SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

CALCIPOTRIOL/BETAMETHASONE 0.005 %/ 0.064 % TOPICAL SUSPENSION GLENMARK

(Topical suspension)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

CALCIPOTRIOL/BETAMETHASONE 0.005 %/ 0.064 % TOPICAL SUSPENSION GLENMARK:

Each gram of topical suspension contains:

Calcipotriene hydrate 52,18 mcg equivalent to calcipotriene 50,0 mcg and betamethasone dipropionate USP 0,643 mg equivalent to betamethasone 0,5 mg.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution (Topical suspension)

CALCIPOTRIOL/BETAMETHASONE 0.005 %/ 0.064 % TOPICAL SUSPENSION GLENMARK:

Viscous, nearly odourless, almost clear, colourless to slightly off-white suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

CALCIPOTRIOL/BETAMETHASONE 0.005 %/ 0.064 % TOPICAL SUSPENSION GLENMARK is indicated for the topical treatment of psoriasis vulgaris of the scalp and body in patients 18 years and older.

4.2 Posology and method of administration

Posology:

CALCIPOTRIOL/BETAMETHASONE 0.005 %/ 0.064 % TOPICAL SUSPENSION GLENMARK should be applied to affected areas on the scalp and body once daily. The recommended treatment period is 4 weeks. **CALCIPOTRIOL/BETAMETHASONE 0.005 %/ 0.064 % TOPICAL SUSPENSION GLENMARK** should be discontinued when control is achieved.

If it is necessary to continue or restart treatment after 4 weeks, treatment should be continued under medical review and under regular medical supervision.

The maximum daily dose should not exceed 15 g, and the maximum weekly dose should not exceed 100 g. The treated area should not be more than 30 % of the body surface.

Children

There is no experience of use in children and adolescents below the age of 18 years.

Method of administration

Patients should shake bottle prior to using calcipotriene and betamethasone dipropionate topical suspension.

Patients should wash their hands after applying the product. Patients should not take a bath or shower or wash their hair right after application of **CALCIPOTRIOL/BETAMETHASONE 0.005 %/ 0.064 % TOPICAL SUSPENSION GLENMARK**.

CALCIPOTRIOL/BETAMETHASONE 0.005 %/ 0.064 % TOPICAL SUSPENSION GLENMARK should not be:

- Used with occlusive dressings unless directed by a healthcare provider.
- Used on the face, groin, or axillae, or if skin atrophy is present at the treatment site.
- Applied to the scalp in the 12 hours before or after any chemical treatments to the hair.

CALCIPOTRIOL/BETAMETHASONE 0.005 %/ 0.064 % TOPICAL SUSPENSION GLENMARK is not for oral, ophthalmic, or intravaginal use.

4.3 Contraindications

CALCIPOTRIOL/BETAMETHASONE 0.005 %/ 0.064 % TOPICAL SUSPENSION GLENMARK is contra-indicated:

- In individuals with known hypersensitivity to calcipotriene and betamethasone or any of the excipients listed in section 6.1.
- In erythrodermic and pustular psoriasis
- In patients with known disorders of calcium metabolism due to content of calcipotriene
- In viral (e.g., herpes or varicella) lesions of the skin, fungal, bacterial or parasitic skin infection, skin manifestations in relation to tuberculosis, perioral dermatitis, atrophic skin, striae atrophicae, fragility of skin veins, ichthyosis, acne vulgaris, acne rosacea, rosacea, ulcers, and wounds (see *section 4.4*) due to the corticosteroid, betamethasone, in **CALCIPOTRIOL/BETAMETHASONE 0.005 %/ 0.064 % TOPICAL SUSPENSION GLENMARK**
- In patients with severe hepatic disorder or severe renal insufficiency
- In pregnancy and lactation, as the use of **CALCIPOTRIOL/BETAMETHASONE 0.005 %/ 0.064 % TOPICAL SUSPENSION GLENMARK** has not been established. Corticosteroids have been shown to be teratogenic in animals following dermal application. As these agents are absorbed percutaneously, teratogenicity following topical application cannot be excluded

4.4 Special warnings and precautions for use

Hypercalcaemia and Hypercalciuria

Hypercalcemia and hypercalciuria have been observed with use of calcipotriene and betamethasone dipropionate topical suspension. If hypercalcemia or hypercalciuria develop, discontinue treatment until parameters of calcium metabolism have normalized. The incidence of hypercalcemia and hypercalciuria following calcipotriene and betamethasone dipropionate topical suspension treatment of more than 8 weeks has not been evaluated.

