

THE EVOLVING TREATMENT LANDSCAPE IN ACNE VULGARIS

**TREATMENTS, MECHANISMS OF ACTION, SAFETY AND
EFFICACY AND ADMINISTRATION**

BEFORE YOU PROCEED: REFLECT BRIEFLY

**ARE YOU FAMILIAR WITH MOST RELEVANT
TREATMENTS FOR ACNE VULGARIS AND HOW THEY
TARGET THE KEY PATHOGENIC FACTORS?**

TREATMENTS FOR ACNE VULGARIS

UNDERSTANDING TREATMENT APPROVALS AND AVAILABILITY

- This micro learning focuses on **evidence-based treatments** for acne vulgaris, as supported by the latest **international guidelines** (American,¹ UK,² and European³) and **scientific data**
- While these treatments are widely recognised in clinical practice, **regulatory approval** and **market availability** vary across **countries**
- The goal of this module is to offer a comprehensive overview of current evidence-based options, regardless of regional variation in approval or access

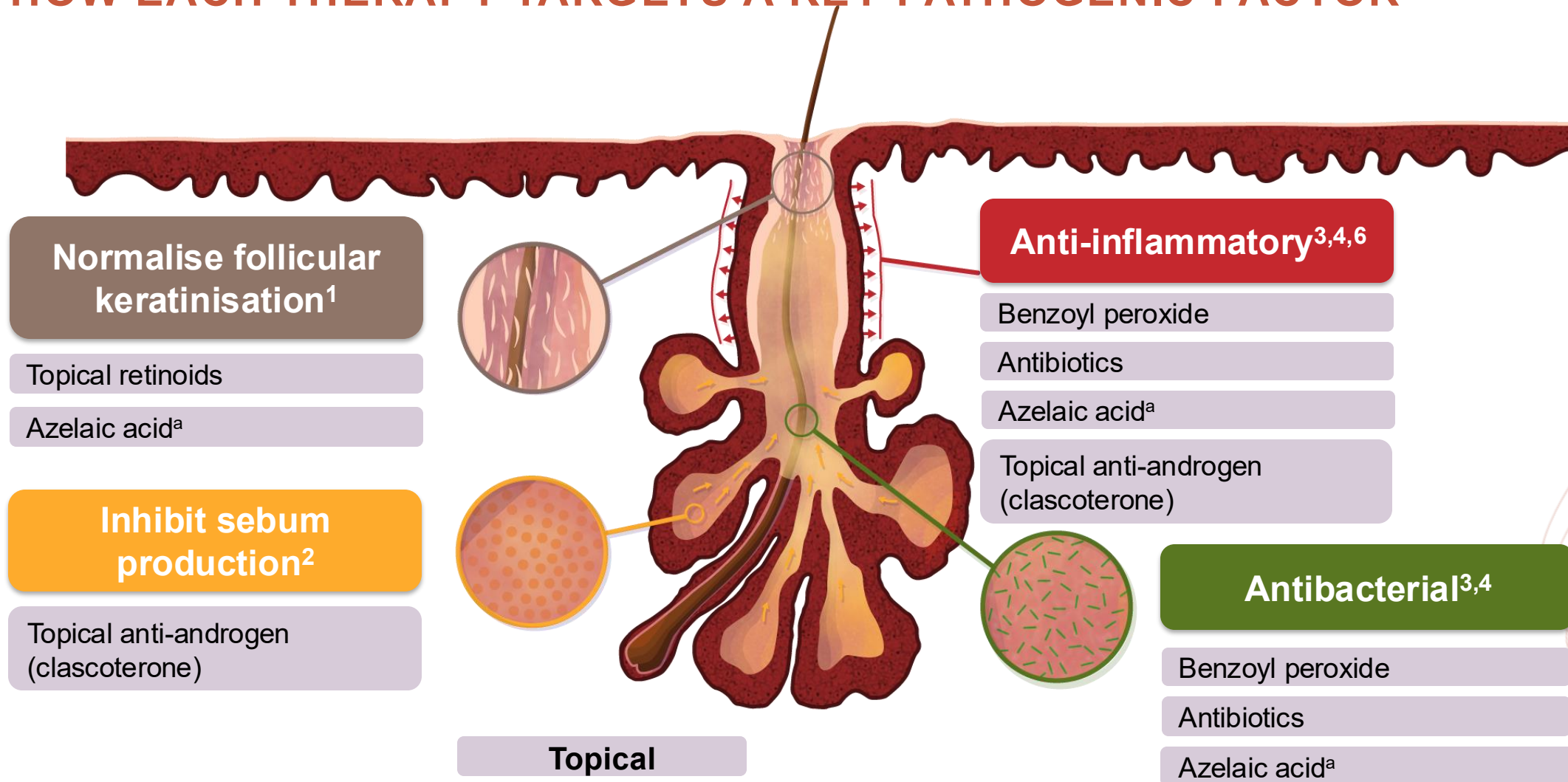
Please note that local prescribing practices, reimbursement, and product availability may differ depending on national regulatory frameworks

