinoïne. On déconseille généralement un antibiotique en monothérapie; des traitements combinés reposant sur divers mécanismes d'action sont recommandés.
- Le trifarotène, la clascotérone, et une combinaison de clindamycine, d'adapalène et de peroxyde de benzoyle (PB) sont 3 nouveaux traitements topiques dont l'efficacité et le profil d'innocuité sont excellents. Pour les patients dont l'acné et les cicatrices sont sévères, l'isotrétinoïne par voie orale demeure le traitement à privilégier.

Actualisation du traitement de l'acné simple pour la pratique canadienne

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Résumé

Objectif Présenter les actualisations effectuées dans les récentes lignes directrices de 2024 de l'American Academy of Dermatology (AAD) sur la prise en charge de l'acné simple (AS) et les mettre en application dans la pratique canadienne, et résumer les pratiques et les traitements courants fondés sur des données probantes, de même que les tendances émergentes dans la prise en charge de l'acné.

Qualité des données Conformément aux directives publiées, une recension a été effectuée dans les bases de données MEDLINE et Embase pour cerner les ouvrages sur l'efficacité et l'innocuité des traitements accessibles et homologués pour l'AS chez des patients âgés de 9 ans et plus aux États-Unis. Les études conformes aux critères liés aux patients ou à la population, à l'intervention, à la comparaison et aux résultats (méthode PICO) ont été extraites et leur qualité a été évaluée au moyen de l'outil de Cochrane sur le risque de biais. Le cadre de référence GRADE (Grading of Recommendations Assessment, Development and Evaluation) a servi à classer la certitude des données probantes comme étant élevée, modérée, faible ou très faible et à catégoriser les recommandations comme étant fortes ou conditionnelles. Le Registre fédéral des médicaments et des produits de santé a ensuite fait l'objet d'une recension à la recherche de traitements approuvés et commercialisés actuellement disponibles au Canada.

Message principal Les traitements topiques intralésionnels, comme le peroxyde de benzoyle, les antibiotiques et les combinaisons à doses fixes ont reçu des recommandations fortes, tandis que les rétinoïdes, la clascotérone, l'acide salicylique et l'acide azélaïque se voyaient attribuer une recommandation conditionnelle. La minocycline topique n'est pas encore accessible au Canada. Les thérapies par voie orale comme la doxycycline et l'isotrétinoïne ont reçu des recommandations fortes, alors que la minocycline, les contraceptifs oraux combinés et la spironolactone obtenaient des recommandations conditionnelles. L'isotrétinoïne demeure la règle d'or pour le traitement de l'acné et des cicatrices sévères; une surveillance fréquente n'est pas nécessaire pour la plupart des patients qui prennent de l'isotrétinoïne par voie orale, et il est improbable qu'elle soit associée à des troubles neuropsychiatriques ou à des maladies inflammatoires de l'intestin. Les corticostéroïdes intralésionnels étaient aussi fortement recommandés pour l'acné à risque élevé de laisser des cicatrices. D'autres facteurs doivent aussi être pris en considération pour les personnes enceintes, à peau de couleur ou qui suivent une thérapie d'affirmation de genre.

Conclusion Les lignes directrices de l'AAD de 2024 offrent un référentiel utile pour la prise en charge de l'AS au Canada. Les cas légers peuvent être pris en charge avec des traitements topiques, tandis que les cas de modérés à sévères nécessitent souvent une médication par voie orale. Un antibiotique en monothérapie est déconseillé; une combinaison avec du peroxyde de benzoyle peut atténuer la résistance aux antibiotiques. Il est recommandé de recourir à des traitements qui utilisent de multiples modalités et mécanismes d'action.

Acne vulgaris (AV) is a prevalent skin condition characterized by pilosebaceous follicle inflammation. Since the last Canadian guidelines for acne management were published in 2016,[1] there have been important advancements and updates to treatment recommendations, highlighting the need for a more current framework. While the American Academy of Dermatology (AAD) released updated guidelines for the management of AV in 2024, the applicability to practitioners in Canada has yet to be assessed.[2] This study aims to provide a comprehensive summary of current evidence-based practices, treatments, and emerging trends in acne management within Canada.

