

AUSTRALIAN PRODUCT INFORMATION – ZATAMIL (MOMETASONE FUROATE) GEL, LOTION, OINTMENT

1 NAME OF THE MEDICINE

Mometasone furoate.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Mometasone furoate 0.1% (1mg/g).

Mometasone furoate is a white to off-white powder which is practically insoluble in water, soluble in acetone and in methylene chloride, slightly soluble in ethanol (96 per cent).

For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

Zatamil Hydrogel is a clear, colourless to straw-coloured gel.

Zatamil Ointment is an opaque white to off-white ointment.

Zatamil Lotion is a clear, colourless to straw-coloured lotion.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Short term (up to four continuous weeks) relief of inflammation and pruritic manifestations of corticosteroid-responsive dermatoses, such as psoriasis and atopic dermatitis.

Zatamil Lotion is suitable for use in scalp psoriasis and applications to other areas of the body.

4.2 DOSE AND METHOD OF ADMINISTRATION

Apply a thin film of the ointment or gel to the affected skin once daily. For Zatamil Lotion few drops should be applied to the affected skin areas including scalp sites once daily; massage gently and thoroughly until the medication disappears.

4.3 CONTRAINDICATIONS

Hypersensitivity to mometasone furoate or to other corticosteroids.

As with other corticosteroids, Zatamil is contraindicated in most viral infections of the skin, tuberculosis, acne rosacea, perioral dermatitis, fungal skin infections and ulcerative conditions.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

For external use only. Avoid contact with eyes.

If irritation or sensitisation develops, treatment should be discontinued and appropriate therapy instituted.

In the presence of an infection, an antibacterial or antifungal agent, as appropriate should be added to the treatment regimen. If the infection does not resolve promptly, corticosteroid therapy should be discontinued until the infection is controlled.

As with all topical corticosteroids in general, systemic absorption will be increased if the product/s is/are applied to large areas of the body, under occlusion, where the epidermal barrier is compromised and where the treatment is long-term. These considerations are especially important in infants and children due to the larger skin surface to bodyweight ratio and the possibility of occlusive napkins and plastic pants being used. Use of corticosteroids in children should be limited to the least amount required for therapeutic effect.

Use in the elderly

Clinical studies in adults have typically included elderly patients. No overall differences in safety or effectiveness were observed between these subjects and younger subjects and other reported clinical experience has not identified differences in responses between the elderly and younger patients. However, greater sensitivity of older individuals cannot be ruled out.

Paediatric use

The use of mometasone furoate 0.1% once daily has been documented in a number of studies in children from 7 months to 12 years of age, with moderate to severe dermatitis involving at least 15% of the body surface area. Duration of treatment was usually only for 3 weeks, with up to 6 weeks in one study. No skin thinning was observed in any of these studies or change in plasma cortisol levels, where this was monitored. In general, mometasone furoate was well tolerated. Local reactions were minor, eg. stinging, and occurred in few patients. However, although mometasone appears to be safe in young children and may have less effect on the HPA axis than other corticosteroids of similar strength, caution is advised when prescribing mometasone or any other corticosteroid for prolonged use in children. Care should be taken that application sites in infants and young children are not occluded with tightly fitting napkins or plastic pants.

Effects on laboratory tests

No data available.

Visual Disturbance

Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

No data available

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No data available.

Use in pregnancy – Pregnancy Category B3

Category B3: Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human foetus having been observed. Studies in animals have shown evidence of an increased occurrence of foetal damage, the significance of which is considered uncertain in humans.

As with corticosteroids in general, studies with mometasone furoate in animals have shown teratogenic effects when administered systemically at relatively low dosage levels. There are no adequate and well controlled studies of the teratogenic effects of corticosteroids in pregnant women. Topical corticosteroids should be used with caution during pregnancy and only if the potential benefit to the patient outweighs the potential risk to the foetus.

Drugs of this class should not be used on pregnant patients in large amounts or for prolonged periods of time.

Use in lactation

Systemically administered corticosteroids are secreted into breast milk but the quantities are too low to have a deleterious effect on the infant. It is not known if topically applied mometasone furoate will be absorbed in sufficient quantity to produce detectable levels in breast milk. Therefore, topical mometasone furoate should be used with caution during breastfeeding and only if the potential benefits to the mother outweigh the potential risks to the infant. Temporary cessation of breastfeeding during treatment may also be considered.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Table 1: Adverse drug reactions in patients treated with mometasone furoate 0.1% w/w dosage forms

System organ class	Adverse drug reactions	
	Frequency category	
	Very rare (< 1/10,000)	Not known.
Infections and infestations	Folliculitis	Infection, Furuncle
Eye disorders		Vision blurred
Nervous system disorders	Burning sensation	Paraesthesia

Skin and subcutaneous tissue disorders	Pruritis	Dermatitis contact, skin hypopigmentation, hypertrichosis, skin striae, dermatitis acneiform, skin atropy
General disorders and administration site conditions		Application site pain, application site reactions

In general, mometasone furoate 0.1%, applied once daily, without occlusion, appears to be well tolerated.