UK, United Kingdom

1. Reynolds RV, et al. J Am Acad Dermatol. 2024;90(5):1006.e1-1006.e30; 2. National Institute for Health and Care Excellence. Acne vulgaris: management NICE guideline [NG198]. Available at: www.nice.org; 2. EDF. S3-Guideline for the Treatment of Acne (Update 2016). Available [here](#) (accessed May 2025)

OVERVIEW OF TOPICAL TREATMENT OPTIONS FOR ACNE VULGARIS

HOW EACH THERAPY TARGETS A KEY PATHOGENIC FACTOR

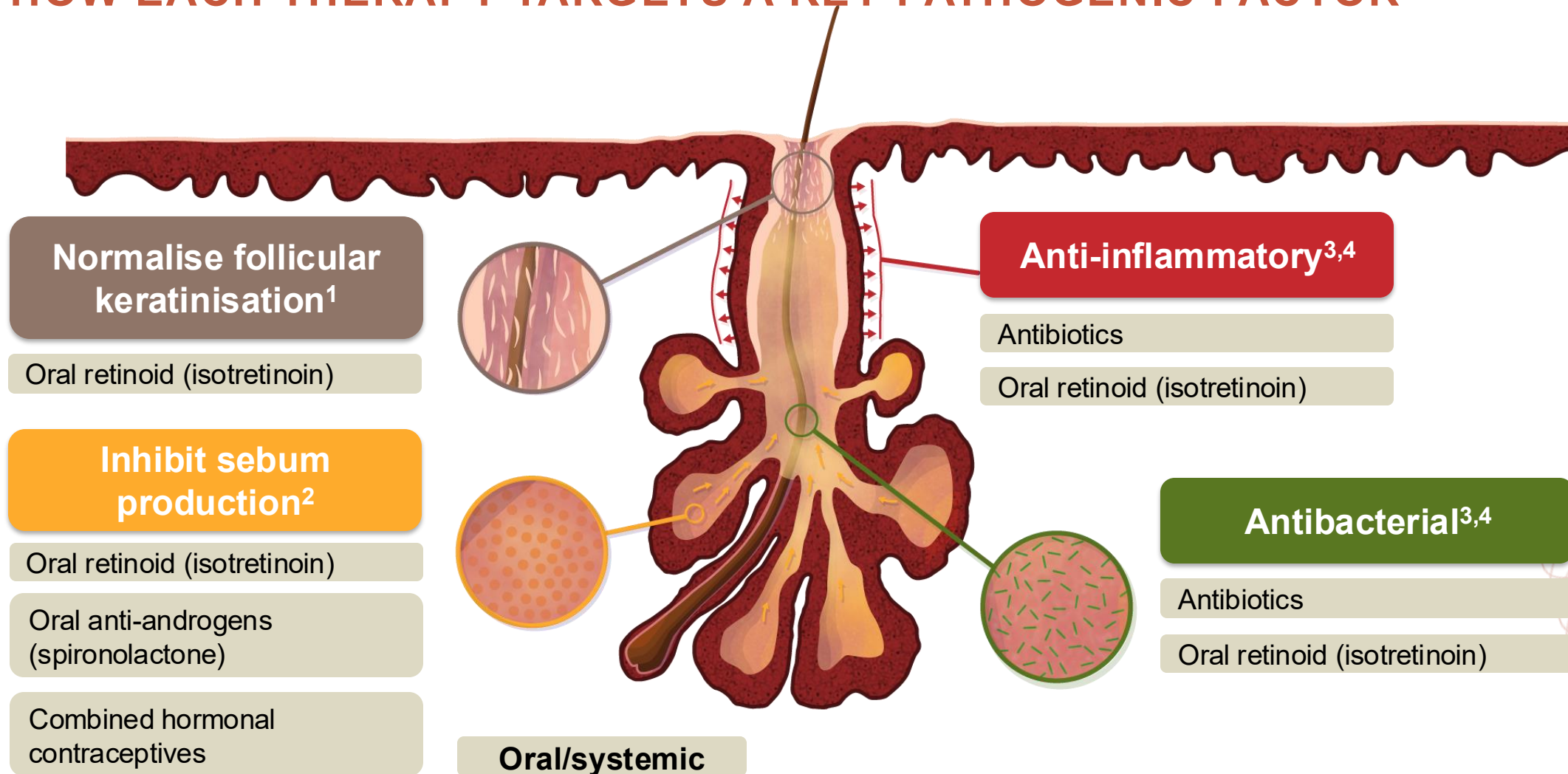


^a Azelaic acid has diverse physiological activities, including antimelanogenic antioxidant effects⁵

1. Sutaria AH, et al. Acne Vulgaris. [Updated 2023 Aug 17]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available [here](#) (accessed June 2025); 2. Hebert A, et al. JAMA Dermatol. 2020;156(6):621-630; 3. DermNet. Benzoyl peroxide. Available [here](#) (accessed June 2025); 4. Reynolds RV, et al. J Am Acad Dermatol. 