Quality of evidence

The 2024 AAD guidelines for the management of AV were selected, as they represent the most recent, evidence-based, and internationally recognized consensus on acne management.[2] As per the published guidelines, a systematic search of MEDLINE and Embase databases was conducted for literature published after 2014 on the effectiveness and safety of available and approved treatments for AV in patients aged 9 or older in the United States. Studies meeting patient or population, intervention, comparison, and outcomes (PICO) criteria were extracted, and quality was assessed using the Cochrane Risk of Bias tool.

The AAD working group comprised dermatologists, pediatric dermatologists, a staff liaison, and a patient representative, and used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to assess evidence certainty and recommendations. The evidence-to-decision framework considered evidence certainty, balance of desirable and undesirable effects, values and preferences, resource use, equity, acceptability, and feasibility.[3]

As there are currently no updated Canadian clinical practice guidelines for the management of AV, the federal Drug and Health Product Register was searched for approved and marketed treatments currently available in Canada. Treatments unavailable in Canada were noted, and Health Canada approvals, prescribing guidelines, and regulatory decisions were considered to ensure alignment with national practice.

Main message

Figure 1 provides a visual summary of the 2024 AAD guidelines modified for Canadian clinical practice.[2]

Topical therapies. Topical therapies are fundamental in the first-line management of AV, either as monotherapy or adjuncts.[1] Combining multiple therapeutic modalities that target different pathogenic mechanisms is advised to enhance efficacy and lower the potential for antibiotic resistance.

Topical retinoids: Retinoids, which are vitamin A analogues, are comedolytic and anti-inflammatory agents. Topical application alters epithelial growth and differentiation, enhancing follicular epithelial cell turnover.[4] Retinoids also improve postinflammatory hyperpigmentation (PIH) and maintain acne clearance.[5] No single topical retinoid outperforms others, as efficacy and tolerability depend on concentration and formulation.[2] **Table 1** summarizes topical retinoids available in Canada.[6-16]

Most topical retinoids are photolabile and should be applied at night. However, adapalene and tretinoin, formulated with microsphere technology, exhibit greater photostability and may be applied during the day. Daily sunscreen should be used concurrently to protect against ultraviolet radiation damage. Higher concentrations may cause irritation, potentially necessitating decreased application frequency and concurrent emollient use. Additionally, most retinoids other than adapalene should not be combined with benzoyl peroxide (BP) due to potential retinoid oxidation and inactivation.

