Professional Information

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

HYDROCORTISONE CREAM GLENMARK (Cream)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

HYDROCORTISONE CREAM GLENMARK 20 mg: Each gram of cream contains 2.0 mg Hydrocortisone Valerate.

Contains antimicrobial preservative: Methyl paraben 2.0 mg per 1 gram of cream.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Cream.

White to off-white homogenous cream.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

HYDROCORTISONE CREAM GLENMARK is a medium potency corticosteroid indicated for the relief of the non-infected inflammatory and pruritic manifestations of corticosteroid responsive dermatoses in adult patients.

4.2 Posology and method of administration

HYDROCORTISONE CREAM GLENMARK should be applied topically to the affected area as a thin film two or three times daily depending on the severity of the condition. Therapy should be discontinued when control is achieved. If no improvement is seen within 2 weeks, reassessment of the diagnosis may be necessary.

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HYDROCORTISONE CREAM GLENMARK should not be used with occlusive dressings unless directed by a medical practitioner. **HYDROCORTISONE CREAM GLENMARK** should not be applied in the diaper area if the patient requires diapers or plastic pants as these garments may constitute occlusive dressing.

4.3 Contraindications

- **HYDROCORTISONE CREAM GLENMARK** is contraindicated in patients who have a history of severe hypersensitivity reactions to hydrocortisone valerate or to any of the other components of the preparation.
- Pregnancy

4.4 Special warnings and precautions for use

General

Systemic absorption of topical corticosteroids can produce reversible hypothalamic-pituitary-adrenal (HPA) axis suppression with the potential for glucocorticosteroid insufficiency after withdrawal of treatment. Manifestations of Cushing's syndrome, hyperglycaemia, and glucosuria can also be produced in some patients by systemic absorption of topical corticosteroids while on treatment.

Patients applying a topical steroid to a large surface area or to areas under occlusion should be evaluated periodically for evidence of HPA axis suppression. This may be done by using the ACTH stimulation, A.M. plasma cortisol, and urinary free cortisol tests.

HYDROCORTISONE CREAM GLENMARK has produced mild, reversible adrenal suppression in adult patients when used under occlusion for 5 days, 15 grams twice a day over 25-60 % body surface area or when used three times a day over 20-30 % body surface area to treat psoriasis for 3-4 weeks.

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If HPA axis suppression is noted, an attempt should be made to withdraw the medicine, to reduce the frequency of application, or to substitute a less potent corticosteroid. Recovery of HPA axis function is generally prompt upon discontinuation of topical corticosteroids. Infrequently, signs and symptoms of glucocorticosteroid insufficiency may occur, requiring supplemental systemic corticosteroids. For information on systemic supplementation, see prescribing information for these products.

Paediatric patients may be more susceptible to systemic toxicity from equivalent doses due to their larger skin surface to body mass ratios. (See *Paediatric Use*).

If irritation develops **HYDROCORTISONE CREAM GLENMARK** should be discontinued and appropriate therapy instituted. Allergic contact dermatitis with corticosteroids are usually diagnosed by observing a failure to heal rather than noting a clinical exacerbation, as with most topical products not containing corticosteroids. Such an observation should be corroborated with appropriate diagnostic patch testing.

If concomitant skin infections are present or develop, an appropriate antifungal or antibacterial medicine should be used. If a favourable response does not occur promptly, use of **HYDROCORTISONE CREAM GLENMARK** should be discontinued until the infection has been adequately controlled.

Laboratory Tests

The following tests may be helpful in evaluating patients for HPA axis suppression: ACTH stimulation test A.M. plasma cortisol test, Urinary free cortisol test.

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Carcinogenesis, mutagenesis and impairment of fertility

Long-term animal studies have not been performed to evaluate the carcinogenic potential or the effect on fertility of topical corticosteroids. Studies to determine mutagenicity with prednisolone and hydrocortisone have revealed negative results.

Paediatric Use

Safety of this product in paediatric patients has not been established. There is no data on adrenal suppression and/or growth suppression. Therefore, **HYDROCORTISONE CREAM GLENMARK** is not recommended for paediatric use.

Because of a higher ratio of skin surface area to body mass, paediatric patients are at a greater risk than adults of HPA axis suppression and Cushing's syndrome when they are treated with topical corticosteroids. They are therefore also at a greater risk of adrenal insufficiency during and/or after withdrawal of treatment. Adverse effects including striae have been reported with inappropriate use of topical corticosteroids in infants and children.

HPA axis suppression, Cushing's syndrome, linear growth retardation, delayed weight gain, and intracranial hypertension have been reported in children receiving topical corticosteroids. Manifestations of adrenal suppression in children include low plasma cortisol levels, and an absence of response to ACTH stimulation. Manifestations of intracranial hypertension include bulging fontanelles, headaches, and bilateral papilledema.

Elderly Use

Clinical studies of **HYDROCORTISONE CREAM GLENMARK** did not include sufficient numbers of subjects aged 65 and older to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

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4.5 Interaction with other medicines and other forms of interaction

No interactions reported.

4.6 Fertility, pregnancy and lactation

Pregnancy:

Corticosteroids have been shown to be teratogenic in laboratory animals when administered systemically at relatively low dosage levels. Some corticosteroids have been shown to be teratogenic after dermal application in laboratory animals.

The use of **HYDROCORTISONE CREAM GLENMARK** is contraindicated during pregnancy.