2024;90(5):1006.e1-1006.e30; 5. Feng X, et al. Clin Cosmet Investig Dermatol. 2024;17:2359-2371; 6. Eichenfield LF, et al. J Drugs Dermatol. 2024 ;23(1):1278-1283.

OVERVIEW OF SYSTEMIC TREATMENT OPTIONS FOR ACNE VULGARIS

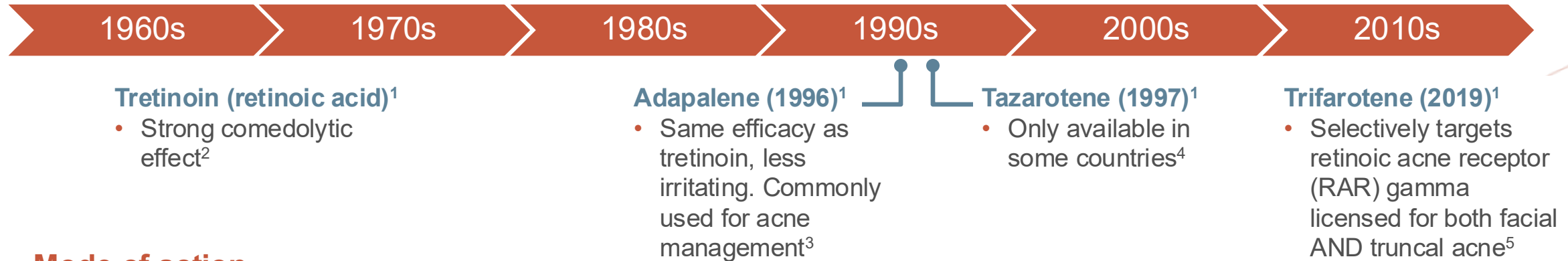
HOW EACH THERAPY TARGETS A KEY PATHOGENIC FACTOR



1. Ganceviciene R, Zouboulis CC. J Dtsch Dermatol Ges. 2010;8 Suppl 1:S47-59; 2. Lam C, Zaenglein AL. Clin Dermatol. 2014;32(4):502-15; 3. Sutaria AH, et al. Acne Vulgaris. [Updated 2023 Aug 17]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available [here](#) (accessed June 2025); 4. Pile HD, et al. Isotretinoin. [Updated 2025 Mar 4]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available [here](#) (accessed June 2025); 5. Reynolds RV, et al. J Am Acad Dermatol. 2024;90(5):1006.e1-1006.e30

TOPICAL RETINOIDS (1/2)