Local adverse reactions:

Mild to moderate stinging, itching, burning, mils skin atrophy and acneiform reactions have been reported in less than 5% of patients.

Other less common reactions reported in less than 1% of patients include erythema furunculosis, dermatitis, abscess, aggravated allergy, disease exacerbation, paraesthesia, dry skin, pimples, folliculitis and popular and pustular formation.

Infrequent local reactions reported with other topical corticosteroids: irritation, hypertrichosis, hypopigmentation, perioral dermatitis, allergic contact dermatitis, maceration of the skin, secondary infection, striae and milaria.

Systemic adverse reactions

Similarly to other topical corticosteroids, mometasone furoate has the potential to suppress the HPA axis. However, in clinical studies of up to 6 weeks duration, the application of mometasone 0.1% once daily, without occlusion, did not affect plasma cortisol

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

Prolonged use over large areas of the body can suppress pituitary adrenal function resulting in secondary adrenal insufficiency. Infants and young children are likely to be particularly susceptible to HPA axis suppression, Cushing's syndrome and growth suppression under these conditions¹. Appropriate symptomatic treatment is indicated. Acute hypercorticoid symptoms are virtually reversible. Treat electrolyte imbalance, if necessary. In cases of chronic toxicity, slow withdrawal of corticosteroids is advised.

If a large amount of Zatamil is accidentally ingested, particularly by a child, contact the Poisons Information Centre. For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

Mometasone furoate is a synthetic 16 α -methyl analogue of beclomethasone for topical use exhibiting anti-inflammatory, anti-pruritic and vasoconstrictor properties.

In laboratory animals, mometasone furoate exhibits potent topical anti-inflammatory activity but approximately half of the suppressive effect on the hypothalamic pituitary adrenal (HPA) axis when compared with equivalent doses of betamethasone valerate. The topical to systemic potency ratio of mometasone furoate is approximately three to ten times that of betamethasone valerate in animal studies.

Mometasone has high lipophilicity and displays greater *in vitro* affinity for glucocorticoid receptors in rat epidermis than betamethasone dipropionate. In humans, using inhibition of UV-B induced erythema as an indicator of anti-inflammatory effect, 0.1% mometasone was found to be equipotent with methylprednisolone aceponate 0.1%ⁱⁱ and 2- to 4-fold better than betamethasone valerate 0.1% and betamethasone dipropionate 0.05%ⁱⁱⁱ in preventing inflammation.

Clinical trials

The Administrative Appeals Tribunal decision provided that equivalence could be established on the satisfactory completion of vasoconstriction assays conducted in accordance with the U.S. Department of Health and Human Services, Food and Drug Administration, Guidance for Industry, Guidance Topical Dermatologic Corticosteroids: *in vivo bioequivalence*, Issue Date: 2 June 1995.

The sponsor submitted satisfactory vasoconstriction assays in compliance with the U.S. Department of Health and Human Services, Food and Drug Administration, Guidance for Industry, Guidance Topical Dermatologic Corticosteroids: *in vivo bioequivalence*, Issue Date: 2 June 1995.

5.2 PHARMACOKINETIC PROPERTIES

Following topical application of radiolabelled mometasone furoate in animals, systemic absorption was minimal in all species studied, ranging from approximately 2% in dogs to 11% in rabbits over a five to seven day period.

In a human study^{iv}, only 0.7% of [³H]mometasone was absorbed into the systemic circulation, after an 8-hour contact time, from an ointment base applied to intact skin, without occlusive dressing. However, only 1.6% of the dose had diffused into the skin while 94% remained on the skin surface. In a similar study, 0.4% was absorbed systemically from a 0.1% mometasone cream.

Another study^v in healthy volunteers found that after repeated application of 10g/day of 0.1% mometasone ointment, under occlusion, for 20 hours/day. For 5 days plasma levels of about 100pg/mL of mometasone furoate were achieved. No metabolites were detected in plasma. Only 0.00076% of the total topically administered dose was excreted in the urine as mometasone furoate, its 6 β -hydroxy metabolite and mometasone itself. Cortisol levels were not affected. In this study, after a single application of 24 hours duration, plasma concentrations peaked at 130pg/mL after 12 hours and declined rapidly after

removal of the ointment to 15pg/mL after 72 hours. These authors concluded that 0.1% mometasone furoate ointment had little possibility of causing systemic effects when used in the manner employed in this study.

