Medicines & Healthcare products Regulatory Agency

Public Assessment Report

National Procedure

Acnecide Face 2.5% w/w Gel

benzoyl peroxide (as hydrous benzoyl peroxide)

PL 10590/0073

Galderma (U.K.) Limited

LAY SUMMARY
Acnecide Face 2.5% w/w Gel
benzoyl peroxide (as hydrous benzoyl peroxide)

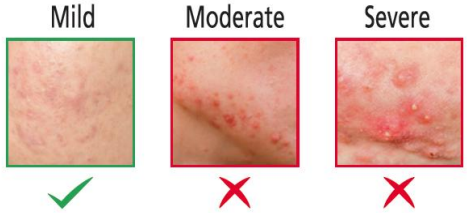
This is a summary of the Public Assessment Report (PAR) for Acnecide Face 2.5% w/w Gel. It explains how this product was assessed and its authorisation recommended, as well as its conditions of use. It is not intended to provide practical advice on how to use this product.

This product will be referred to as Acnecide Face Gel in this lay summary for ease of reading.

For practical information about using Acnecide Face Gel, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

What is Acnecide Face Gel and what is it used for?
This application is a full-dossier application. This means that the results of pharmaceutical, non-clinical and clinical tests have been submitted to show that this medicine is suitable for treating the specified indications.

Acnecide Face Gel is for the treatment of mild acne on the face, in adults and adolescents 12 years and over. Mild acne appears as predominantly blackheads and whiteheads and there are few or no spots and pimples and no inflamed spots.
The patient should a look at the diagrams below showing the different types of acne:



How does Acnecide Face Gel work?
Acnecide Face Gel contains the active ingredient benzoyl peroxide which kills the bacteria (germs) known as *Cutibacterium acnes*, one of the main causes of acne.

How is Acnecide Face Gel used?
The pharmaceutical form of this medicine is a gel, and the route of administration is topical (on the skin, face only).

The main dosing recommendation is as follows:

In adults and adolescents aged 12 years and over
Unless the patient's doctor or pharmacist has told otherwise:
- the patient should wash the affected area with a mild skin cleanser and water and gently pat the skin dry.
- the patient should apply the gel in a thin layer to all the affected areas of the face, avoiding contact with sensitive areas such as eyes, mouth, nose lining and neck.
- When the patient first uses Acnecide Face Gel apply the gel once daily before going to bed.
The patient may feel mild burning and notice slight reddening and peeling of the skin during the first few days. If the patient has more severe redness, burning, irritation and peeling then the patient should stop treatment and let the skin go back to normal before restarting treatment.

- If Acnecide Face Gel does not affect the patient's skin or has only mild burning and slight reddening and peeling after 2-3 days of use, they can apply the gel twice a day, in the morning and evening. If this causes more severe skin symptoms (burning, irritation, redness, peeling) then they should go back to using Acnecide Face Gel only once a day. If the patient's skin remains more severely irritated they should stop treatment and let the skin go back to normal before restarting treatment once a day.
- If the patient gets severe skin irritation at any time whilst using Acnecide Face Gel they should stop the treatment. If the patient's skin does not recover after stopping treatment, they should seek a doctor's advice.
- Using a moisturiser after application can help to reduce any irritation the treatment may cause.

The patient should avoid exposure to strong sunlight while using Acnecide Face Gel. If exposure is unavoidable, they should use a sun-protection product with a protection factor of at least SPF 30 and UVA protection and apply Acnecide Face Gel in the evening.

Children and adolescents aged less than 12 years
Acnecide Face Gel should not be used by children less than 12 years of age

For further information on how Acnecide Face Gel is used, refer to the PIL and Summary of Product Characteristics (SmPC) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

This medicine can be obtained without a prescription.

The patient should always take the medicine exactly as their doctor/pharmacist has told them. The patient should check with their doctor or pharmacist if they are not sure.

What benefits of Acnecide Face Gel have been shown in studies?
Acnecide Face Gel is a line extension of the existing product Acnecide 5% w/w Gel (PL 10590/0006). The approved extension application, concerning the registration of the different strength (i.e. 2.5%) is based on non-clinical and clinical studies carried out by the applicant and bibliographical references.