TRETINOIN, ADAPALENE, TAZAROTENE AND TRIFAROTENE^a



Mode of action

- Primary: **Desquamation & normalise keratinization.** Promote shedding of abnormal epithelium, altering microclimate in microcomedones^{1,2,6}
- Resolves mature comedones and prevents the formation of new ones⁶
- Enhances the penetration and effectiveness of other topical treatments like antibiotics⁷
- Reduces inflammation by activating TLR-2 (Toll-like receptor 2), reducing acne-related redness and swelling⁸
- No direct antibacterial effect: Makes follicles more accessible to antimicrobials, creating synergistic effects^{2,6,9}

^a May vary according to country

1. Baldwin H, et al. Am J Clin Dermatol. 2021;22(3):315-327; 2. Leyden J, et al. Dermatol Ther (Heidelb). 2017;7(3):293-304; 3. Tu P, et al. J Eur Acad Dermatol Venereol. 2001;15 Suppl 3:31-6; 4. Han G, et al. J Clin Aesthet Dermatol. 2020;13:E59-E65; 5. Annunziata MC, et al. Dermatol Ther (Heidelb). 2025;15(2):245-264; 6. Motamedi M, et al. J Cutan Med Surg. 2022;26(1):71-78; 7. Dreno B. Drugs. 2004;64:2389-97; 8. Zhang B, et al. Biomed Dermatol 3, 4 (2019); 9. Dessinioti C, Katsambas A. Dermatol Ther (Heidelb). 2024;14(1):31-44

TOPICAL RETINOIDS (2/2)

TRETINOIN, ADAPALENE, TAZAROTENE AND TRIFAROTENE

Clinical effects

- Possible acne flare in the first weeks due to increased epidermal proliferation^{1,2}
- Stimulates blood flow and collagen production,^{3,4} speeding up healing

Pharmacokinetics

- Minimal systemic absorption⁵

Side effects^{6,7}

- Erythema, dryness, itching, stinging (varies by vehicle, skin type, frequency, and mode of application)
- Trifarotene receptor specific aimed to enhance tolerability

Indications

- Topical retinoids can be used by both males and females⁸
 - should be avoided in pregnancy and in patients aiming to conceive⁷
- For comedonal and mild inflammatory acne, and / or as part of maintenance therapy^{7,9}
- Often used in combination with benzoyl peroxide or antibiotics and can be effective for mild, moderate and severe acne⁷

1. Del Rosso JQ, editors. J Clin Aesthet Dermatol. 2008;1:41-3; 2. Dreno B, et al. J Drugs Dermatol. 2022;21:734-740; 3. Harvard Health Publishing. Do retinoids really reduce wrinkles? Available [here](#) (accessed June 2025); 4. Sitohang IBS, et al. Int J Womens Dermatol. 2022;8(1):e003; 5. Chien A, et al. J Drugs Dermatol. 2018;17(12):s51-55; 6. Motamedi M, et al. J Cutan Med Surg. 2022;26(1):71-78; 7. NICE. Acne vulgaris: Topical retinoids. Available [here](#) (accessed June 2025); 8. Dermatology Advisor. Racial and Sex Differences Observed in the Efficacy of Once-Daily Tretinoin for Acne. Available [here](#) (accessed June 2025); 9. DermNet. Topical retinoids. Available [here](#) (accessed June 2025)

Annunziata MC, et al. Dermatol Ther (Heidelb). 2025;15(2):245-264;



BENZOYL PEROXIDE¹

A KEY TOPICAL TREATMENT FOR ACNE

History

- Leading over-the-counter topical treatment¹
- Widely used since the late 1970s¹

Mode of action¹

- Primary: Powerful **antimicrobial**: Rapidly reduces *C. acnes* by 90% and free fatty acids by 40% within days
- Anti-inflammatory: Reduces oxygen free radicals, stimulates epidermal mitosis
- Slightly comedolytic

Pharmacokinetics¹

- Decomposes in light, rapidly metabolised to benzoic acid on skin, no systemic absorption