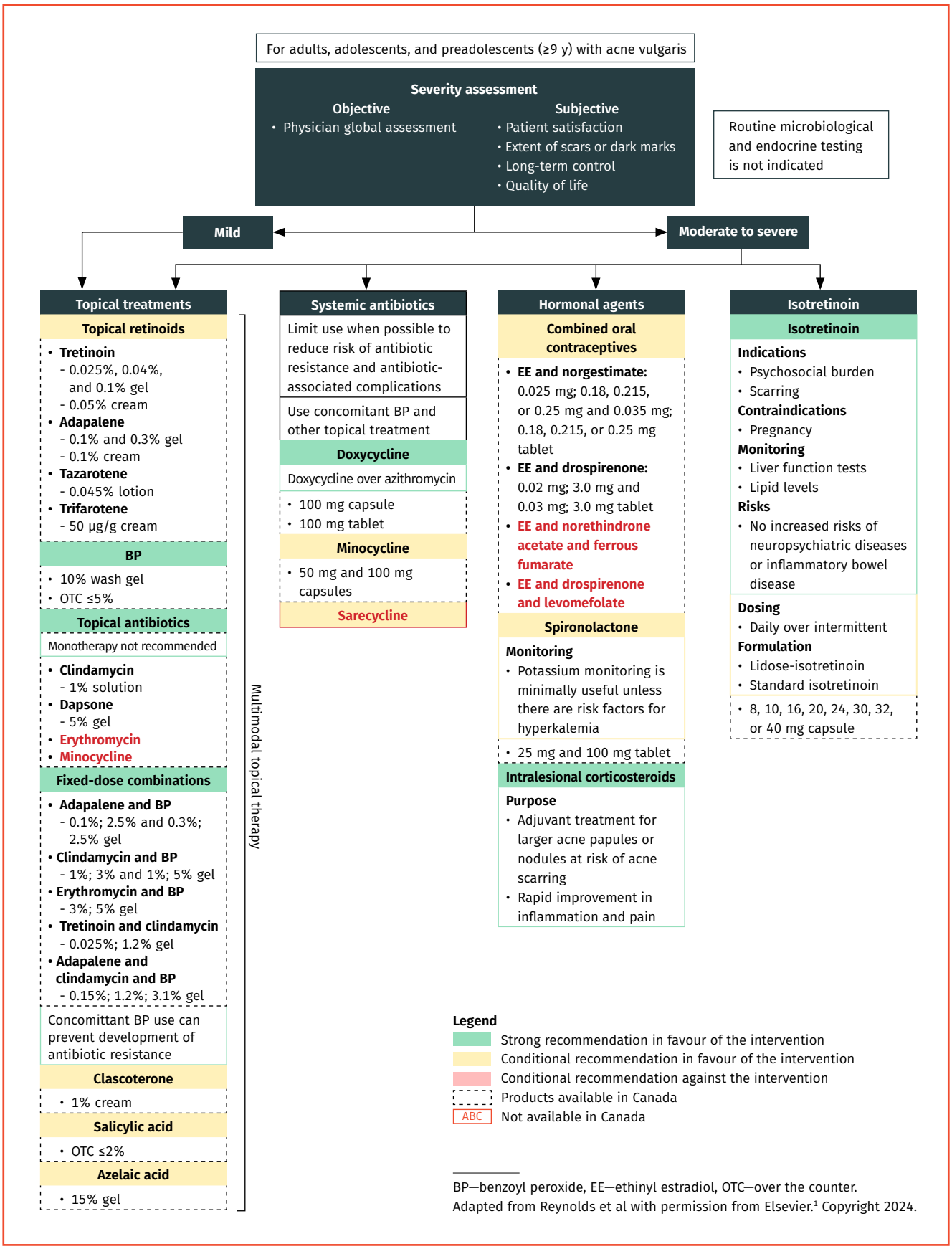
BP: In Canada, BP is available over the counter (OTC) in concentrations of 5% or less, or as a prescription of 10% cleansing gel. It functions as a topical antimicrobial agent, reduces the presence of irritating free fatty acids, and has mild comedolytic properties.[17,18] Products with lower concentrations and wash-off formulations are typically well tolerated.[19] Side effects include burning, dryness, fabric staining, and bleaching.[20] There have been no reported instances of BP-resistant *Cutibacterium acnes*, highlighting its advantage amid growing antibiotic resistance concerns.

Topical antibiotics: **Table 2** summarizes topical antibiotics available in Canada for AV.[21-25] Topical erythromycin is not available in Canada at acne-recommended concentrations, and topical minocycline is approved by the Food and Drug Administration but not available in Canada. No evidence supports the superiority of a single topical antibiotic.[2] Monotherapy is discouraged due to increased risk of antibiotic resistance. Combining antibiotics with BP is recommended for improved efficacy and decreased antibiotic resistance. Specific combinations, such as BP and dapsone or sulfacetamide, can lead to orange-brown skin discoloration that washes off, although avoidable by applying BP and antibiotics at different times.

Fixed-dose topical combinations: **Table 3** summarizes branded and generic fixed-dose topical combinations available in Canada.[26-30] Combination BP with adapalene or clindamycin is recommended. Retinoid-antibiotic combinations are also advised.[1] In August 2024, Health Canada approved a topical triple-combination of clindamycin, adapalene, and BP for patients with AV older than 12 years.[31] Adverse effects associated with fixed-dose combinations reflect the safety profiles of the individual agents in summation.[2]

Topical clascoterone: Topical clascoterone, a first-in-class topical antiandrogen, inhibits androgen receptors and blocks androgen-mediated sebum production and abnormal keratinization.[32] Twice-daily 1% clascoterone cream is approved in Canada as AV monotherapy in patients aged 12 years or older.[33]

Figure 1. Management of acne vulgaris



BP—benzoyl peroxide, EE—ethinyl estradiol, OTC—over the counter.
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Table 1. Topical retinoids available in Canada for treatment of acne vulgaris

