1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

PERSIVATE OINTMENT 5 mg/5 g

PERSIVATE 5 mg/5 g cream

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 g of PERSIVATE OINTMENT contains betamethasone valerate equivalent to 5 mg betamethasone.

Each 5 g of PERSIVATE cream contains betamethasone valerate equivalent to 5 mg betamethasone.

Preservative*:*

PERSIVATE cream: Chlorocresol 1 % *m/m*

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

PERSIVATE OINTMENT is a soft, smooth, translucent whitish ointment.

PERSIVATE cream is a soft, smooth, homogenous, white cream.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

PERSIVATE is indicated for the treatment of non-infected steroid responsive dermatoses.

4.2 Posology and method of administration

Posology

Adults

PERSIVATE OINTMENT: Apply to the affected areas 2 or 3 times daily by gentle inunction or use with occlusive dressings.

PERSIVATE cream: Apply to the affected areas 2 to 3 times daily by gently inunction.

Paediatric population

PERSIVATE should not be used on infants and young children.

Method of administration

For topical administration.

4.3 Contraindications

PERSIVATE is contraindicated in:

- Patients with hypersensitivity to betamethasone or to any excipients in PERSIVATE (see section 6.1).
- Skin lesions caused by infection with viruses (e.g. herpes simplex, vaccinia or varicella), fungi (e.g. candidiasis, tinea) or bacteria (e.g. impetigo).
- Long term use is contraindicated in patients with diabetes mellitus or tuberculosis.
- Rosacea, acne vulgaris, peri-oral dermatitis, peri-anal and genital pruritus, tuberculosis of the skin, varicose ulcers, untreated cutaneous infections and pruritis without inflammation.

- Nappy areas of infants for flexural eruptions or dermatoses in children under one year of age, including dermatitis.
- Pregnancy (see section 4.6).

4.4 Special warnings and precautions for use

FOR EXTERNAL USE ONLY.

KEEP OUT OF REACH OF CHILDREN.

Hypersensitivity

PERSIVATE should be used with caution in patients with a history of local hypersensitivity to other corticosteroids. Local hypersensitivity reactions (*see section 4.8)* may resemble symptoms of the condition under treatment.

Hypercortisolism

Manifestations of hypercortisolism (Cushing's syndrome) and reversible hypothalamic-pituitary-adrenal (HPA) axis suppression, leading to glucocorticosteroid insufficiency, can occur in some individuals as a result of increased systemic absorption of topical steroids.

Depression of the hypothalmic-pituitary-adrenal axis with consequent suppression of the adrenal gland may occur, and may be precipitated by an infection or trauma. These effects are most likely to be severe in children.

If either of the above are observed, gradually reduce the use of PERSIVATE by reducing the frequency of application, or by substituting a less potent corticosteroid. Abrupt withdrawal of treatment may result in glucocorticosteroid insufficiency (see section 4.8).

Systemic absorption

Systemic absorption of topically applied PERSIVATE may occur, particularly under the following

conditions; when large quantities are used, or when application is made to wide areas of the body or to damaged skin, and when the occlusive dressing technique is applied.

Risk factors for increased systemic effects are:

- Potency and formulation of topical steroid.
- Duration of exposure.
- Application to a large surface area.
- Use on occluded areas of skin e.g. on intertriginous areas or under occlusive dressings.
- Increasing hydration of the stratum corneum.
- Use on thin skin areas such as the face.
- Use on broken skin or other conditions where the skin barrier may be impaired.
- In comparison with adults, children may absorb proportionally larger amounts of topical corticosteroids and thus be more susceptible to systemic adverse effects. This is because children have an immature skin barrier and a greater surface area to body weight ratio compared with adults.

Paediatric population

In children under 12 years of age, treatment courses should be limited to five days and occlusion should not be used; long-term continuous topical corticosteroid therapy should be avoided where possible, as adrenal suppression can occur (see section 4.3).

Infection risk with occlusion

Bacterial infection is encouraged by the warm, moist conditions within skin folds or caused by occlusive dressings. When using occlusive dressings, the skin should be cleansed before a fresh dressing is applied.

Use in Psoriasis

PERSIVATE should be used with caution in psoriasis as rebound relapses, development of tolerances, risk of generalised pustular psoriasis and development of local or systemic toxicity due to impaired barrier function of the skin have been reported in some cases. If used in psoriasis careful patient supervision is important.

The treatment of psoriasis with PERSIVATE may provoke the pustular form of the disease.

Application to the face

Prolonged application to the face is undesirable as this area is more susceptible to atrophic changes; therefore, treatment courses should be limited to five days and occlusion should not be used.

Application near eyes

PERSIVATE should be used with caution near the eyes and should be used for short courses only. Application to the eyes has produced corneal ulcers, raised intraocular pressure, and reduced visual function.