What are the possible side effects of Acnecide Face Gel?
For the full list of all side effects reported with this medicine, see Section 4 of the PIL or the SmPC available on the MHRA website.

If a patient gets any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in the product information or the PIL that comes with the medicine. Patients can also report suspected side effects themselves, or a report can be made on their behalf by someone else who cares for them, directly via the Yellow Card scheme at https://yellowcard.mhra.gov.uk or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

Because Acnecide Face Gel is a line extension of the existing product Acnecide 5% w/w Gel, its benefits and possible side effects are taken as being the same as Acnecide 5% w/w Gel.

Why was Acnecide Face Gel approved?
It was concluded that Acnecide Face Gel has been shown to be effective as topical therapy for mild acne affecting the face, when comedones (blackheads and whiteheads) predominate, and there are few or no papules and pustules (acne spots and pimples) and no inflamed spots. Furthermore, the side effects observed with use of this product are considered to be typical for this type of treatment. Therefore, the MHRA decided that the benefits are greater than the risks and recommended that this medicine can be approved for use.

What measures are being taken to ensure the safe and effective use of Acnecide Face Gel?
As for all newly-authorised medicines, a Risk Management Plan (RMP) has been developed for Acnecide Face Gel. The RMP details the important risks of Acnecide Face Gel, how these risks can be minimised, any uncertainties about Acnecide Face Gel (missing information), and how more information will be obtained about the important risks and uncertainties.

There are no safety concerns associated with use of Acnecide Face Gel.

The information included in the SmPC and the PIL is compiled based on the available quality, non-clinical and clinical data, and includes appropriate precautions to be followed by healthcare professionals and patients. Side effects of Acnecide Face Gel are continuously monitored and reviewed including all reports of suspected side-effects from patients, their carers, and healthcare professionals.

An RMP and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

Other information about Acnecide Face Gel
A marketing authorisation application for Acnecide Face Gel was received by the MHRA on 02 December 2021, and a marketing authorisation was granted in the United Kingdom (UK) on 23 May 2025.

The full PAR for Acnecide Face Gel follows this summary.

This summary was last updated in June 2025.

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I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the application for Acnecide Face 2.5% w/w Gel could be approved.

The product is indicated in adults and adolescents aged 12 years and over and is approved for the following indications:

- Topical therapy for the treatment of mild acne affecting the face, when comedones (blackheads and whiteheads) predominate, and there are few or no papules and pustules (acne spots and pimples) and no inflamed spots.

The name of the active substance is benzoyl peroxide (as hydrous benzoyl peroxide), which belongs to the pharmacotherapeutic group of anti-acne preparations for topical use.

Benzoyl peroxide is an established and effective keratolytic agent with antibacterial properties. It has been shown to be effective in reducing the local population of *Cutibacterium acnes* leading to a reduction in the production of irritant fatty acids in the sebaceous glands.

This application was approved under Regulation 50 of The Human Medicines Regulation 2012, as amended (previously Article 8(3) of Directive 2001/83/EC, as amended), a full-dossier application.

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for this product at all sites responsible for the manufacture, assembly and batch release of this product.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

Advice was sought from the Commission on Human Medicines (CHM) on 22nd February 2024. Following subsequent provision by the applicant of additional data the CHM were reassured on the quality and efficacy of the product.

A marketing authorisation application for Acnecide Face Gel was received by the MHRA on 02 December 2021, and marketing authorisation was granted in the United Kingdom (UK) on 23 May 2025.

II QUALITY ASPECTS

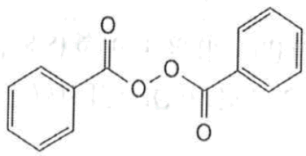
II.1 Introduction

This product consists of gel, each gram of gel contains 25 mg (2.5%) benzoyl peroxide (as hydrous benzoyl peroxide).
In addition to benzoyl peroxide, this product also contains the following excipients:
Docusate sodium
Disodium edetate
Poloxamer
Carbomer
Propylene glycol (E1520)
Acrylates copolymer
Glycerol
Colloidal anhydrous silica
Purified water
Sodium hydroxide (for pH adjustment)

The finished product is packaged in white low-density polyethylene tubes of a pack size of 15 g.
Satisfactory specifications and Certificates of Analysis have been provided for all packaging components. All primary packaging complies with the current regulations concerning materials in contact with food.