AGENT	MECHANISM OF ACTION AND RECEPTORS	DOSE	ADVERSE EFFECTS	PRECAUTIONS AND SPECIAL CONSIDERATIONS	CONTRAINDICATIONS
Tretinoin	• Vitamin A derivative • Reduces follicular cell cohesion and microcomedone formation • Enhances mitotic activity and accelerates follicular turnover • Expels comedones • Targets RAR-α, RAR-β, RAR-γ, and RXR[5]	Gel: 0.01%, 0.025%, or 0.05% applied every day at bedtime[6] Cream: 0.01%, 0.025%, 0.05%, or 0.1% applied every day at bedtime[6]	• Application site reaction or contact dermatitis • Dryness • Burning • Stinging • Exfoliation • Pruritus	• Start with lower concentrations or lesser frequency (eg, every other day) and increase as tolerated • Photolabile; avoid use with BP • Use with caution in patients with eczema-prone skin • Apply a thin layer to the affected area, not to the individual spots • Avoid application near eyes, mouth, and mucosal areas[7] • Use a gentle, noncomedogenic moisturizer to reduce irritation	Contraindicated in pregnancy and those planning pregnancy
Tretinoin microsphere formulation	• Vitamin A derivative • Reduces follicular cell cohesion and microcomedone formation • Accelerates follicular cell turnover • Targets RAR-α, RAR-β, RAR-γ, and RXR[5]	Gel: 0.04% or 0.1% applied every day[7]	Same as tretinoin	Less photolabile than tretinoin but otherwise similar	Same as tretinoin
Adapalene	• Naphthoic acid derivative • Modulates differentiation of follicular epithelial cells • Exfoliates mature microcomedones • Has anti-inflammatory properties • Binds to RAR-β and RAR-γ[7]	Gel: 0.1% or 0.3% applied every day[7,8] Cream: 0.1% applied every day[9]	Same as tretinoin	Photostable; can be applied during the day[9]	Should be avoided in pregnancy and those planning pregnancy
Tazarotene 0.045%	• Synthetic acetylenic retinoid • Downregulates keratinocyte differentiation and proliferation • Upregulates antiproliferative mechanisms • Exhibits anti-inflammatory effects • Binds to RAR-β and RAR-γ[10]	Lotion: 0.045% applied every evening[11,12]	Same as tretinoin	Same as tretinoin	Contraindicated in pregnancy and those planning pregnancy
Trifarotene	• Terphenyl acid derivative • Weakens adhesion between keratinocytes • Enhances proteolysis of elastin and collagen • Possesses anti-inflammatory effects • Binds specifically to RAR-γ[13]	Cream: 0.005% applied every evening[14]	• Erythema • Scaling • Dryness • Stinging • Burning[15]	Only retinoid approved for truncal acne[14]	Same as tretinoin

BP—benzoyl peroxide, RAR—retinoic acid receptor, RXR—retinoid X receptor.

Table 2. Topical antibiotics available in Canada to treat acne vulgaris

TOPICAL ANTIBIOTIC	MECHANISM OF ACTION	DOSE	ADVERSE EFFECTS	PRECAUTIONS AND SPECIAL CONSIDERATIONS
Clindamycin	• Lincosamide • Anti-inflammatory and antibacterial effects against *Cutibacterium acnes* • Prevents peptide bond formation and inhibits bacterial protein synthesis[20]	Solution: 1% thin film applied twice a day	• Skin dryness • Irritation • Extremely rare risk of antibiotic-associated diarrhea (eg, *Clostridioides difficile*)[21,22]	• Should not be used as monotherapy • Only effective for inflammatory acne
Dapsone	• Sulfone • Primarily anti-inflammatory, also has antibacterial effects against *C acnes* • Prevents dihydrofolic acid synthesis and inhibits bacterial protein synthesis[23]	Gel: 5% pea-sized amount applied in a thin layer twice a day	• Oiliness • Peeling • Dryness • Application site erythema • Concurrent use with BP may cause temporary orange-brown skin discoloration (can be washed off)[24]	• Best used for inflammatory acne, not for comedonal acne • May take 6-8 wk to see substantial improvements • Should be avoided in patients with hypersensitivity to dapsone or sulfonamides

BP—benzoyl peroxide.