If applied to the eyelids, care is needed to ensure that the preparation does not enter the eye, as cataract and glaucoma might result from repeated exposure.

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.

Concomitant infection

If a secondary microbial skin infection is present suitable concomitant antimicrobial therapy should be instituted.

Appropriate antimicrobial therapy should be used whenever treating inflammatory lesions which have become infected. Any spread of infection requires withdrawal of topical corticosteroid therapy and administration of appropriate antimicrobial therapy.

Chronic leg ulcers

PERSIVATE should not be used to treat infections and ulcers of the leg. It causes delayed wound healing and increased liability to infections.

PERSIVATE should not be applied to any skin crease areas.

Topical corticosteroids should not be used to treat the dermatitis around chronic leg ulcers, as this use may be associated with a higher occurrence of local hypersensitivity reactions and an increased risk of local infection (see section 4.3).

Topical steroid withdrawal syndrome

Long term continuous or inappropriate use of topical steroids can result in the development of rebound flares after stopping treatment (topical steroid withdrawal syndrome). A severe form of rebound flare can develop which takes the form of a dermatitis with intense redness, stinging and burning that can spread beyond the initial treatment area. It is more likely to occur when delicate skin sites such as the face and flexures are treated. Should there be a reoccurrence of the condition within days to weeks after successful treatment a withdrawal reaction should be suspected. Reapplication should be with caution and specialist advise is recommended in these cases or other treatment options should be considered.

The use of PERSIVATE during pregnancy is not recommended.

Treatment should be discontinued if unfavourable reactions are seen. Regular review should be made of the necessity for continuing therapy.

Excipients

PERSIVATE contains chlorocresol. Chlorocresol can cause allergic reactions. PERSIVATE should be discontinued if this occurs.

4.5 Interaction with other medicines and other forms of interaction

CYP3A4 Inhibitors

Co-administered drugs that can inhibit CYP3A4 (e.g. ritonavir, itraconazole) have been shown to inhibit the metabolism of corticosteroids leading to increased systemic exposure. The extent to which this interaction is clinically relevant depends on the dose and route of administration of the corticosteroids and the potency of the CYP3A4 inhibitor.

4.6 Fertility, pregnancy and lactation

The use of PERSIVATE is contraindicated in pregnancy (see section 4.3).

Pregnancy

Corticosteroids have been shown to be teratogenic in animals following dermal application. As these medicines are absorbed percutaneously, teratogenicity following topical application, cannot be excluded.

The use of PERSIVATE during pregnancy is not recommended.

Breastfeeding

The safe use of PERSIVATE during breastfeeding has not been established.

It is not known whether topical administration of PERSIVATE could result in sufficient systemic absorption to produce detectable amounts in breast milk.

If used during breastfeeding, PERSIVATE should not be applied to the breasts to avoid accidental ingestion by the infant.

Fertility

There is no data in humans to evaluate the effect of topical corticosteroids on fertility.

4.7 Effects on ability to drive and use machines

PERSIVATE has minor influence on the ability to drive or operate machinery.

Since adverse reactions such as blurred vision have been reported, patients should not drive, use machinery or perform any tasks that require concentration until they are certain that PERSIVATE does not adversely affect their ability to do so safely (see section 4.4 and 4.8).

4.8 Undesirable effects

a) Tabulated list of adverse reactions

System organ class	**Frequent**	**Less frequent**	**Frequency unknown** (cannot be estimated from the available data)
Infections and infestations		Opportunistic infection	
Immune system disorders		Hypersensitivity, generalised rash	
Endocrine disorders		Hypothalamic-pituitary adrenal (HPA) axis suppression Cushingoid features (e.g. moon face, central obesity), delayed weight gain/growth retardation in children, hyperglycaemia/glucosuri	

		a, decreased endogenous cortisol levels	
Metabolism and nutrition disorders		Increased weight/obesity	
Nervous system disorders			Benign intracranial hypertension
Eye disorders		Glaucoma, cataract	Vision, blurred (see also section 4.4)
Vascular disorders		Hypertension	
Skin and subcutaneous tissue disorders	Pruritus, local skin burning /skin pain	Allergic contact dermatitis /dermatitis, erythema, rash, urticaria, pustular psoriasis, skin thinning* / skin atrophy*, skin wrinkling*, skin dryness*, striae*, telangiectasias*, dilatation of superficial blood vessels, pigmentation, hypopigmentation changes*,hypertrichosis, exacerbation of underlying symptoms, alopecia, trichorrhexis	Withdrawal reactions - redness of the skin which may extend to areas beyond the initial affected area, burning or stinging sensation, itch, skin peeling, oozing pustules. (see section 4.4), loss of elasticity, ecchymoses , bruising, purpura, Rosacea-like dermatitis, perioral dermatitis, acneiform eruptions,
Musculoskeletal and connective tissue disorders		Osteoporosis,	
General disorders and administrative site conditions		Application site irritation/pain	

**Skin features secondary to local and/or systemic effects of hypothalamic-pituitary adrenal (HPA) axis suppression.*

b) Description of selected adverse reactions

Changes are particularly likely to occur on the face and when occlusive dressings are used.