II.2 ACTIVE SUBSTANCE(S)

INN: benzoyl peroxide (as hydrous benzoyl peroxide)
Chemical Name: Dibenzoyl peroxide, Benzoyl peroxide
Molecular Formula: $C_{14}H_{10}O_4$
Chemical Structure:



Molecular Weight: 242.23
Appearance: White or almost white, amorphous or granular powder
Solubility: Sparingly soluble in water and alcohol. Soluble in benzene, acetone, chloroform and ether.

The information related to the active substance was provided in an ASMF. The Active substance is the subject of a Ph.Eur. monograph.

Synthesis of the active substance from the designated starting materials has been adequately described and appropriate in-process controls and intermediate specifications are applied. Satisfactory specifications are in place for all starting materials and reagents, and these are supported by relevant Certificates of Analysis.

Appropriate proof-of-structure data have been supplied for the active substance. All potential known impurities have been identified and characterised.

An appropriate specification is provided for the active substance. Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications. Batch analysis data are provided and comply with the proposed specification. Satisfactory Certificates of Analysis have been provided for all working standards.

Suitable specifications have been provided for all packaging used. The primary packaging has been shown to comply with current regulations concerning materials in contact with food.

Appropriate stability data have been generated supporting a suitable retest period when stored in the proposed packaging.

II.3 DRUG PRODUCT(S)

Pharmaceutical development

A satisfactory account of the pharmaceutical development has been provided.

All excipients comply with either their respective European/national monographs, or a suitable in-house specification. Satisfactory Certificates of Analysis have been provided for all excipients.

No excipients of animal or human origin are used in the finished product.

This product does not contain or consist of genetically modified organisms (GMO).

Manufacture of the product(s)

A description and flow-chart of the manufacturing method has been provided.

Satisfactory batch formulation data have been provided for the manufacture of the product, along with an appropriate account of the manufacturing process. The manufacturing process has been validated and has shown satisfactory results.

Finished Product Specification(s)

The finished product specifications at release and shelf-life are satisfactory. The test methods have been described and adequately validated. Batch data have been provided that comply with the release specifications. Certificates of Analysis have been provided for any working standards used.

Stability

Finished product stability studies have been conducted in accordance with current guidelines, using batches of the finished product stored in the packaging proposed for marketing. Based on the results, a shelf-life of before the first opening: 2 years and after the first opening: 3 months, with the storage conditions: “Do not store above 25ºC” is accepted.

II.4 Discussion on chemical, pharmaceutical and biological aspects

The grant of a marketing authorisation is recommended.

III NON-CLINICAL ASPECTS

III.1 Introduction

The pharmacology, pharmacokinetics and toxicology of the active substance is well known. As such, no new non-clinical studies have been conducted in support of this application and none are required.

III.2 Pharmacology
No new pharmacology data were provided, and none were required for this application.

III.3 Pharmacokinetics
No new pharmacokinetic data were provided, and none were required for this application.

III.4 Toxicology
No new toxicology data were provided, and none were required for this application.

III.5 Ecotoxicity/Environmental Risk Assessment
A full Environmental Risk Assessment (ERA) was submitted with this application, and no increased environmental exposure to the active substance is anticipated on introduction of this product to the market.

The effects of the finished product on the environment have been fully characterised, in-line with current guidance. No further action regarding the environmental fate of this products is required.

III.6 Discussion on the non-clinical aspects
The grant of a marketing authorisations is recommended.

IV CLINICAL ASPECTS

IV.1 Introduction
As this application is for a line extension of the existing product Acnecide 5% w/w Gel (PL 10590/0006), in support of the application, the following clinical studies were submitted:

