SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Monovo 1 mg/g crème

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One gram of cream contains 1 mg of mometasone furoate (0.1% mometasone furoate).

Excipients with known effect:
72.00 mg of cetostearyl alcohol (type A), emulsifying; 10.00 mg of cetyl alcohol and 13 microgram of butylated hydroxytoluene /1 gram cream.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Cream
A white cream.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Monovo is indicated for the symptomatic treatment of inflammatory skin conditions which respond to external treatment with glucocorticoids, such as atopic dermatitis and psoriasis (excluding widespread plaque psoriasis).
Monovo should be used to treat skin complaints where a topical mometasone preparation is indicated.

4.2 Posology and method of administration

Adults, including elderly patients adolescents and children aged 2 years and older:
A thin film of Monovo should be applied to the affected skin area once daily.

Strong topical corticosteroids generally should not be applied to the face without close monitoring by the physician.

Monovo should not be used for long periods (over 3 weeks) or on large areas (over 20% of body surface area).
In children aged 2 years and older a maximum of 10% of the body surface area should be treated. It should not be used occlusively or intertriginously. Treatment duration is limited to a maximum of 3 weeks.
Use of a weaker corticosteroid is often advisable when there is a clinical improvement.

Children below 2 years:
Monovo is a potent group III glucocorticoid. It should not be used in children below 2 years due to insufficient data on safety.

For application on the skin (cutaneous use).

4.3 Contraindications

Monovo is contraindicated in patients with

- hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- facial rosacea
- acne vulgaris
- perioral dermatitis
- perianal and genital pruritus
- napkin eruptions
- bacterial (e.g. impetigo), viral (e.g. herpes simplex, herpes zoster, chickenpox (varicella)) and fungal (e.g. candida or dermatophyte) infections
- tuberculosis
- syphilis
- post-vaccine reactions

The use of Monovo on the eyelids is contraindicated.

4.4 Special warnings and precautions for use

Any contact with the eyes, and use on the eyelids should be avoided.
Monovo should not be applied to broken skin and mucous membranes.
Caution should be observed in patients who are hypersensitive to any other corticosteroid. If irritation or sensitization develops with the use of Monovo, treatment should be withdrawn and appropriate therapy instituted.
Should an infection develop, use of an appropriate antifungal or antibacterial agent should be instituted. If a favorable response does not occur promptly, the corticosteroid should be discontinued until the infection is adequately controlled.
Local and systemic toxicity is common especially following long continued use on large areas of damaged skin, in flexures and with occlusion. Caution should be exercised when large areas of the body are treated and long term continuous therapy should be avoided in all patients irrespective of age.
Topical steroids may be hazardous in psoriasis for a number of reasons including rebound relapses following development of tolerance, risk of centralized pustular psoriasis and development of local or systemic toxicity due to impaired barrier function of the skin. If used in psoriasis careful patient supervision is important.
As with all potent topical glucocorticoids, avoid sudden discontinuation of treatment. When long term topical treatment with potent glucocorticoids is stopped, a rebound phenomenon can develop which takes the form of dermatitis with intense redness, stinging and burning. This can be prevented by slow reduction of the treatment, for instance continue treatment on an intermittent basis before discontinuing treatment.
Hyperglycaemia and glucosuria can occur in some patients after topical application due to systemic absorption.
Glucocorticoids can change the appearance of some lesions and make it difficult to establish an adequate diagnosis and can also delay the healing.

Monovo contains emulsifying cetostearyl alcohol and cetyl alcohol which may cause local skin reactions (e.g. contact dermatitis) as well as butylated hydroxytoluene which may cause local skin reactions (e.g. contact dermatitis), or irritation to the eyes and mucous membranes.

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 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

4.6 Fertility, pregnancy and lactation

Fertility
No effects known.

Pregnancy
Corticosteroids cross the placenta. There is very limited data on the use of topical mometasone during pregnancy. After systemic use of high dose corticosteroids, effects on the foetus/neonate has been described (intra-uterine growth retardation, adrenocortical suppression, cleft palate).
Animal studies have shown reproduction toxicity and teratogenicity (see section 5.3). The potential risk for humans is unknown.
Although systemic exposure is limited, Monovo should only be used during pregnancy after careful consideration of the benefit/risk assessment.

