



# AZCLEAR Action Medicated Lotion

This leaflet answers some common questions about AZCLEAR Action Medicated Lotion

**Product Description:**

AZCLEAR Action Medicated Lotion is a white to off-white glossy lotion

**Active Substance:**

AZCLEAR Action Medicated Lotion contains azelaic acid 20% w/w as the active ingredient.

**Pharmacodynamics / Pharmacokinetics:**

*Pharmacodynamics*

1. Antimicrobial effect on acne related organisms  
Azelaic acid possesses bacteriostatic properties *in vitro* against a variety of aerobic organisms, including *Staphylococcus aureus*, *Staphylococcus epidermis*, *Proteus mirabilis*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Candida albicans* and the anaerobe *Propionibacterium acnes*. At high concentrations (>250 mmol/L) it is bactericidal against *S. epidermis* and *P. acnes* *in vitro*. Studies suggest azelaic acid may inhibit cellular protein synthesis resulting in an antimicrobial action.

Topical application of a 20%w/w azelaic acid cream to acne affected skin for two to three months, resulted in pronounced reductions in the densities of superficial cutaneous microflora as well as intrafollicular micrococaceae (≥99.9%) and intrafollicular *Propionibacterium* sp. (97.7%). Comedo biopsy sections similarly demonstrated marked reductions in bacteria and spore numbers. Skin surface lipids obtained from areas treated with topical azelaic acid exhibited significant decreases in their free fatty acid content. A study into the follicular concentration of azelaic acid after a single topical application of a 20%w/w azelaic acid cream, have demonstrated that the peak concentration of azelaic acid in the pilosebaceous follicle was in excess of that required to inhibit protein synthesis by 50% in both *S. epidermis* and *P. acnes* *in vitro*. While all these effects are suggestive of a direct bacteriostatic or bactericidal action of azelaic acid *in vivo*, the possibility that they might be mediated indirectly through azelaic acid induced alterations to cutaneous microenvironment cannot be excluded.

2. Antikeratinising effect on the follicular epidermis  
Numerous *in vitro* studies on the effects of azelaic acid on epidermal and dermal cell proliferation and viability have been performed. These studies suggest that rather than being a general protein synthesis inhibitor, azelaic acid has an antikeratinising effect specifically inhibiting the synthesis of cytoplasmic proteins during the terminal stages of keratinocyte differentiation.

*In vivo*, azelaic acid appears to influence the differentiation of human keratinocytes by reducing the synthesis of filaggrin (keratin filament aggregating protein) and may thus act as an antikeratinising agent. Topical application of 20%w/w azelaic acid cream to normal, seborrhoea and acne affected skin resulted in alterations in the pattern of epidermal keratinisation. Light and electron microscopic examination of the epidermis revealed reductions in the number and size of keratohyaline granules and tonofilament bundles in the stratum corneum, intercellular oedema and marked reductions in the thickness of the horny layer in acro infundibular areas. Immunocytochemistry suggested an effect of azelaic acid in the terminal phase of epidermal keratinisation, with restoration of the normal pattern of filaggrin distribution occurring in the epidermal granular and horny layers of seborrhoea and acne affected skin. On the basis of this antikeratinising action, it has been suggested that an azelaic acid induced reduction in follicular hyperkeratosis may partly account for the beneficial effect in acne.

3. Antiinflammatory action

*In vitro*, azelaic acid acted as a scavenger of reactive oxygen species (oxy radicals), inhibiting the hydroxylation of aromatic compounds and the peroxidation of arachidonic acid induced by reactive hydroxy radicals. At non toxic concentrations

(≤ 20 mmol/L) azelaic acid reduced the cyto toxic effects of hydroxy radicals generated by UV irradiation or diphenol auto oxidation on melanoma and lymphoma derived cell cultures. Azelaic acid has additionally been shown to decrease superoxide anion and hydroxy radical generation by neutrophils. These studies have demonstrated that azelaic acid inhibits the generation and action of oxy radicals in biological systems.

Therefore, the ability of azelaic acid to reduce inflamed acne lesions may possibly be due to its oxy radical scavenging properties. Alternatively, the antiinflammatory effect may be indirectly attributed to antimicrobial action on the cutaneous microflora.

4. Effect on the sebaceous gland

In humans, it appears unlikely that azelaic acid has any direct effect on the functional activity of the sebaceous gland, as topical administration of 20% w/w cream for periods of three to six months to individuals with acne, seborrhoea or normal skin had no significant effect on sebum excretion rate, sebum composition or sebaceous gland morphology. Nevertheless, patients with acne reported subjectively gradual and progressive reduction in skin greasiness after one to two months treatment with azelaic acid (15% w/w cream).

