

Trifarotene

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This is the corrected
version of the article.

Correction noticed
available at:

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Approved indication: acne

Aklief (Galderma) cream containing 50 microgram/gram

Acne vulgaris is a common skin condition of adolescents, which is mild and self-limiting in many cases. However, it sometimes persists into the 30s and 40s age groups and the more severe forms at any age may lead to lowering of self-esteem and mood disorders. Permanent scarring can also occur. Acne is thought to develop due to abnormal follicular keratinocyte hyperproliferation causing follicular plugs and increased sebum production with subsequent overgrowth of bacteria such as *Cutibacterium acnes*. Clinical manifestations range from comedones to painful cysts.

Management is guided by the severity of the skin lesions. Topical retinoid monotherapy is preferred for the treatment of mild comedonal acne. For moderate to severe acne, a combination of topical therapies, or oral drugs such as antibiotics, is recommended. Other treatments include oral isotretinoin for refractory acne and combined oral contraceptives when appropriate.

Trifarotene is a terphenyl acid derivative with retinoid-like activity. Retinoids work by binding to retinoic acid receptors (RAR), of which there are three isoforms (alpha, beta and gamma). RAR-gamma is the most widely distributed in the skin and is thought to be the most relevant in the development of acne. Trifarotene is the only topical retinoid that is a selective RAR-gamma agonist.¹ It has anti-inflammatory and comedolytic properties.

There were two identical phase III randomised placebo (vehicle)-controlled multi-site trials (PERFECT 1 and PERFECT 2).^{2,3} These trials included patients of nine years of age and older, with moderate facial and truncal acne, but no cysts or nodules. PERFECT 1 had 1208 participants and PERFECT 2 had 1212. The investigators' assessments found that over 12 weeks trifarotene applied once daily reduced inflammatory and non-inflammatory lesions on the face and trunk more than placebo. Lesions on the trunk took longer to start improving than on the face.³


In the PERFECT trials, most adverse events were mild with transient local irritation consistent with other topical retinoids, with mild-moderate erythema, scaling, dryness and burning, worse on the face than the trunk. Nine patients had severe symptoms such as sunburn and allergic dermatitis.³ A longer term, non-comparative, multi-site trial studied the efficacy and safety of trifarotene over 52 weeks.⁴ A total of 453 patients aged nine years and over with moderate

acne were enrolled and 348 completed the study. Thirteen (2.9%) patients discontinued treatment because of adverse events related to trifarotene. Overall, 218 (48.1%) patients experienced adverse events, mostly during the first three months, with 57 (12.6%) participants having cutaneous symptoms. The most common effects were pruritus (4.6% patients), irritation (4.2%) and sunburn (1.8%). Three patients had severe cutaneous adverse effects.⁴

While global trials included patients from nine years of age, trifarotene is approved in Australia for patients aged 12 years and above for the topical treatment of acne of the face and the trunk when many comedones, papules or pustules are present. However, safety and efficacy have not been evaluated in people aged 65 years and over, nor in those with renal and hepatic impairment. Trifarotene is contraindicated during pregnancy and for women planning to become pregnant. A discussion about contraception may be appropriate. Systemic exposure is low and it is estimated that most of the drug will be eliminated within four days of the last application of the cream.

Treatment should be assessed after three months and may be continued if necessary and for maintenance. In the long-term trial, lesions improved over time with 57.9% of patients having their face and trunk clear or almost clear at week 52.⁴

Trifarotene potentially is a useful addition to the topical treatments for acne. Due to its targeting of the RAR-gamma receptor, it may improve acne compared to other topical retinoids, although it has not been directly compared to them in trials. As with other topical retinoids, patients should be warned about erythema, scaling and dryness, and advised to use a moisturiser during treatment, as well as sunscreen to help avoid sunburn.

 manufacturer provided additional useful information.

REFERENCES

1. Thoreau E, Arlabosse J-M, Bouix-Peter C, Chambon S, Chantalat L, Daver S, et al. Structure-based design of trifarotene (CD5789), a potent and selective RAR γ agonist for the treatment of acne. *Bioorg Med Chem Lett* 2018;28:1736-41. <https://doi.org/10.1016/j.bmcl.2018.04.036>
2. Aubert J, Piwnica D, Bertino B, Blanchet-Réthoré S, Carlavan I, Déret S, et al. Nonclinical and human pharmacology of the potent and selective topical retinoic acid receptor- γ agonist trifarotene. *Br J Dermatol* 2018;179:442-56. <https://doi.org/10.1111/bjd.16719>
3. Tan J, Thiboutot D, Popp G, Gooderham M, Lynde C, Del Rosso J, et al. Randomized phase 3 evaluation of trifarotene 50 μ g/g cream treatment of moderate facial and truncal acne. *J Am Acad Dermatol*. 2019;80:1691-9. <https://doi.org/10.1016/j.jaad.2019.02.044>
4. Blume-Peytavi U, Fowler J, Kemény L, Draelos Z, Cook-Bolden F, Dirschka T, et al. Long-term safety and efficacy of trifarotene 50 μ g/g cream, a first-in-class RAR- γ selective topical retinoid, in patients with moderate facial and truncal acne. *J Eur Acad Dermatol Venereol* 2020;34:166-73. <https://doi.org/10.1111/jdv.15794>

The Transparency Score is explained in [New drugs: transparency, Vol 37 No 1, Aust Prescr 2014;37:27.](#)

At the time the comment was prepared, information about this drug was available on the websites of the [Food and Drug Administration](#) in the USA, and the [Therapeutic Goods Administration](#).

Update

Antipsychotic switching tool [Update 3]

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The online tool by Nicholas Keks et al has been updated. [View updated tool \(v4\).](#)

It includes a clarification that the paliperidone depot-to-depot advice applies to the once-monthly long-acting injection.

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