- SUM.0325 Efficacy Evaluation of Benzac W5 and Benzac AC in the Reduction of P. acnes
- SRE.105041 Benzaknen® 5% Gel in combination with Dermotivin® Soft Liquid soap and noncomedogenic Cetaphil® Dermacontrol Moisturizer SPF30 in the treatment of mild-to-moderate acne vulgaris
- SRE.2585 A treatment regimen comparison of 5% benzoyl peroxide gel versus 5% benzoyl peroxide gel and 0.1% adapalene gel in subjects with mild to moderate acne vulgaris
- SRE.27122 Multiple-dose safety study of GK530G in healthy male subjects
- Study SUM.0323 Comparison of Benzac AC 5% Gel with Westwood's Desquam E and Benzac AC Gel Vehicle for *acne vulgaris*
- Study SRE.18058 Treatment Regimen Comparison of Benzoyl Peroxide Gel 5% versus Benzoyl Peroxide Gel 5% and Differin® (adapalene gel) Gel 0.1% in Subjects with Acne Vulgaris
- Study CR.U9401 Efficacy Evaluation of 5% Benzac AC® Wash vs. Benzac AC® Wash Vehicle in Patients with Mild to Moderate Acne Vulgaris
- SPR.18094 AMulti-Center, Randomized, Double-Blind, Parallel Group Study to Evaluate the Safety And Efficacy of a Fixed Combination of Adapalene 0.1% / Benzoyl Peroxide 2.5%
- (Adapalene/Benzoyl Peroxide Topical Gel) Gel Compared to Each Monad and Topical Gel Vehicle in Subjects with Acne Vulgaris
- SPR.18087 A Multicenter, Randomized, Double-Blind, Parallel-Group Study to Demonstrate the Efficacy and Safety of Adapalene/Benzoyl Peroxide Topical Gel

Compared with Adapalene Topical Gel, 0.1%; Benzoyl Peroxide Topical Gel, 2.5% and Topical Gel Vehicle in Subjects with Acne Vulgaris

- Study SRE.2018 In-Use Test Comparing the European Formulation of Benzac AC Wash 5% with the Formulation of Benzac AC Wash 5% Commercially Available in the US
- Study SRE.2687 Determination of the cumulative irritation potential of a combination product with adapalene 0.1% plus benzoyl peroxide 2.5% in a gel after repeated applications to the skin of healthy Subjects in comparison with adapalene gel 0.1%, benzoyl peroxide gel 2.5% and 10% and tazarotene gel 0.1%
- Study SUM.0321 Twenty-One-Day Cumulative Irritancy Potential of Benzac Ac 5, Benzac AC Vehicle, Benzac W5 and Desquam E
- Study SRE.2674 Intra-individual evaluation of cutaneous tolerance of a one daily application of a combination adapalene 0.1% and benzoyl peroxide 2.5% or 5% gel compared to benzoyl peroxide 2.5%, 5% or 10% in healthy volunteers
- SPR.27124 A Multicenter, Randomized, Double-Blinded, Vehicle-Controlled Parallel Group
- Efficacy and Safety Study of 2 Different Concentrations of CD1579 Gels versus Vehicle in the Treatment of Acne Vulgaris.

Background on the condition and current treatment options

Acne vulgaris is a common chronic skin condition, secondary to blockage or inflammation of the pilosebaceous units. It principally affects the face (99% of people), the back (60%), and the chest (15%). Acne is estimated to affect 9.4% of the global population. It affects mainly postpubescent teens, but can persist into adulthood. Acne results from androgen-induced increased sebum production, altered keratinisation, and proliferation of *Cutibacterium acnes*, causing acute inflammation of the pilosebaceous unit.

Benzoyl peroxide is a widely used topical acne medication in dermatology. Its use is well-established for the treatment of acne vulgaris in adults and children from 12 years old. The applicant provides a review of guidelines for the treatment of acme. Among others, in the 2016 European Guidelines, single agent therapy with benzoyl peroxide is recommended for comedonal acne (low strength recommendation) and mild to moderate papulopustular acne (medium strength recommendation). The strength of recommendation depends on the level of evidence.

NHS England recommends that patients should be encouraged to manage mild acne with long term use of over-the-counter products.

NICE issued a guideline on the medical management of acne in June 2021. Fixed combinations of BPO 2.5% with adapalene or clindamycin were considered first line choices. Single agent treatment with BPO 5% was recommended as an alternative treatment to the preferred options for mild to moderate and moderate to severe acne vulgaris, if the treatments were contraindicated, or the person wished to avoid using a topical retinoid, or an antibiotic (topical or oral). No guidance was issued by NICE on the use of 2.5% or 10% BPO formulations.

International guidelines recommend the use of BPO 2.5% in patients with more sensitive skin and to increase tolerance when initiating treatment.