Breast-feeding
It is not known whether mometasone is excreted into breast milk. Monovo should only be administered to nursing mothers after careful consideration of the benefit/risk assessment. During the lactation period, Monovo must not be applied in the breast area.

4.7 Effects on ability to drive and use machines

Monovo has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Adverse reactions are listed in Table 1 according to MedDRA system organ class and in decreasing frequency defined as follows:

Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1,000 to <1/100)
Rare (≥1/10,000 to <1/1,000)
Very rare (<1/10,000)
Not known (frequency cannot be estimated from the available data)

Undesirable effects that have been reported in connection with external corticosteroid treatment include:

Table 1: Treatment-related adverse reactions reported by body system and frequency

Infections and infestations	
Uncommon:	Secondary infection.
Eye disorders	
Not known:	Vision, blurred (see also section 4.4)
Vascular disorders	
Very rare:	Telangiectasis.
Skin and subcutaneous tissue disorders	
Common:	Mild to moderate burning sensations at the application site, tingling/stinging, pruritus, bacterial infections, paraesthesia, furunculosis, local skin atrophy.
Uncommon:	Striae, irritation, hypertrichosis, hypopigmentation, perioral dermatitis, maceration of the skin, allergic contact dermatitis, papulous rosacea like dermatitis (facial skin), acneiform reactions, capillary brittleness (ecchymoses), miliaria, dryness, sensitisation (mometasone), folliculitis.

An increased risk of systemic effects and local undesirable effects exists with frequent dosing, treatment of large areas or in the long term and also the treatment of intertriginous areas or with occlusive dressings.
Hypopigmentation or hyperpigmentation has been reported in isolated cases (rare) in connection with other steroids and may therefore occur with Monovo.
Side effects which have been reported with systemic glucocorticoids – including adrenal suppression – may also occur with topically applied glucocorticoids.
Paediatric patients may demonstrate greater susceptibility to topical corticosteroid-induced hypothalamic-pituitary-adrenal axis suppression and Cushing's syndrome than mature patients because of a larger skin surface to body weight ratio. Chronic corticosteroids therapy may interfere with the growth and development of children.
Intracranial hypertension has been reported in paediatric patients receiving topical corticosteroids. Manifestations of intracranial hypertension include bulging fontanelles, headaches and bilateral papilloedema.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation 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 via the national reporting system listed in Appendix V

4.9 Overdose

Excessive long-term use of external corticosteroids may suppress HPA axis function and give rise to secondary adrenocortical insufficiency. If suppression of the HPA axis has been reported, it should be

endeavoured, with the usual caution being exercised in these situations, to reduce the frequency of applications or to try to withdraw the drug.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Corticosteroids, Dermatological preparations; Corticosteriods, potent (Group III)
ATC Code: D07AC13
Monovo is a potent glucocorticoid, group III.
The active substance, mometasone furoate, is a synthetic, non-fluorinated glucocorticoid with a furoate ester in position 17.
Like other corticosteroids for external use, mometasone furoate exhibits marked anti-inflammatory activity and marked anti-psoriatic activity in standard animal predictive models.
Monovo was shown to have an equivalent pharmacodynamic (vasoconstriction) response profile to the reference product containing 1mg/g mometasone furoate when applied to normal skin. The calculated AUC ratio of Monovo to the reference product in the vasoconstrictor assay was 97.06%.
The therapeutic index of mometasone furoate (a ratio of desired to unwanted effects) determined from relevant literature data suggests that mometasone belongs to a category of topical glucocorticoids, in which desired effects clearly outweigh unwanted effects.
In the croton oil assay in mice, mometasone (ED50 = 0.2 μg/ear) was equipotent to betamethasone valerate after single application and about 8 times as potent after five applications (ED50 = 0.002 μg/ear /day versus 0.014 μg/ear/day).
In guinea pigs, mometasone was approximately twice as potent as betamethasone valerate in reducing m.ovalis-induced epidermal acanthosis (i.e. anti-psoriatic activity) after 14 applications.