However inflammation and/or other disease processes in the skin may increase percutaneous absorption. Over the longer term, occlusive dressings substantially increase percutaneous absorption.

The low levels absorbed systematically after topical administration and the rapid elimination can be considered responsible for the low systemic activity and minimal effect on the hypothalamic-pituitary-adrenal (HPA) axis.^{vi}

In animal studies, 75% of a subcutaneously or peritoneally administered dose was excreted in the faeces, after metabolism in the liver.^{vi} Due to the very low levels detected in plasma, metabolism in humans has not been studied.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available.

Carcinogenicity

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Each gram of **Zatamil Hydrogel** contains mometasone furoate 1mg in a gel base of hexylene glycol, purified water, hypromellose and citric acid.

Each gram of **Zatamil Ointment** contains mometasone furoate 1mg in an ointment base of soft white paraffin, light liquid paraffin, hexylene glycol, polyethylene, cetostearyl alcohol, purified water, colloidal anhydrous silica, citric acid.

Each gram of **Zatamil Lotion** contains mometasone furoate 1mg in a lotion base of ethanol, propylene glycol, purified water, hypromellose and citric acid.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Zatamil Hydrogel: Store below 25°C.

Zatamil Ointment: Store below 25°C.

Zatamil Lotion: Store below 25°C. Do not refrigerate.

6.5 NATURE AND CONTENTS OF CONTAINER

Zatamil Hydrogel: 45g, 15g and 5g* in laminate tube with a tamper evident seal packed into a carton.

Zatamil Ointment: 45g, 15g and 5g* in laminate tube with a tamper evident seal packed into a carton.

Zatamil Lotion: 30mL in plastic dropper bottle packed into a tamper evident carton.

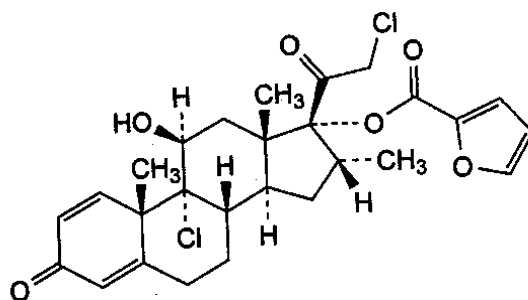
*not currently available.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure



CAS number

83919-23-7

7 MEDICINE SCHEDULE (POISONS STANDARD)

Zatamil Hydrogel: 45g (S4), 15g (S3)

Zatamil Ointment: 45g (S4), 15g (S3)

Zatamil Lotion 30mL (S4).

8 SPONSOR

Ego Pharmaceuticals Pty Ltd.
13-31 Malcolm Road, Braeside, Victoria 3195
AUSTRALIA (ACN 005 142 361)

9 DATE OF FIRST APPROVAL

This product information was approved by the Therapeutic Goods Administration on 10 May 2012.

The TGA approved registration following a contested hearing heard before the Administrative Appeals Tribunal and then the making the orders to effect registration (see the clinical trials section).

10 DATE OF REVISION

14 August 2020.

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
7	Medicine Schedule (Poisons Standard) information amended to include 15g Schedule 3 packs for Zatamil Hydrogel and Zatamil Ointment.

ⁱ Memorandum: Department of Health and Human Services. Public Health Service. Food and Drug Administration. Centre for Drug Evaluation and Research. September 26, 2003. Postmarketing Safety review PID D030565.

ⁱⁱ Keckes A, Heger-Mahn D, Kleine Kuhlmann R and Langer L: Comparison of the local and systemic side effects of methylprednisolone aceponate and mometasone furoate applied as ointments with equal anti-inflammatory activity. *Journal of the American Academy of Dermatology* 29:576:58-580. 1993.

ⁱⁱⁱ Bjerring P: Comparison of the bioactivity of mometasone furoate 0.1% fatty cream, betamethasone dipropionate 0.05% cream and betamethasone valerate 0.1% cream in humans. *Skin Pharmacology*. 6:187-192, 1993.

^{iv} Samson C, Peets E, Winter-Sperry R and Wolkoff H: Mometasone furoate – Elocon®-A medium potency topical corticosteroid with favourable efficacy/safety profile : In *Topical Corticosteroids*. Maibach HI and Surber C (eds). Basel, Karger. 1992. pp462-479.

^v Higashi N, Katagiri K: Percutaneous absorption of a 0.1% mometasone furoate ointment fate, excretion and adrenocortical suppression [in Japanese]. *Skin Research* 32(3):394-402. 1990.

^{vi} Degreef H and Dooms-Gooseens A: The new corticosteroids: Are they effective and safe. *Dermatologic Clinics*. 11(1):155-160.