Clascoterone is associated with minimal to no skin irritation. Clascoterone also lacks systemic anti-androgenic effects due to its epidermal hydrolysis to cortexolone.[34] Given its recent approval, limited safety data on combination treatments containing clascoterone exist.

Despite a high level of evidence for clascoterone, it is conditionally recommended in the AAD guidelines due to high costs in the United States, which limits its accessibility.[2] No studies have examined the safety of clascoterone during pregnancy and lactation.[35]

Other topical agents: Salicylic acid and azelaic acid are 2 conditionally recommended topical comedolytics approved in Canada for AV (**Table 4**).[2,36-40] Salicylic acid and lower concentrations of azelaic acid are available OTC, whereas 15% azelaic acid is obtainable through prescription only. Azelaic acid offers additional antibacterial, anti-inflammatory, and antipigmentary properties, and is the AV treatment of choice during pregnancy.[41]

Systemic antibiotics. **Table 5** outlines oral antibiotics approved for AV in Canada.[42,43] All systemic antibiotics in the 2024 AAD guidelines are available in Canada except sarecycline. Systemic antibiotic use should generally not exceed 3 to 4 months.[44,45] Tetracyclines are contraindicated during pregnancy and lactation, and in children younger than 9 years due to risks of permanent enamel hypoplasia.[46]

Hormonal therapy

Combined oral contraceptives (COCs): COCs use the anti-androgenic properties of ethinyl estradiol (EE) to reduce ovarian androgen production, elevate sex hormone–binding globulin, and reduce free testosterone levels.[47] In the 2024 AAD guidelines, COCs are conditionally recommended for AV treatment based on moderate-certainty evidence on efficacy, variations in cultural beliefs, and individual values regarding contraception in general.[2]

COCs are approved for acne in female patients seeking oral contraception. Notably, combinations of norethindrone, EE, and ferrous fumarate, and of drospirenone, EE, and levomefolate are not currently available in Canada. For female patients aged 14 years and older, formulations containing drospirenone and EE may be used. For female patients aged 15 years and older, formulations containing norgestimate and EE may be considered. Other COCs approved in Canada for AV include combinations of EE and cyproterone acetate, and of EE and levonorgestrel.

No consistent differences in acne response exist between COC dosages, with no single COC showing superiority.[2] Typically, improvement is observed 3 to 6 months after initiating COC monotherapy.[48] Early combination of COCs with other acne therapies, such as tetracycline antibiotics or spironolactone, may expedite and increase efficacy. The combination of COCs with rifampin or griseofulvin has been associated with diminished COC efficacy.[49]

Before prescribing COCs, a thorough medical assessment, including baseline blood pressure measurement and pregnancy status, must be conducted. Recommendations for patients with specific characteristics are detailed in the 2015 World Health Organization (WHO) medical eligibility criteria for contraception.[50]

Oral spironolactone: Spironolactone competitively inhibits testosterone and dihydrotestosterone binding to androgen receptors.[51-53] It may impede 5-α reductase activity and increase steroid hormone–binding globulin levels.[54,55] Oral spironolactone is not FDA-approved for treating AV, but is commonly prescribed off-label