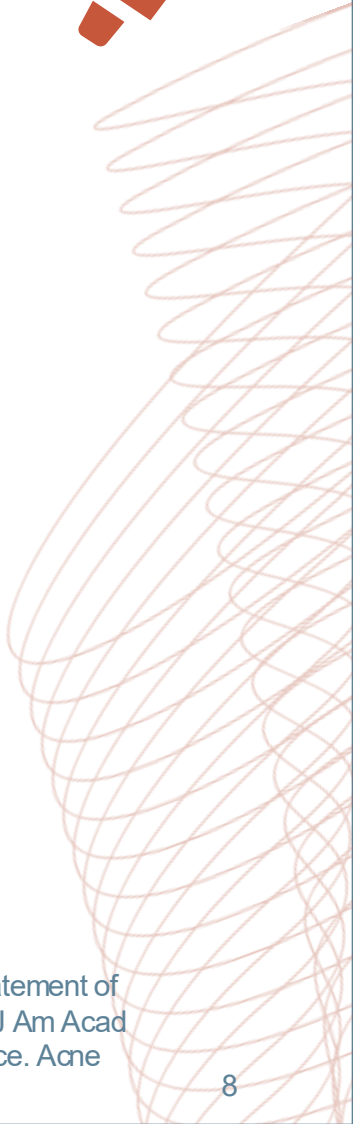
Side effects

- Moderate irritation, dryness, scaling¹
- Bleaches clothes, bed linen, hair¹
- Rare contact allergy¹
- Recent safety concerns²
 - No issues when stored at correct temperature^{3,4}
 - The American Academy of Dermatology recommends patients to store the product at room temperature or cooler⁴

Indication

- Suitable for individuals aged 12 and above⁵
- Mild inflammatory acne, part of combination therapies in moderate to severe acne^{6,7}

1. Plewig, G., Kligman, A.M. (1993). Benzoyl Peroxide. In: ACNE and ROSACEA. Springer, Berlin, Heidelberg. https://doi.org/10.1007/978-3-642-97234-8_75; 2. AAD statement of Benzoyl Peroxide in OTC Personal Care Products. Available [here](#) (accessed June 2025); 3. Garate D, et al. J Am Acad Dermatol. 2024;91(5):966-8; 4. Veenstra J, et al. J Am Acad Dermatol. 2024;91(3):533-4; 5. NHS. Who can and cannot use benzoyl peroxide. Available [here](#) (accessed June 2025); 6. National Institute for Health and Care Excellence. Acne vulgaris: management NICE guideline [NG198]. Available at: www.nice.org; 7. Nast A, et al. JEADV. 2016;30:1261-1268



AZELAIC ACID^{1,2}

History¹

- Approved by the FDA in 2002 for papulopustular rosacea; now commonly used as a second-line treatment for acne vulgaris

Mode of action^{1,2}

- Comedolytic, higher concentrations (e.g. ~20–30%) are **anti-bacterial**; anti-inflammatory effects, lightening effect on hyperpigmentation
- Acts through multiple mechanisms

Pharmacokinetics¹

- Poor percutaneous absorption (3-5% retained in the skin), enhanced with gel formulations (up to 8%)

Efficacy¹

- Effective in treating both non-inflammatory and inflammatory acne, with significant improvement in post-inflammatory hyperpigmentation
- Slow onset of action^a

Safety / side effects¹

- Well tolerated; Mild irritation

Indication¹

- Suitable for individuals aged 12 and above
- Safe in pregnancy³

^a Personal note

FDA, Food and Drug Administration

1. Feng X, et al. Clin Cosmet Investig Dermatol. 2024;17:2359-2371; 2. Plewig, G., Melnik, B. and Chen, W.C. (2019) Plewig and Kligman's Acne and Rosacea. 4th Edition, Springer, Berlin (chapter 7); 3. Ly S, et al. Dermatol Ther (Heidelb). 2023;13(1): 115-130



TOPICAL ANTI-ANDROGEN

CLASCOTERONE IS A TOPICAL TREATMENT OPTION FOR ACNE IN MALES AND FEMALES



History

- Clascoterone cream was approved by the FDA in 2020 and by the UK MHRA in 2025 based on 2 Phase 3 studies^{1,2}

Mode of action

- First-in-class topical anti-androgen, reduces **sebum production**³
- Anti-inflammatory: Inhibits the transcription of androgen-responsive genes including inflammatory cytokines³