The 2016 US guidelines of care recommend the use of benzoyl peroxide 2.5%, 5%, or 10% in gel, wash, or cream, for the treatment of mild to moderate acne vulgaris and consider that maintenance treatment is normally required to maintain a satisfactory clinical response. Lower concentrations (e.g., 2.5-5%), water based, and wash-off agents are considered better tolerated in patients with more sensitive skin. Guidelines indicate that higher concentrations than the 2.5% and 5% concentrations may cause more irritation. Skin tolerance to BPO varies

between individuals. The 10% BPO concentration would benefit mostly acne sufferers who can tolerate the lower concentrations of BPO well and need a more potent treatment. An example would be truncal acne that affects more than half of the acne sufferers, and which is usually less sensitive to irritation by anti-acne products than the face.

All studies were conducted in line with current Good Clinical Practice (GCP).

IV.2 Pharmacokinetics

Benzoyl peroxide applied topically is metabolized in the skin to benzoic acid before systemic penetration. Benzoic acid is widely used in food, cosmetic and pharmaceutical applications and consumer exposure occurs by the oral and dermal route. The acceptable daily intake for benzoic acid and its salts was established by the Joint FAO/WHO Expert Committee on Food Additives at 5 mg/kg/day of benzoic acid equivalent.
Nonclinical data showed that percutaneous absorption figures in vivo were reported by Nacht (1981) with BPO applied topically as a 10% aqueous emulsion and Wepierre (1983) with BPO applied topically as a 5% gel: 4.5% and 4.3% of BPO penetrated the skin, respectively, reaching the systemic circulation as benzoic acid.
The applicant notes that for a patient treated with 2.5 g of BPO 2.5%, or 5% or 10% gel, the exposure to benzoic acid would represent 10% or less of the acceptable daily intake of benzoic acid as established for food additives.

The applicant further provides a clinical study to support this (Study SRE.27122). Within the framework of the development of a fixed-combination of adapalene and benzoyl peroxide 2.5% aqueous gel for Japan, a single-centre, randomized, evaluator-blinded, vehicle-controlled study adult healthy males was conducted to evaluate the local tolerability of the combination (referred to as GK530G) and of benzoyl peroxide monads (2.5% and 5% aqueous gels), and to investigate the systemic exposure to adapalene and benzoyl peroxide after 5-day repeated topical application to the face (Study SRE.27122).
The results confirm that systemic penetration of benzoyl peroxide, assessed through measurement of the BA metabolite is extremely limited. The efficacy of benzoyl peroxide relies on local activity at the skin surface and does not depend on systemic absorption.

IV.3 Pharmacodynamics

Benzoyl peroxide (BPO) is a peroxide. Its main properties are antibacterial, keratolytic and comedolytic. It also has anti-inflammatory and wound healing activity. Benzoyl peroxide has been shown to be effective in reducing the local population of C. acnes (*Cutibacterium acnes*). Investigations into the penetration of topically applied benzoyl peroxide through the skin and its systemic disposition have shown limited penetration as unchanged material in the stratum corneum, followed by diffusion into the epidermis and dermis with conversion into benzoic acid (BA), and elimination of unchanged benzoate in the urine.

The antibacterial activity of BPO 2.5%, 5% and 10% formulations has been extensively evaluated. The three concentrations all have highly potent antibacterial activity against C. acnes as demonstrated in open trials after C. acnes sampling of the pilosebaceous unit or the skin surface, as well as a literature review covering additionally the 2.5% and 10% strengths to support this.
After two weeks of daily treatment, BPO 10% once daily decreases the amount of C. acnes in pilosebaceous follicles by 98% (n=9) (Fulton 1974), BPO 5% twice daily reduces the number of C. acnes on the skin surface by 98% (n=9) and BPO 2.5% twice daily decreases the number of C. acnes on the skin surface by 99% (n=10). A one year-long study did not show changes in the drug sensitivity to antibiotics of BPO Gels 2.5% and 5%.