Effects on Endocrine System

Hypothalamic-Pituitary-Adrenal Axis Suppression

Calcipotriene and betamethasone dipropionate topical suspension can cause reversible hypothalamic-pituitary-adrenal (HPA) axis suppression with the potential for clinical glucocorticosteroid insufficiency. This may occur during treatment or upon withdrawal of treatment. Factors that predispose a patient to HPA axis suppression include the use of high potency steroids, large treatment surface areas, prolonged use, use of occlusive dressings, altered skin barrier, liver failure, and young age.

Evaluation for HPA axis suppression may be done by using the adrenocorticotropic hormone (ACTH) stimulation test. If HPA axis suppression is documented, gradually withdraw calcipotriene and betamethasone dipropionate topical suspension, reduce the frequency of application, or substitute with a less potent corticosteroid.

Cushing's Syndrome and Hyperglycaemia

Cushing's syndrome and hyperglycaemia may occur due to the systemic effects of the topical corticosteroid. These complications are rare and generally occur after prolonged exposure to excessively large doses, especially of high-potency topical corticosteroids.

Additional Considerations for Endocrine Adverse Reactions

Use of more than one corticosteroid-containing product at the same time may increase the total systemic corticosteroid exposure.

CALCIPOTRIOL/BETAMETHASONE 0.005 %/ 0.064 % TOPICAL SUSPENSION GLENMARK is not recommended for use in children younger than 18 years.

Allergic Contact Dermatitis with Topical Corticosteroids

Allergic contact dermatitis to a topical corticosteroid is usually diagnosed by observing a failure to heal rather than a clinical exacerbation. Such an observation should be corroborated with appropriate diagnostic patch testing.

Allergic Contact Dermatitis with Topical Calcipotriene

Allergic contact dermatitis has been observed with use of topical calcipotriene. Such an observation should be corroborated with appropriate diagnostic patch testing.

Ophthalmic Adverse Reactions

Use of topical corticosteroids, including calcipotriene and betamethasone dipropionate topical suspension, may increase the risk of posterior subcapsular cataracts and glaucoma. Cataracts and glaucoma have been reported with the post marketing use of topical corticosteroid products (see section 4.8). Avoid contact of calcipotriene and betamethasone dipropionate topical suspension with eyes. Calcipotriene and betamethasone dipropionate topical suspension may cause eye irritation. Advise patients to report any visual symptoms and consider referral to an ophthalmologist for evaluation.

Local adverse reactions

CALCIPOTRIOL/BETAMETHASONE 0.005 %/ 0.064 % TOPICAL SUSPENSION GLENMARK contains a potent group III-steroid and concurrent treatment with other steroids on the same treatment area must be avoided. Skin of the face and genitals are very sensitive to corticosteroids. **CALCIPOTRIOL/BETAMETHASONE 0.005 %/ 0.064 % TOPICAL SUSPENSION GLENMARK** should not be used in these areas. The patient must be instructed in correct use of **CALCIPOTRIOL/BETAMETHASONE 0.005 %/ 0.064 % TOPICAL SUSPENSION GLENMARK** to avoid application and accidental transfer to the face, scalp, mouth or eyes. Hands must be washed after each application to avoid accidental transfer to these areas.

Concomitant skin infections

When lesions become secondarily infected, they should be treated with anti-microbiological therapy. However, if infection worsens, treatment with **CALCIPOTRIOL/BETAMETHASONE 0.005 %/ 0.064 % TOPICAL SUSPENSION GLENMARK** should be stopped (see section 4.3).

Discontinuation of treatment

When treating psoriasis with topical corticosteroids, such as contained in **CALCIPOTRIOL/BETAMETHASONE 0.005 %/ 0.064 % TOPICAL SUSPENSION GLENMARK**, there may be a risk of generalised pustular psoriasis or of rebound effects when discontinuing treatment. Medical supervision should therefore continue in the post-treatment period.

Long-term use

With long-term use there is an increased risk of local and systemic corticosteroid adverse reactions. The treatment should be discontinued in case of adverse reactions related to long- term use of corticosteroid (see section 4.8).