Pharmacokinetics

- Only local, not systemic, antiandrogenic activity⁴

Efficacy

- Clascoterone is effective in the treatment of acne vulgaris, showing statistically significant improvements in all primary and secondary efficacy endpoints⁴

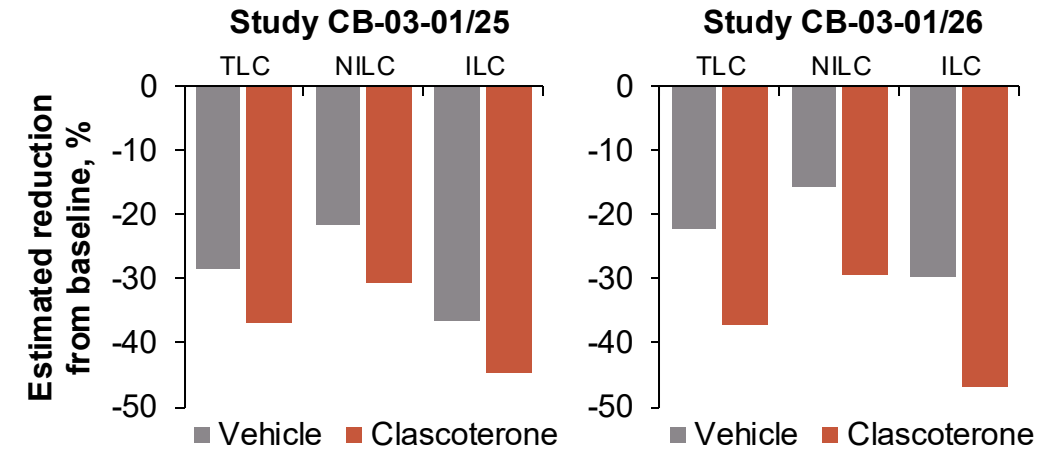
Safety / side effects

- Adverse events rates are low and mostly mild⁴
 - The predominant local skin reaction was trace or mild erythema

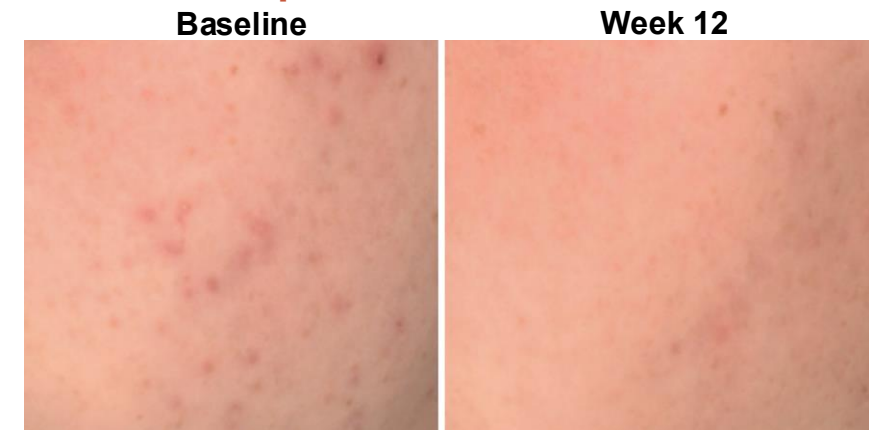
Indication

- Suitable for individuals aged 12 and above³
- Clascoterone can be used as part of a multimodal approach with other fixed combination products or oral therapies available for acne management, addressing more key pathophysiological factors

Efficacy – change in lesion reduction⁴



Improvement of acne⁴



FDA, Food and Drug Administration; MHRA, Medicines and Healthcare Products Regulatory Agency; UK, United Kingdom

1. Piszczatoski CR, Powell J. Clin Ther. 2021;43(10):1638-1644; 2. FirstWord PHARMA. Cosmo and Glenmark Announces UK MHRA Approval of Winlevi for Treatment of Acne. Available [here](#) (accessed June 205); 3. Eichenfield LF, et al. J Drugs Dermatol. 2024;23(1):1278-1283; 4. Hebert A, et al. JAMA Dermatol. 2020 ;156(6):621-630;