*Pharmacokinetics*

A study of percutaneous absorption of azelaic acid from a single topical dose (5 grams) of Skinoren Cream, has estimated 3.6% is systemically absorbed within three days. Another study determined the percutaneous absorption of azelaic acid when dissolved in an oil in water emulsion, polyethylene glycol anhydrous ointment or carboxyvinyl gel at 15% w/w, as 3.0%, 3.6% and 8.1% respectively over 12 hours.

These results are suggestive of a connection between the rate of percutaneous absorption from topical application and whether azelaic acid is dispersed or dissolved in the formulation. A formulation containing dispersed azelaic acid can expect a slower rate of percutaneous absorption of 3.6%/3 days compared to an increased rate of 3.0-8.1%/12 hours from a formulation containing dissolved azelaic acid. Percutaneous absorption is directly proportional to penetration of azelaic acid through the skin and into the dermis. However processes such as binding of the drug to the stratum corneum or subcutaneous fat to form a reservoir or metabolism by cutaneous enzymes must also be taken into account. It has been suggested that following topical application of Skinoren Cream, 3.6% of the azelaic acid dose will be percutaneous absorbed, up to 10% will be present in the epidermis and dermis while 3-5% will be in the stratum corneum. In a study using Skinoren Cream, the level of azelaic acid present in the pilosebaceous follicles after a single topical application was found to increase as the amount of azelaic acid present on the skin surface decreased. As both percutaneous absorption and concentration of azelaic acid within the pilosebaceous follicle are related to penetration of the drug through the skin, a direct relationship probably exists between percutaneous absorption and the penetration of azelaic acid into the pilosebaceous follicle.

Both Skinoren Cream and AZCLEAR Action Medicated Lotion contain a similar uniform dispersion of azelaic acid at a 20%w/w level with a typical crystal size of <10 µm. Percutaneous absorption of azelaic acid from AZCLEAR Action Medicated Lotion and therefore penetration into the pilosebaceous follicle, is expected to be equivalent to that from Skinoren Cream.

**Indication:**

AZCLEAR Action Medicated Lotion is indicated for non-inflamed or inflamed mild to moderate acne vulgaris. It is also indicated as maintenance therapy after oral therapy

has been discontinued and as a combined therapy with oral antibiotics (tetracycline, erythromycin, minocycline, doxycycline, trimethoprim).

**Recommended Dose:**

Before touching your face wash and rinse your hands thoroughly. Apply a small amount of AZCLEAR Action Medicated Lotion directly onto acne, massaging well. Use in the morning and at night to help your acne problem disappear. Improvement may not become visible until after 4 weeks. A doctor or pharmacist should be consulted if the condition has not improved within 8 weeks.

**Mode of Administration:**

Topical

**Contraindications**

Known sensitivity to any of the ingredients.

**Warnings and Precautions:**

Avoid contact with eyes. Initial mild irritation may occur. If severe irritation occurs discontinue use.

**Interactions with Other Medicaments:**

No interactions known

**Pregnancy and lactation:**

The safety of azelaic acid is well reported and, when used in topical medication, is a category B1 drug as defined in 'Prescribing medicines in pregnancy – 4th edition' approved by the Australian Drug Evaluation Committee. Category B1 drugs are those which have been taken by only a limited number of pregnant women and women of child-bearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the foetus having been observed. Studies in animals have not shown evidence of an increased occurrence of foetal damage.

**Adverse Effects / Undesirable Effects:**

Mild transient symptoms such as itching, burning or irritation may be experienced.

**Overdose and Treatment:**

Not applicable (topical preparation).

**Storing Condition:**

Store below 30°C.

**Dosage Form and Packaging available:**

AZCLEAR Action Medicated Lotion is a white to off-white glossy lotion in a 25g tube, packed in a carton.

**Date of Revision of Package Insert:**

17th November 2022

**Shelf life:**

The shelf life of AZCLEAR Action Medicated Lotion is 3 years.

**Note:**

This information is limited. For further information please consult your doctor or pharmacist.  
• You may want to read this leaflet again, please do not throw it away until you have finished using your medicine.

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ARTWORK

23/10/2023

START DATE

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JOB NUMBER

Leaflet

TYPE

H: 200 x W: 148 mm

SIZE

AzClearAction Medicated Lotion 25g LEAFLET (MAL)

JOB DESCRIPTION

Eliza

PROJECT LEADER

Anthony

DESIGNER

EGO PHARMACEUTICALS 21-31 Malcolm Road Braeside VIC 3195.  
THIS ARTWORK HAS BEEN DEVELOPED IN ACCORDANCE TO BRIEF PROVIDED, COMPLEMENTARY TO RELEVANT REGULATIONS.  
Whilst every effort has been made to ensure that all information on this proof is correct, final responsibility for checking is with the project manager.

COLOURS



Black

ARTWORK  
VERSION

1

PRINTER FINISHES

N/A