5.2 Pharmacokinetic properties

Results from percutaneous absorption studies have indicated that systemic absorption following topical application of mometasone furoate cream 0.1% is minimal. The results show that about 0.4% of the active ingredient is absorbed by the intact skin in 8 hours (without using an occlusive dressing).
Characterization of metabolites was not feasible owing to the small amounts present in plasma and excreta.

5.3 Preclinical safety data

Acute Toxicity

Type of Animal	**Type of Application**	**LD50 (mg/kg)**
Mouse	**subcutaneous**	**200 – 2000**
Rat	**subcutaneous**	**200**
Dog	**subcutaneous**	**>200**
Mouse	**oral**	**>2000**
Rat	**oral**	**>2000**

Chronic Toxicity
In various toxicity studies with chronic use in which excessive quantities of the active ingredient (670 times the therapeutic dose) were applied over 6 months, only symptoms typical of corticoid overdose were found: reduced weight gain; muscular atrophy; distended abdomen; decrease in lymphocytes and eosinophilic granulocytes and increase in neutrophilic leucocytes; increase in serum transaminases (SGPT and SGOT), cholesterol and triglycerides; lipidaemia; organ changes (atrophy of the spleen and thymus, local skin atrophy, increases in liver and kidney weight and reduced osteogenesis).
These changes were generally more pronounced and more frequent in animals which were given the comparison substance, betamethasone valerate. Neither of the two substances exhibited unusual systemic effects.

Genotoxicity
Tests on gene mutations were negative. However, mometasone induced chromosome mutations in-vitro but only at cell-toxic concentrations. Similar effects were not observed in thorough in-vivo tests, so a mutagenic risk can be ruled out with sufficient certainty.

Carcinogenicity
Long-term carcinogenicity studies of mometasone furoate have been conducted by the inhalation route in rats (2 years) and mice (19 months). No statistically significant increase in the incident of tumours was observed at doses up to 67 mcg/kg in rats or 160 mcg/kg in mice.

Reproduction Toxicity
Animal tests on the effect of mometasone furoate on embryonic development in rabbits revealed depressed body weight from 0.15 mg/kg/BWT upwards.
After topical treatment of rabbits, the progeny suffered various types of malformation, such as crooked front paws, cleft palate, gallbladder agenesis and umbilical hernia. In the rat, embryo-lethal effects from 7.5 µg//kg/BWT (subcutaneous) and poor development from 0.3 mg/kg/BWT (topical) (depressed body weight, delayed ossification) and substance-related increase in umbilical hernia were observed. When the drug was administered to mothers close to the birth date, protracted labour and difficult births were observed. Mometasone furoate had no effects on the fertility of rats.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Purified water
White soft paraffin (contains butylated hydroxytoluene (E321) as antioxidant)
Liquid paraffin
2-Methylpentane-2,4-diol
Emulsifying cetostearyl alcohol (type A, contains disodium/potassium hydrogen phosphate for pH adjustment)
Macrogol cetostearyl ether
Cetyl alcohol
Glycerol
Citric acid
Sodium citrate
Xanthan gum

6.2 Incompatibilities

When treating the genital or anal area with Monovo, the ingredients white soft paraffin and liquid paraffin can lead to a reduction in the functional capability of latex products (e.g. condoms, diaphragms) when used simultaneously and might thereby impair the safety of these products.

6.3 Shelf life

2 years

Shelf-life after first opening: 6 months.

6.4 Special precautions for storage

Do not store above 25 °C.

6.5 Nature and contents of container

The cream is filled in PE/aluminium laminate tubes fitted with a white polypropylene screw cap in a cardboard carton. Carton of 1 tube.

Tubes with 10g, 15g, 20g, 25g, 30g, 35g, 50g, 60g, 70g, 90g and 100g of cream
Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements

7. MARKETING AUTHORISATION HOLDER

Almirall Hermal GmbH
Scholtzstraße 3
21465 Reinbek
Duitsland

8. MARKETING AUTHORISATION NUMBER(S)

RVG 105118

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Datum van eerste verlening van de vergunning: 18 april 2011
Datum van laatste verlenging: 10 maart 2016

10. DATE OF REVISION OF THE TEXT

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