ANTIBIOTICS FOR THE TREATMENT OF ACNE

GUIDELINE DRIVEN ANTIBIOTIC USE



- Oral antibiotics remain important but should be limited due to global AMR concerns¹⁻³
 - Limit treatment to 3 months (up to 6 months in select cases)^{1,2}
 - Combine with benzoyl peroxide to reduce resistance¹
- Prefer doxycycline, lymecycline, or sarecycline (narrow spectrum) over minocycline^{1,2}
 - Avoid minocycline due to the risk of severe eruptions and neurological side effects²
- Limit trimethoprim-sulfamethoxazole due to risk of rare, but severe hypersensitivity reactions¹
 - Stevens-Johnson syndrome/toxic epidermal necrolysis
 - Acute respiratory failure
- Reserve macrolides (e.g. erythromycin) for specific cases only²
 - e.g. during pregnancy or in patients where tetracyclines are contraindicated
- Stop antibiotics once control is achieved and start maintenance therapy^{1,3,4}

AMR, antimicrobial resistance

1. Reynolds RV, et al. J Am Acad Dermatol. 2024;90(5):1006.e1-1006.e30; 2. National Institute for Health and Care Excellence. Acne vulgaris: management NICE guideline [NG198]. Available at: www.nice.org; 3. Nast A, et al. JEADV. 2016;1261-1268; 4. Zaenglein AL, et al. J Am Acad Derm. 2016;74:945-73.e33

ORAL RETINOID

ISOTRETINOIN



History¹

- Discovered in 1971, registered for severe acne since 1982

Mode of action¹

- Primary: Apoptosis-mediated **sebum suppression** in sebaceous glands
- Changes gene-expression leading to altered terminal differentiation of keratinocytes and anti-inflammatory effects

Pharmacokinetics¹

- Systemic absorption: rapidly absorbed, bioavailability 25%, significantly increased with intake of fatty food

Efficacy²

- Most effective acne drug

Safety / side effects¹

- Teratogenic
- Strict contraception in all women in childbearing age
- Side effects like vitamin-A hypervitaminosis (xeroderma, lipid/liver enzyme elevations [among others])
- Conflicting data on depression/suicidal intents

Indication¹

- Conglobate acne, severe acne, scarring acne, acne resistant to other therapies

1. Plewig, G., Melnik, B. and Chen, W.C. (2019) Plewig and Kligman's Acne and Rosacea. 4th Edition, Springer, Berlin (chapter 7);

2. Huang CY, et al. Ann Fam Med. 2023;21:358-369

COMBINED HORMONAL CONTRACEPTIVES



History

- Introduced in the 1960s as birth control¹

Mode of action

- Reduce **sebaceous gland activity**, mediated by a reduced level of circulating androgens²

Pharmacokinetics

- Orally absorbed, metabolised by the liver, and reduces free androgens³

Efficacy

- Efficient in the treatment of acne and reduce inflammatory and comedonal lesions⁴
- Full effect after 6–9 months of use⁵
- No superiority of one combined hormonal contraceptive over the other for the treatment of acne⁶

Safety / side effects

- Generally well-tolerated⁵
- Systematic reviews exhibit an increased risk of breast cancer and cervical cancer⁵

Indication

- Although not licensed for acne in all countries may help moderate to severe acne in females and may be used when a female with acne requires contraception or requires them for hormonal reasons^{4,7}
- Contraindicated in the case of genetic clotting disorders, positive history of venous thromboembolism, heart disease, hypertension, obesity, smoking in women older than 35 years of age, diabetes mellitus, liver disease, migraine and headache, prolonged immobilisation, history of breast, endometrial and liver malignancy, pregnancy and breastfeeding, and hypersensitivity to any component of the product⁵

1. Christin-Maitre S. Best Pract Res Clin Endocrinol Metab. 2013;27(1):3-12; 2. Zaenglein AL, et al. J Am Acad Derm. 2016;74:945-73.e33; 3. Elliman A. BMJ Sex Reprod Health. 2000;26:109-111; 4. Arowojolu AO, et al. Cochrane Database Syst Rev. 2012;2012(7):CD004425; 5. Plewig, G., Melnik, B. and Chen, W.C. (2019) Plewig and Kligman's Acne and Rosacea. 4th Edition, Springer, Berlin (chapter 7); 6. Reynolds RV, et al. J Am Acad Dermatol. 2024;90(5):1006.e1-1006.e30; 7. National Institute for Health and Care Excellence. Acne vulgaris: management NICE guideline [NG198]. Available at: www.nice.org