Dermal embryofoetal developmental studies were conducted in rabbits and rats with hydrocortisone valerate cream. Hydrocortisone valerate cream was administered topically for 4 hours/day, rather than the preferred 24 hours/day, during the period of organogenesis in rats (gestational days 5-16) and rabbits (gestational days 6-19).

Topical doses of hydrocortisone valerate up to 9 mg/kg/day (54 mg/m^2/day) were administered to rats and 5 mg/kg/day (60 mg/m^2/day) were administered to rabbits. In the absence of maternal toxicity, a significant increase in delayed skeletal ossification in foetuses was noted at 9 mg/kg/day [2.5 x the Maximum Recommended Human Dose (MRHD) based on body surface area (BSA) comparisons] in the rat study. No malformations in the foetuses were noted at 9 mg/kg/day (2.5 x MRHD based on BSA comparisons) in the rat study. Indicators of embryofoetal toxicity, significant decrease in foetal weight at 2 mg/kg/day (1 x MRHD based on BSA) and a significant increase in post-implantation loss and embryo resorption at 5 mg/kg (3 x MRHD based on BSA), were noted in the rabbit study.

A significant increase in delayed skeletal ossification in foetuses was noted at 5 mg/kg/day (3 x the MRHD based on BSA comparisons) in the rabbit study.

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Increased numbers of foetal malformations (e.g., cleft palate, omphalocele and clubbed feet) were noted at 5 mg/kg/day (3 x MRHD based on BSA comparisons) in the rabbit study.

Breastfeeding:

Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in human milk. Because many drugs are excreted in human milk, caution should be exercised when **HYDROCORTISONE CREAM GLENMARK** is administered to a nursing woman.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

4.8 Undesirable effects

a. Summary of the safety profile

The following local adverse reactions have been reported with topical corticosteroids, and they may occur more frequently with the use of occlusive dressings.

b. Tabulated adverse reactions

Tabulated list of adverse reactions for **HYDROCORTISONE CREAM GLENMARK**

System Organ Class	Frequency	Undesirable effect
Infections and infestations	Common	Infection, fungal infection
Gastrointestinal disorders	Common	Gastrointestinal disorder
Skin and subcutaneous tissue disorders	Very common	Stinging
	Common	Eczema, burning skin, skin irritation, eczema, pruritus, rash, rash maculopapular, dry skin
	Unknown	Itching, folliculitis, hypertrichosis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis,

		maceration of the skin, secondary infection, skin atrophy, striae, miliaria.
General disorders and administration site conditions	Common	Application site reaction

Description of selected adverse reactions:

Local adverse reactions may occur with use of topical corticosteroids and may be more likely to occur with occlusive use, prolonged use or use of higher potency corticosteroids. Some local adverse reactions may be irreversible.

Reactions may include atrophy, striae, telangiectasias, burning, itching, irritation, dryness, folliculitis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, secondary infection, and miliaria.

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 "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Topically applied **HYDROCORTISONE CREAM GLENMARK** can be absorbed in sufficient amounts to produce systemic effects (see *section 4.3*).

Treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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A 21.5.1 Corticosteroids and analogues

Hydrocortisone valerate cream USP, 0.2% contains hydrocortisone valerate, 11,21-dihydroxy-17-[(1-oxopentyl)oxy]-(11β)-pregn-4-ene-3,20-dione, a synthetic corticosteroid for topical dermatologic use. The corticosteroids constitute a class of primarily synthetic steroids used topically as anti-inflammatory and antipruritic medicines.

Hydrocortisone valerate has anti-inflammatory, antipruritic and vasoconstrictive properties. The mechanism of the anti-inflammatory activity of the topical steroids, in general, is unclear. However, corticosteroids are thought to act by the induction of phospholipase A2 inhibitory proteins, collectively called lipocortins. It is postulated that these proteins control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of their common precursor arachidonic acid. Arachidonic acid is released from membrane phospholipids by phospholipase A2.

5.2 Pharmacokinetic properties

The extent of percutaneous absorption of topical corticosteroids is determined by many factors including the vehicle and the integrity of the epidermal barrier. Occlusive dressings with hydrocortisone for up to 24 hours have not been demonstrated to increase penetration; however, occlusion of hydrocortisone for 96 hours markedly enhances penetration. Topical corticosteroids can be absorbed from normal intact skin. Inflammation and/or other disease processes in the skin may increase percutaneous absorption.

Studies performed with hydrocortisone valerate cream USP, 0.2% indicate that they are in the medium range of potency as compared with other topical corticosteroids.

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6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Citric acid monohydrate, methyl paraben, polyoxyl strearyl ether, propylene glycol, purified water, sepineo P 600, sodium lauryl sulfate, steareth-100, stearyl alcohol, white petroleum.Absolute ethyl alcohol, docetaxel, nitrogen polysorbate 80.

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

None.

6.5 Nature and contents of container

HYDROCORTISONE CREAM GLENMARK:

Pack: 15 g

A filled and crimped 15 g Aluminium tube packed in a carton along with a leaflet.

Pack: 45 g

A filled and crimped 45 g Aluminium tube packed in a carton along with a leaflet.

Pack: 60 g

A filled and crimped 60 g Aluminium tube packed in a carton along with a leaflet.

6.6 Special precautions for disposal and other handling

None.

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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)

55/21.5.1/0072

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

19 September 2023

10. DATE OF REVISION OF THE TEXT