Table 3. Branded and generic fixed-dose topical combinations available in Canada

FIXED-DOSE COMBINATION	DOSE	ADVERSE EFFECTS	PRECAUTIONS	CONTRAINDICATIONS
0.1% adapalene and 2.5% BP	Gel: thin film applied every day at bedtime	• Desquamation • Stinging • Dryness • Burning • Erythema • Dermatitis • Hyperpigmentation • Hypopigmentation • Pruritus • Swelling • Conjunctivitis • Pharyngeal edema[25]	None	Contraindicated in pregnancy and those planning pregnancy
0.3% adapalene and 2.5% BP	Gel: thin film applied every day at bedtime	Same as 0.1% adapalene and 2.5% BP	Higher concentration may increase risk of skin irritation[25]	Contraindicated in pregnancy and those planning pregnancy
1% clindamycin and 5% BP	Gel: thin film applied every day	• Scaling • Dryness • Erythema • Sunburn • Burning • Irritation • Dermatitis[26]	BP may bleach clothing	None
1% clindamycin and 3% BP	Gel: thin film applied every day	Same as 1% clindamycin and 5% BP	None	None
3% erythromycin and 5% BP	Gel: thin film applied every day	• Peeling • Itching • Burning sensation • Erythema • Facial inflammation • Eye irritation • Nasal irritation • Skin discoloration • Oiliness • Skin tenderness • Pruritus • Edema[27]	BP may bleach clothing	None
0.025% tretinoin and 1.2% clindamycin	Gel: thin film applied every day at bedtime	• Application site irritant dermatitis • Erythema • Dryness • Irritation • Pruritus • Scaling[28]	None	None
1.2% clindamycin, 0.15% adapalene, and 3.1% BP	Gel: thin film applied every day at bedtime	• Mild to moderate application site irritation • Scaling • Dryness • Erythema • Burning or stinging[29]	BP may bleach clothing	• The only triple fixed-combination therapy approved in Canada • Contraindicated in pregnancy and those planning pregnancy

BP—benzoyl peroxide.

in female patients. The typical starting dose for AV is 50 mg daily, gradually increased to 100 to 200 mg daily based on response and tolerance.

Risks include menstrual irregularities, breast tenderness, and headaches. Specifically, its use in men is limited due to the risk of feminizing side effects such as gynecomastia and decreased libido. Use during pregnancy may increase risk of feminization in male fetuses.[56] No significant evidence links spironolactone to breast, ovarian, bladder, kidney, gastric, or esophageal cancer.

Table 4. Other conditionally recommended topical agents approved in Canada for treatment of acne vulgaris

AGENT	MECHANISM OF ACTION	DOSE	ADVERSE EFFECTS	PRECAUTIONS AND SPECIAL CONSIDERATIONS	CONTRAINDICATIONS
Salicylic acid	• Keratolytic agent • Desquamation of hyperkeratotic epithelium	• Cream: various concentrations, thin layer applied 1-3 times daily • Cleaners: various concentrations, use to cleanse twice a day or every day • Gel: various concentrations, applied 1-2 times per wk[35]	• Localized burning • Desquamation • Exfoliation • Irritation[36]	Avoid contact with eyes, lips, and mucous membranes	While systemic exposure to salicylic acid is contraindicated in pregnancy due to the risk of fetal harm (eg, salicylate toxicity and teratogenicity), the amount absorbed from typical cosmetic and OTC acne products is minimal. Studies show that when applied topically, especially at concentrations of ≤2%, systemic absorption is negligible, making it unlikely to cause fetal harm
Azelaic acid	• Dicarboxylic acid • Bactericidal against *Cutibacterium acnes*, *Staphylococcus aureus*, and *S epidermidis* • Anti-inflammatory and antioxidative properties • Mild keratolytic effects inhibit comedonal formation[37]	Gel: 15% applied in a thin film twice a day[38]	• Burning • Stinging • Tingling • Contact dermatitis • Desquamation • Erythema • Itching • Irritation • Dryness • Rash[38]	• Considered a safe option for acne treatment in pregnant individuals[39] • Can be effective for mild rosacea and treat postinflammatory pigmentation	None

OTC—over the counter, *S epidermidis—Staphylococcus epidermidis*.

Table 5. Oral antibiotics approved for acne vulgaris treatment in Canada

ORAL ANTIBIOTIC	MECHANISM OF ACTION	DOSE	ADVERSE EFFECTS	PRECAUTIONS AND SPECIAL CONSIDERATIONS	CONTRAINDICATIONS
Doxycycline	• Tetracycline • Anti-inflammatory and antibacterial effects against *Cutibacterium acnes*	Hyclate tablet or capsule: 100 mg every day or twice a day	• Esophagitis • GI upset • Diarrhea • Photosensitivity • Vulvovaginal candidiasis • Rare risk of intracranial hypertension (pseudotumor cerebri)[41]	• Concurrent use with systemic retinoids may increase the risk of pseudotumor cerebri • Take with plenty of water and do not lie on your back immediately or sleep after taking the medication to prevent esophagitis • Avoid taking with dairy products, calcium, iron, or other multivitamins or supplements containing metal ions as they can interfere with absorption	• Infants and children <9 y (risk of permanent enamel hypoplasia or discoloration) • Pregnancy • Breastfeeding
Minocycline	Same as doxycycline	Capsule: 50 mg or 100 mg twice a day or every day	Similar to doxycycline but with less photosensitivity and GI side effects. Rare adverse effects: • Vertigo • Autoimmune hepatitis • Skin hyperpigmentation • Drug-induced lupus • Hypersensitivity syndrome[42]	Same as doxycycline	Same as doxycycline