ORAL ANTI-ANDROGEN

SPIRONOLACTONE

History

- Spironolactone used off-label to treat acne vulgaris in women¹
 - Based on the evidence for use in two independent large clinical studies^{1,2}

Mode of action

- An oral anti-androgen to reduce **sebum production**^{1,2}

Efficacy

- Improves acne compared to placebo¹ and doxycycline²
- Greater improvements at 6 months than at 3 months¹

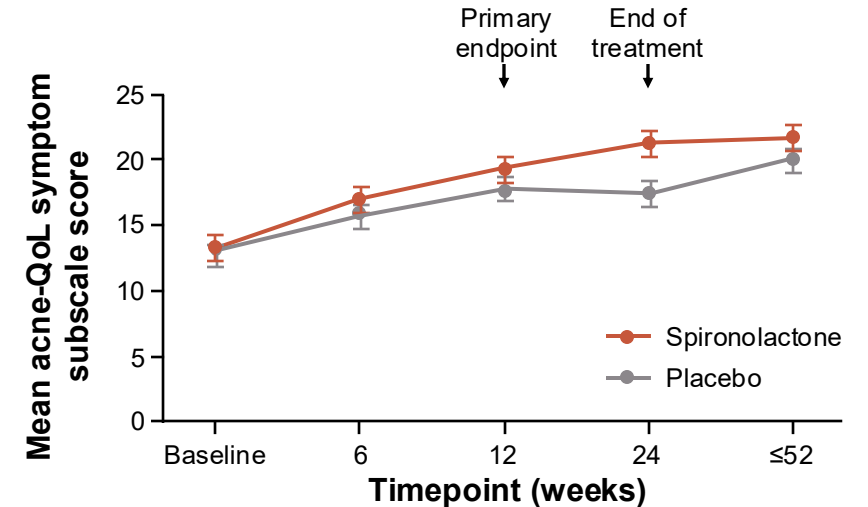
Safety / side effects

- Well tolerated^{1,2}
 - SAFA trial: more headaches (no SAEs)²
 - Most spironolactone-related AEs in the FASCE study were mild to moderate events of irregular menstruation and did not lead to withdrawal of the patients from treatment¹

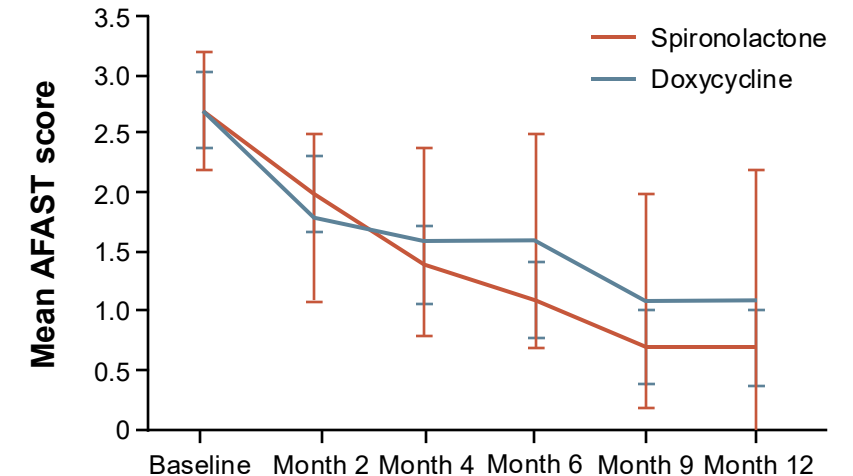
Indication

- May be an effective alternative to oral antibiotics for women with persistent acne who have not responded to first-line topical treatments²

Mean Acne-QoL symptom subscale score by time point for each treatment group²



Evolution of the global AFAST score¹



AE, adverse event; Acne-QoL, Acne-Specific Quality of Life; AFAST, Adult Female Acne Scoring Tool; SAE, serious adverse events

1. Dréno B, et al. Acta Derm Venereol. 2024;104:adv26002; 2. Santer M, et al. Drug Ther Bull. 2023;62(1):6-10