Unevaluated use

There is no experience with the use of **CALCIPOTRIOL/BETAMETHASONE 0.005 %/ 0.064 % TOPICAL SUSPENSION GLENMARK** in guttate psoriasis.

Concurrent treatment and UV exposure

There is limited experience for the use of **CALCIPOTRIOL/BETAMETHASONE 0.005 %/ 0.064 % TOPICAL SUSPENSION GLENMARK** in combination with other topical anti-psoriatic products at the same treatment area, other anti-psoriatic medicines administered systemically or with phototherapy.

During **CALCIPOTRIOL/BETAMETHASONE 0.005 %/ 0.064 % TOPICAL SUSPENSION GLENMARK** treatment, patients should limit or avoid excessive exposure to either natural or artificial sunlight.

4.5 Interaction with other medicines and other forms of interaction

No interaction studies have been performed with **CALCIPOTRIOL/BETAMETHASONE 0.005 %/ 0.064 % TOPICAL SUSPENSION GLENMARK**.

4.6 Fertility, pregnancy and lactation

Safety and efficacy in pregnancy and lactation have not been established (see section 4.3).

Pregnancy

CALCIPOTRIOL/BETAMETHASONE 0.005 %/ 0.064 % TOPICAL SUSPENSION GLENMARK is contraindicated in pregnancy (See Section 4.3). Calcipotriene and betamethasone dipropionate topical suspension may increase the potential risk of having a low-birth-weight infant..

Breastfeeding

Caution should be exercised when prescribing [CALCIPOTRIOL/BETAMETHASONE 0.005 %/ 0.064 % TOPICAL SUSPENSION GLENMARK] to women who are breast feeding. The patient should be instructed not to use **CALCIPOTRIOL/BETAMETHASONE 0.005 %/ 0.064 % TOPICAL SUSPENSION GLENMARK** on the breast when breastfeeding or directly to the nipple and areola to avoid direct infant exposure.

4.7 Effects on ability to drive and use machines

CALCIPOTRIOL/BETAMETHASONE 0.005 %/ 0.064 % TOPICAL SUSPENSION GLENMARK has no or negligible influence on the ability to drive and to use machines.

4.8 Undesirable effects

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Tabulated summary of post-marketing adverse reactions

The adverse reactions are listed by system organ class and absolute frequency.

System Organ Class	Adverse Reactions	Frequency Category
Infection and infestations	Folliculitis, skin infection, furuncle	Less frequent
Immune system disorders	Hypersensitivity	Less frequent
Endocrine disorders	Hirsutism, Cushings syndrome	Less frequent

Metabolism and nutrition disorders	Hypercalcaemia	Frequency unknown
Eye disorders	Blurred vision	Frequency unknown
Skin and subcutaneous tissue disorders	Pruritus	Frequent
	Burning sensation of skin, skin pain or irritation, folliculitis, dermatitis, erythema, acne, dry skin, exacerbation of psoriasis, rash, pustular rash, pustular psoriasis, skin hypopigmentation	Less frequent
	Hair colour changes	Frequency unknown
General disorders and administration site conditions	Rebound effect, application site pruritus	Less frequent

Betamethasone

Skin and subcutaneous tissue disorders	Skin atrophy, telangiectasia, striae, folliculitis, hypertrichosis, perioral dermatitis, allergic contact dermatitis, depigmentation, colloid milia, pustular psoriasis	Less frequent
General disorders and administration site conditions	Adrenocortical suppression, cataract, infections, impaired glycaemic control of diabetes mellitus, increase of intra-ocular pressure	Frequency unknown

Calcipotriene

General disorders and administration site conditions	Hypercalcaemia, inhibition of the	Frequency unknown

	adrenal cortex, application site reactions, pruritus, skin irritation, burning and stinging sensation, dry skin, erythema, rash, dermatitis, psoriasis aggravated, photosensitivity and hypersensitivity reactions, angioedema, facial oedema, hypercalcaemia, hypercalciuria	

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

4.9 Overdose

Usage 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. Excessive prolonged use of topical corticosteroids may result in adrenocortical suppression which is usually reversible. Symptomatic and supportive treatment may be indicated.