Lipophilic properties of benzoyl peroxide enhance its penetration into the pilosebaceous duct. Benzoyl peroxide has demonstrated exfoliative and keratolytic properties. Due to its irritant effect, benzoyl peroxide increases turnover rate of epithelial cells, thereby peeling the skin, thus preventing the plugging and fostering the unplugging of pilosebaceous glands. Benzoyl peroxide also has anti-inflammatory and wound-healing properties, which are beneficial in the treatment of acne. How benzoyl peroxide affects sebum secretion rate remains a point of debate

IV.4 Clinical efficacy

In support of the application, the following was submitted:
The clinical evidence base supporting the efficacy of Acnecide Face 2.5% w/w Gel consists of trials in the context of the clinical development of the fixed combination adapalene 0.1% and BPO 2.5% (studies SPR.27124, SPR.18094 and SPR.18087). In these studies, the efficacy of the 2.5% BPO monad developed by the applicant for the fixed combination adapalene 0.1% and BPO 2.5% is supported in a direct comparison with vehicle (study SPR.27124). Additionally descriptive analyses of the studies SPR.18094 and SPR.18087, indicate that BPO 2.5% gel monad had numerically superior efficacy to vehicle for all primary endpoints and that its efficacy was close to that of the adapalene 0.1% monad. No statistical analysis comparing BPO 2.5% gel monad with vehicle was performed in these studies. The applicant has also performed a literature review and has provided bibliographical studies as additional evidence for the efficacy of the BPO 2.5% formulations used in these studies.
Existing guidelines state that, for topical products, differences in formulation, may significantly influence the efficacy and/or safety. In summary, BPO is acknowledged as an active and effective treatment for acne. The 2.5% strength has already been approved in the UK and is therefore considered efficacious. The literature summary provided with the dossier, along with the clinical overview, offers sufficient evidence to support the efficacy and safety of the 2.5% BPO formulation.

IV.5 Clinical safety

Phase 1 dermal tolerance studies in healthy subjects using benzoyl peroxide AC gels 2.5%, 5% and 10% or AC wash 5%, showed good local tolerance. In addition, analyses of AEs in clinical studies in healthy subjects and patients with acne vulgaris indicated that benzoyl peroxide topical formulations caused mainly mild to moderate, transient and local AEs including irritation, erythema, scaling, dryness, stinging/burning, pruritus and tightness.
The literature review of 8 prospective randomized studies evaluating the safety of other BPO 2.5% gels confirm the good local tolerability of this concentration. Most subjects had no or only mild application site reactions which occurred during the first two weeks after treatment onset and resolved quickly. The tolerance of BPO 2.5% and 5% gels, was comparable. Long-term treatment was well tolerated.
Overall, the literature review indicates that although application site irritation was more pronounced with the BPO 10% gels compared with the lower concentrations, no significant difference was found in withdrawals due to adverse effects.

<u>Post marketing experience</u>

The safety profile of topical BPO is well characterised.

The majority of adverse events reported with benzoyl peroxide formulations represent local skin reactions. Detailed information on adjusting posology to mitigate the potential for the commonest local skin reactions are given in section 4.2 (posology and method of administration) and 4.4 (special warnings and precautions for use) of the SmPC for Acnecide

Face 2.5% w/w Gel (a GSL product). Local skin reactions as well as allergic contact dermatitis, swelling of the face, allergic reactions, including application site hypersensitivity and anaphylaxis are included in section 4.8 (undesirable effects) of the SmPC.

IV.6 Risk Management Plan (RMP)

The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulation 2012, as amended. The applicant proposes only routine pharmacovigilance and routine risk minimisation measures for all safety concerns. This is acceptable.

IV.7 Discussion on the clinical aspects

The grant of a marketing authorisation is recommended for this application.

V USER CONSULTATION

A full colour mock-up of the Patient Information Leaflet (PIL) was provided with the application in accordance with legal requirements, including user consultation.

VI OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the product is acceptable. The non-clinical and clinical data submitted have shown the positive benefit/risk of this product, in adults and adolescents aged 12 years and over, for topical therapy in the treatment of mild acne affecting the face when comedones (blackheads and whiteheads) predominate and there are few or no papules and pustules (acne spots and pimples) and no inflamed spots.

The Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling are satisfactory, and in line with current guidelines.

In accordance with legal requirements, the current approved UK version of the SmPC and PIL for this product are available on the MHRA website.

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Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations where significant changes are made are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the marketing authorisation are recorded in the current SmPC and/or PIL available on the MHRA website.

Application type	**Scope**	**Product information affected**	**Date of grant**	**Outcome**	**Assessment report attached Y/N**