GI—gastrointestinal.

Per the 2024 AAD guidelines, potassium level monitoring is not required unless patients have an increased risk of hyperkalemia from medical comorbidities (eg, hypertension, diabetes mellitus, chronic kidney disease), advanced age, or medications impacting renal or adrenal function.[2]

Intralesional corticosteroids: Intralesional corticosteroids may be used as adjuvant therapy for larger acne lesions, but should be used judiciously in patients at high risk of scarring or in patients requiring rapid relief of inflammation and pain.[57] Adverse effects may include localized atrophy, systemic absorption, and adrenal suppression.[58] These effects may be minimized with lower concentrations and volumes. Oral corticosteroids are not recommended.[2]

Oral isotretinoin. Isotretinoin is the only approved treatment for severe nodular AV in Canada. It reduces sebum secretion by shrinking sebaceous glands, limiting sebum-dependent *C acnes* growth. Isotretinoin prevents comedone formation by normalizing keratinization and reducing inflammation.[59,60] **Table 6** summarizes relevant updates for isotretinoin.[1] All on-market brands available in Canada are summarized in **Figure 1**.[2] Notably, a new micronized form of isotretinoin offers improved absorption over conventional formulations and does not rely on lipid vesicles for uptake, allowing it to be taken without food.[61]

Isotretinoin is indicated for severe or refractory acne in patients aged 12 and older with scarring or psychosocial distress.[59,62] Dosage starts at 0.3 to 1 mg/kg daily until a cumulative dose of 120 to 150 mg/kg is achieved.[63] Studies suggest that higher cumulative doses are associated with lower recurrence rates.[64]

Daily isotretinoin is conditionally recommended over intermittent dosing.[2] This approach typically leads to greater reductions in Global Acne Grading System score and lesion counts, but may carry a higher risk of adverse effects.[65-67] Low-dose regimens may have similar efficacy and relapse rates as higher doses, although more evidence is needed.[2]

Adverse effects may involve the mucocutaneous, musculoskeletal, and ophthalmic systems, and typically resolve after discontinuation.[68] Before initiating oral isotretinoin, serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels, fasting triglyceride levels, total cholesterol level, and human chorionic gonadotropin tests are needed at baseline and every 8 weeks.[3] Complete blood count monitoring is not recommended in patients who are otherwise healthy. Due to isotretinoin's potent teratogenicity, strict safety protocols are recommended for patients who may become pregnant. Although no formal protocols exist in Canada, clinicians are responsible for counselling patients on the importance of effective contraception during isotretinoin therapy.

Special considerations

Pregnancy: The safety and efficacy of many acne treatments during pregnancy and lactation cannot be confirmed, as these populations are frequently excluded from clinical trials.[69] Isotretinoin, spironolactone,