Occlusive dressings are associated with maceration of the skin and miliaria. Local infection may be worsened and spread enhanced.

c) Paediatric population

Growth retardation in children has been reported.

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 requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

Aspen Pharmacare:

E-mail: Drugsafety@aspenpharma.com

Tel: 0800 118 088/+27 (0)11 239-6200

4.9 Overdose

Symptoms

Topically applied betamethasone valerate as contained in PERSIVATE may be absorbed in sufficient amounts to produce systemic effects. Acute overdosage is very unlikely to occur, however, in the case of chronic overdosage or misuse the features of hypercortisolism may occur (*see section 4.4)*.

Management

Treatment is supportive and symptomatic.

In the event of overdose, betamethasone valerate as contained in PERSIVATE should be withdrawn gradually by reducing the frequency of application, or by substituting a less potent corticosteroid because of the risk of glucocorticosteroid insufficiency.

Further management should be as clinically indicated or as recommended by the national poisons centre, where available.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and Class A 13.4.1 Corticosteroids with or without anti-infective agents.

Pharmacotherapeutic group: Corticosteroids, potent (group III)

ATC code: D07AC

Mechanism of action

Betamethasone valerate is a potent topical corticosteroid which exhibits anti-inflammatory and anti-allergic properties when applied to the skin and mucosa.

The mechanism of action is related to causing vasoconstriction, stabilizing lysosomal membranes, suppressing cell division and suppressing the immune response.

Pharmacodynamic effects

Topical corticosteroids have anti-inflammatory, antipruritic, and vasoconstrictive properties.

5.2 Pharmacokinetic properties

Absorption

Topical corticosteroids can be systemically absorbed from intact healthy skin. The extent of percutaneous absorption of topical corticosteroids is determined by many factors, including the vehicle and the integrity of the epidermal barrier. Occlusion, inflammation and/or other disease processes in the skin may also increase percutaneous absorption.

Distribution

The use of pharmacodynamic endpoints for assessing the systemic exposure of topical corticosteroids is necessary because circulating levels are well below the level of detection.

Biotransformation

Once absorbed through the skin, topical corticosteroids are handled through pharmacokinetic pathways similar to systemically administered corticosteroids. They are metabolised, primarily in the liver.

Elimination

Topical corticosteroids are excreted by the kidneys. In addition, some corticosteroids and their metabolites are also excreted in the bile.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

PERSIVATE OINTMENT: Beeswax white, cholesterol, propylene glycol, stearyl alcohol, white soft paraffin.

PERSIVATE cream: Cetyl alcohol, chlorocresol, citric acid monohydrate (for pH adjustment), disodium hydrogen phosphate (for pH adjustment), emulsifying wax, liquid paraffin, propylene glycol, purified water.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

PERSIVATE OINTMENT:
White HDPE Jar: 36 months
Aluminium tube: 60 months
PERSIVATE cream:
White HDPE Jar: 36 months
Aluminium tube: 48 months

6.4 Special precautions for storage

Store in an airtight container at or below 25 °C.

Protect from light.

Keep in original packaging until required for use.

6.5 Nature and contents of container

PERSIVATE OINTMENT:

15 g is packed in an aluminium collapsible tube, sealed with a white, self-piercing, high density polyethylene screw-cap, and placed in a unit cardboard carton together with a leaflet.

500 g is packed into a white round high density polyethylene jar sealed with a white, polypropylene screw-cap.

PERSIVATE cream:

15 g is packed in an aluminium collapsible tube, sealed with a white, self-piercing, high density polyethylene screw-cap, and placed in a unit cardboard carton together with a leaflet.

500 g is packed into a white round high density polyethylene jar sealed with a white, polypropylene screw-cap.

Not all packs and pack sizes are necessarily marketed.

6.6 Special precautions for disposal

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

8. REGISTRATION NUMBER

PERSIVATE OINTMENT: L/13.4.1/395

PERSIVATE cream: L/13.4.1/382

9. DATE OF FIRST AUTHORISATION

Date of registration:

PERSIVATE OINTMENT: 06 June 1980

PERSIVATE cream: 15 June 1981

10. DATE OF REVISION OF TEXT

01 May 2024

Die Afrikaanse Professionele Inligting is op versoek beskikbaar. Mediese Blitslyn: 0800 118 088.

Botswana:	S2
PERSIVATE OINTMENT:	BOT0901496
PERSIVATE cream:	B9322635

Namibia:	NS2
PERSIVATE OINTMENT:	90/13.4.1/001108
PERSIVATE cream:	90/13.4.1/001109

ZA_PERSCOMB_2405_00