Daivonex® Ointment

Daivonex® ointment contains 50µg/g (0.005% w/w) calcipotriol.
Off white to yellowish white translucent ointment.
Pack sizes: 15 g, 30 g and 100 g. Not all pack sizes are marketed in the country.

Properties
Daivonex® ointment is a topical formulation of the vitamin D derivative, calcipotriol, which induces differentiation and suppresses proliferation of skin cells (keratinocytes). Daivonex® ointment thus normalises abnormal cell proliferation and differentiation in psoriatic skin.

Indications
Psoriasis vulgaris.

Dosage and administration
Adults:
Daivonex® ointment should be applied to the affected area twice daily. For some patients adequate maintenance therapy may be achieved with less frequent application. The maximum amount used by an adult in one week should not exceed 100 g (equivalent to 5 mg of calcipotriol). If using other calcipotriol containing medicinal products concomitantly, the total weekly dose of all calcipotriol containing medical products, including Daivonex® ointment, should not exceed 5 mg of calcipotriol.

Contraindications
Hypersensitivity to the active substance or to any of the excipients.
Due to the content of calcipotriol, Daivonex® ointment is contraindicated in patients with known disorders of calcium metabolism (see Special warnings and precautions for use).

Fertility, pregnancy and lactation
Pregnancy
Safety for use of calcipotriol during human pregnancy has not been established. When calcipotriol was administered orally in animals, reproductive toxicity has been shown. Calcipotriol should not be used during pregnancy unless clearly necessary.
Breast-feeding
It is unknown whether calcipotriol is excreted in human milk. Caution should be exercised when prescribing Daivonex® ointment to women who breast-feed. The patient should be instructed not to use Daivonex® ointment on the breast when breast-feeding.
Fertility
Studies in rats with oral doses of calcipotriol demonstrated no impairment of male and female fertility.

Use in Children
Safety and efficacy in the treatment of children have not yet been established.

Special warnings and precautions for use
Effects on calcium metabolism
Due to the content of calcipotriol, hypercalcaemia may occur if the maximum weekly dose is exceeded. Serum calcium is normalised when treatment is discontinued. The risk of hypercalcaemia is minimal when the recommendations relevant to calcipotriol are followed. The maximum weekly dose in adults is 100 g of cream or ointment (equivalent to 5 mg of calcipotriol) or 60 ml of scalp solution (equivalent to 3 mg of calcipotriol). When cream, ointment or cutaneous solution are applied together, the total dose of calcipotriol should not exceed 5 mg per week.
Local adverse reactions
Daivonex® ointment should not be applied to the face. The patient must be instructed in correct use of the product to avoid accidental transfer to the face and eyes. Hands must be washed after each application to avoid accidental transfer to these areas. Daivonex® ointment should be used with caution in skin folds as this may increase the risk of developing adverse reactions (see Undesirable effects).
UV exposure
During Daivonex® ointment treatment, physicians are recommended to advise patients to limit or avoid excessive exposure to either natural or artificial sunlight. Daivonex® ointment should be used with UVR only if the physician and patient consider that the potential benefits outweigh the potential risks.

Due to lack of data, Daivonex® ointment should be avoided in guttate, erythrodermic, and pustular psoriasis.
Adverse reactions to excipients
Daivonex® ointment contains propylene glycol as an excipient which may cause skin irritation.

Effects on the ability to drive and use machines
Daivonex® ointment has no or negligible influence on the ability to drive and use machines.

Undesirable effects
The estimation of the frequency of adverse reactions is based on a pooled analysis of data from clinical studies and spontaneous reporting.
The most frequently reported adverse reactions during treatment are pruritus, skin irritation and erythema.
Systemic reactions (hypercalcaemia and hypercalciuria) have been reported. The risk of developing such reactions increases if the recommended total dose is exceeded (see Special warnings and precautions for use).

Adverse reactions are listed by MedDRA SOC and the individual adverse reactions are listed starting with the most frequently reported. Within each frequency grouping, adverse reactions are presented in the order of decreasing seriousness.

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)

Infections and infestations	
Uncommon (≥1/1,000 to <1/100)	Folliculitis
Immune system disorders	
Rare (≥1/10,000 to <1/1,000)	Hypersensitivity
Metabolism and nutrition disorders	
Rare (≥1/10,000 to <1/1,000)	Hypercalcaemia
Skin and subcutaneous tissue disorders	
Common (≥1/100 to <1/10)	Psoriasis aggravated Dermatitis Erythema Skin exfoliation Skin burning sensation Skin irritation Pruritus
Uncommon (≥1/1,000 to <1/100)	Rash* Dry skin
Rare (≥1/10,000 to <1/1,000)	Photosensitivity reaction Skin oedema Urticaria Seborrhoeic dermatitis
Renal and urinary disorders	
Rare (≥1/10,000 to <1/1,000)	Hypercalciuria
General disorders and administration site conditions	
Common (≥1/100 to <1/10)	Application site pain
Uncommon (≥1/1,000 to <1/100)	Application site pigmentation changes

* Various types of rash reactions such as rash erythematous, rash maculo-papular, rash morbilliform, rash papular and rash pustular have been reported.

Overdose
Use above the recommended dose may cause elevated serum calcium which subsides when treatment is discontinued. The symptoms of hypercalcaemia include polyuria, constipation, muscle weakness, confusion and coma.

Interaction with other medicinal products and other forms of interaction
No interaction studies have been performed with Daivonex®.

Preclinical safety data
The effect on the calcium metabolism is approximately 100 times less than that of the hormonally active form of vitamin D_3.
A dermal carcinogenicity study in mice revealed no special hazard to humans.
In a study where albino hairless mice were repeatedly exposed to both ultraviolet (UV) radiation and dermally administered calcipotriol for 40 weeks at dose levels corresponding to 9, 30 and 90 µg/m^2/day (equivalent to 0.25, 0.84, 2.5 times the maximum recommended daily dose for a 60 kg adult, respectively), a reduction in the time required for UV radiation to induce the formation of skin tumours was observed (statistically significant in males only), suggesting that calcipotriol may enhance the effect of UV radiation to induce skin tumours. The clinical relevance of this finding is unknown.

Storage
Do not store above 30°C.

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