Table 6. Updates to oral isotretinoin use in acne vulgaris

NO.	RECOMMENDATION
1	Oral isotretinoin is indicated for severe nodular acne. However, patients with severe psychosocial burden, those prone to scarring, and those with acne refractory to conventional treatments should be considered as candidates for oral isotretinoin
2	ALT and lipid profile should be measured before and after 8 wk of initiation of oral isotretinoin
3	Checking baseline complete blood count or monitoring it during treatment is not required except in patients with a known blood disorder affecting blood counts
4	Creatine kinase monitoring is not required except in patients experiencing severe musculoskeletal pain
5	For persons with pregnancy potential, pregnancy prevention is mandatory with oral isotretinoin treatment
6	Daily dosing regimen may result in improved treatment outcomes compared to intermittent dosing. However, daily dosing is associated with a higher withdrawal rate due to adverse effects
7	Both standard isotretinoin and lidose-isotretinoin are effective. Standard isotretinoin demonstrates improved bioavailability when taken with a high-fat meal, whereas the bioavailability of lidose-isotretinoin is less influenced by whether it is taken with food
8	Population-based studies and recent evidence have not identified increased risk of neuropsychiatric conditions (depression, anxiety, or suicidal thoughts) in patients undergoing isotretinoin treatment. Multiple studies indicate that treating patients with severe acne using oral isotretinoin may improve their quality of life, reduce symptoms, and decrease the overall risk of anxiety and depression
9	There is insufficient evidence to link the use of oral isotretinoin with an increased risk of inflammatory bowel disease
10	Insufficient evidence exists to warrant postponing treatment with superficial chemical peels, hair removal lasers and lights, and vascular and nonablative laser treatments for patients currently receiving or who have recently received oral isotretinoin

ALT—alanine aminotransferase.
Data from Reynolds et al.[1]

tazarotene, and trimethoprim-sulfamethoxazole (TMP-SMX) are well-established teratogenic agents. Tetracycline antibiotics should be avoided after the first trimester, as it may cause permanent teeth discoloration and inhibit fetal bone growth. Erythromycin is generally safe, but erythromycin estolate should be avoided due to risk of hepatotoxicity. Topical azelaic acid, clindamycin, BP, and salicylic acid are safe for use during pregnancy.[70] No increased risk of congenital malformations and spontaneous abortions has been observed with tretinoin or adapalene; however, patients are typically encouraged to avoid these medications due to risk of systemic absorption.[71-73] Novel topical anti-androgens, such as clascoterone, are also generally avoided given the limited data on fetal risks. Hormonal therapies, including oral contraceptives, are contraindicated.

Skin of colour: Patients with Fitzpatrick skin types III to VI have an increased risk of PIH after inflammatory acne or treatments causing irritation.[74] Azelaic acid and combination adapalene-BP may decrease PIH severity.[75-78] Isotretinoin can improve existing PIH, but side effects like dermatitis may increase risk of PIH.[79-81] While 0.05% tretinoin lotion is associated with improved baseline hyperpigmentation, high-concentration retinoids may increase PIH risk.[79,82-84]

Transgender individuals: Spironolactone is not advised in transmasculine individuals taking testosterone therapy, as it may block masculinization and cause irregular bleeding, breast tenderness, and gynecomastia.[85,86] COCs are not contraindicated in this population.[85] Concurrent testosterone and isotretinoin may increase hepatotoxicity, requiring regular liver function tests and lipid panels.[87] Transfeminine individuals undergoing feminization therapy with estrogen and spironolactone are less likely to develop acne.[88-90] Moderate to severe acne should be treated before potential chest reconstruction to optimize conditions for surgical success.[91]

Conclusion

The AAD 2024 guidelines for the management of AV provide a valuable framework for Canadian clinicians to optimize outcomes. Mild cases of AV are generally managed with topical treatments, while more severe cases often require systemic medications such as antibiotics or isotretinoin. Antibiotic monotherapy is generally discouraged; combination treatments using various mechanisms of action are recommended. Trifarotene, clascoterone, and a combination of clindamycin, adapalene, and BP are 3 new topical treatments with excellent efficacy and safety profiles. For patients with severe acne and scarring, oral isotretinoin remains the criterion standard treatment.

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Contributors

All authors contributed to conceptualizing and designing the study; to collecting, analyzing, and interpreting the data; and to preparing the manuscript for submission.

Competing interests

Samantha Keow and **Grace Xiong** declare no conflicts of interest. **Dr Mohannad Abu-Hilal** has been a speaker or advisor, or has received honoraria from AbbVie, Biojamp, Boehringer Ingelheim, Bristol Myers Squibb, Celltrion, Eli Lilly, Galderma, Hikma Pharmaceuticals, Incyte, Janssen, Leo, L'Oreal, La Roche Posay, Medexus, Novartis, Pfizer, Recordati, Sanofi Regeneron, and Sun Pharma.

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