In case of systemic toxicity due to chronic use, **CALCIPOTRIOL/BETAMETHASONE 0.005 %/ 0.064 % TOPICAL SUSPENSION GLENMARK** treatment must be discontinued gradually.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 13.8.1 Preparations for psoriasis

Pharmacotherapeutic group: Antipsoriatics. Other antipsoriatics for topical use, Calcipotriol, combinations. ATC Code: D05AX5

CALCIPOTRIOL/BETAMETHASONE 0.005 %/ 0.064 % TOPICAL SUSPENSION GLENMARK combines the pharmacological effects of calcipotriene hydrate as a synthetic vitamin D3 analogue and betamethasone dipropionate as a synthetic corticosteroid.

Calcipotriene is a vitamin D analogue. It is suggested that calcipotriene induces differentiation and suppresses proliferation of keratinocytes. This is the proposed basis for its effect in psoriasis. The underlying antiproliferative mechanism of vitamin D in keratinocytes involves the induction of the growth inhibitory factor transforming growth factor-β and of cyclin-dependent kinase inhibitors, with subsequent growth arrest in the G1 phase of the cell cycle plus down-regulation of the two proliferation factors early growth response-1 and polo-like kinase-2.

In addition, vitamin D has an immunomodulatory effect, suppressing activation and differentiation of Th17/Th1 cells while inducing a Th2/Treg response.

In psoriasis, corticosteroids suppress the immune system, particularly pro-inflammatory cytokines and chemokines, thereby inhibiting T-cell activation. At the molecular level, corticosteroids act via the intracellular glucocorticoid receptor and the anti-inflammatory function is due to transrepression of pro-inflammatory transcription factors such as nuclear factor κB, activator protein-1, and interferon regulatory factor-3.

The dipropionate of betamethasone is a glucocorticoid exhibiting the general properties of corticosteroids. In pharmacological doses, corticosteroids are used primarily for their anti-inflammatory and/ or immunosuppressive effects. The exact mechanism of action of corticosteroids in psoriasis is uncertain.

In combination, calcipotriene monohydrate and betamethasone dipropionate promote greater anti-inflammatory and anti-proliferative effects than either component alone.

5.2 Pharmacokinetic properties

Absorption

The systemic effect of calcipotriene and betamethasone dipropionate topical suspension in psoriasis was investigated.

Elimination

Metabolism

Calcipotriene: Calcipotriene metabolism following systemic uptake is rapid and occurs in the liver. The primary metabolites of calcipotriene are less potent than the parent compound.

Calcipotriene is metabolized to MC1046 (the α,ß-unsaturated ketone analogue of calcipotriene), which is metabolized further to MC1080 (a saturated ketone analogue). MC1080 is the major metabolite in plasma. MC1080 is slowly metabolized to calcitroic acid.

Betamethasone dipropionate: Betamethasone dipropionate is metabolized to betamethasone 17-propionate and betamethasone, including the 6ß-hydroxy derivatives of those compounds by hydrolysis. Betamethasone 17-propionate (B17P) is the primary metabolite.

5.3 Preclinical safety data

Studies in rats with oral doses of up to 54 mcg/kg/day (324 mcg/m^2/day) of calcipotriene indicated no impairment of fertility or general reproductive performance. Studies in male rats at oral doses of up to 200 mcg/kg/day (1,200 mcg/m^2/day), and in female rats at oral doses of up to 1000 mcg/kg/day (6000 mcg/m^2/day), of betamethasone dipropionate indicated no impairment of fertility.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Butylated hydroxytoluene, hydrogenated castor oil, mineral oil. polyoxypropylene stearyl ether, vitamin E.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 25 °C.

Do not refrigerate.

KEEP OUT OF THE REACH OF CHILDREN.

6.5 Nature and contents of container

Carton containing 60 g topical suspension in an opaque white HDPE bottle with white nozzle and 20 mm red ribbed screw cap along with leaflet.

6.6 Special precautions for disposal and other handling

No special requirements. Any unused product or waste material should be disposed of in accordance with local requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Glenmark Pharmaceuticals South Africa (Pty) Ltd

34 Monte Carlo Crescent,

Block A, First floor,

Kyalami Park,

Midrand,

1684

8. REGISTRATION NUMBER(S)

54/13.8.1/0523.522

9. DATE OF FIRST AUTHORISATION/ RENEWAL OF THE AUTHORISATION

3 June 2025

10. DATE OF REVISION OF TEXT

8 May 2025