SCHEDULING STATUS
S4

1. NAME OF THE MEDICINE
PEVISONE® CREAM 150mg/15mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Econazole nitrate 150 mg/15 g
Triamcinolone acetonide 15 mg/15 g

Preservative:
Benzoic acid 0,2 % *m/m*
Antioxidant:
Butylated hydroxyanisole 0,02 % *m/m*

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Cream.
Soft, white cream with faint odour.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
PEVISONE CREAM is indicated for the treatment of steroid-responsive inflammatory dermatoses with econazole-sensitive mycotic.

4.2 Posology and method of administration
PEVISONE CREAM should be applied sparingly to the skin lesions no more than 2 times daily, preferably once in the morning and once in the evening. PEVISONE CREAM should not be applied with an occlusive dressing, or to large skin areas of the body.

The duration of treatment with PEVISONE CREAM should be until the inflammatory symptoms subside but no longer than 2 weeks; after 2 weeks of therapy with PEVISONE CREAM, continue therapy as needed with a preparation containing econazole or econazole nitrate alone.

4.3 Contraindications
- Hypersensitivity to econazole nitrate, triamcinolone acetonide or any of the excipients listed in section 6.1.
- Specific skin conditions such as varicella, herpes simplex or other viral infections of the skin, or fresh vaccination sites and tuberculosis skin lesions.
- PEVISONE CREAM should not be used in children less than 3 months of age.
- Pregnancy and breastfeeding (see section 4.6).

4.4 Special warnings and precautions for use
For external use only: PEVISONE CREAM is not for ophthalmic or oral use.

Avoid prolonged applications to thin skin and to the face. Potent topical corticosteroid preparations (triamcinolone as contained in PEVISONE CREAM) should not be applied to any skin crease areas.

If a reaction suggesting hypersensitivity or chemical reaction occurs, treatment should be discontinued.

PEVISONE CREAM applied to the skin can be absorbed in sufficient amounts to produce systemic effects, including adrenal suppression. Systemic absorption may be increased by various factors such as application over a large skin surface area, application to damaged skin, application under occlusive skin dressings and prolonged duration of therapy.

Repeated application and/or prolonged application of PEVISONE CREAM in the periorbital region may induce cataracts, ocular hypertension, or increase the risk of glaucoma in patients.

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.

PEVISONE CREAM is associated with skin thinning and atrophy, striae, rosacea, perioral dermatitis, acne telangiectasis, purpura, hypertrichosis and delayed wound healing.

Topical PEVISONE CREAM may lead to increased risk of dermatological superinfection or opportunistic infection.

Paediatric patients may demonstrate greater susceptibility to topical corticosteroid-induced HPA (hypothalamic-pituitary-adrenal) – axis suppression and Cushing's syndrome than mature patients because of a higher ratio of skin surface to body mass. Caution should be exercised when PEVISONE CREAM is administered to paediatric patients and treatment should be discontinued if signs of HPA axis suppression or Cushing's syndrome occur.

The following special precautions are recommended:
(a) If a secondary microbial skin infection is present, suitable concomitant anti-microbial therapy should be instituted.
(b) PEVISONE CREAM should be used with particular caution in facial dermatoses, and only for short periods. Steroid rosacea-like facies may be produced.
(c) PEVISONE CREAM preparations should be used with caution near the eyes.
(d) PEVISONE CREAM should be used for short courses only.
(e) Regular review should be made of the necessity for continuing therapy with PEVISONE CREAM.
(f) PEVISONE CREAM should not be used in the nappy areas in infants for flexural eruptions and they should not be used in infants and young children at all.
(g) The treatment of psoriasis with PEVISONE CREAM may provoke the pustular form of the disease.

Excipients
PEVISONE CREAM contains benzoic acid as a preservative and butylated hydroxyanisole as an antioxidant.
Benzoic acid may cause non-immunologic immediate contact reactions by a possible cholinergic mechanism.

Butylated hydroxyanisole may cause local skin reactions (e.g. contact dermatitis) or irritation

to the eyes and mucous membranes.

4.5 Interaction with other medicines and other forms of interaction
PEVISONE CREAM is a known inhibitor of CYP3A4/2C9. After cutaneous application clinical relevant interactions have been reported with oral anticoagulants. Therefore, in patients taking oral anticoagulants, such as warfarin or acenocoumarol, prothrombin time (INR) should be monitored.

4.6 Fertility, pregnancy and lactation
Pregnancy
Corticosteroids such as PEVISONE CREAM have been shown to be teratogenic in animals following dermal application. As these medicines are absorbed percutaneously, teratogenicity following topical application cannot be excluded. Therefore, PEVISONE CREAM should not be used during pregnancy (see section 4.3).

Breastfeeding
Safety in lactation has not been established.
Mothers on PEVISONE CREAM should not breastfeed their infants (see section 4.3).

Fertility
Safety has not been established.

4.7 Effects on ability to drive and use machines
None known.

4.8 Undesirable effects
a. Summary of the safety profile
Adverse reactions reported during clinical trials:
Adverse reactions are listed below by system organ class and frequency. Frequencies are defined as: Very common (≥ 1/10); common (≥ 1/100, < 1/10); uncommon (≥ 1/1 000, < 1/100); rare (≥ 1/10 000, < 1/1 000); very rare (< 1/10 000).

The safety of PEVISONE CREAM was evaluated in 182 adults who participated in 4 clinical trials and evaluated in 101 children (ages 3 months to 10 years) who participated in 1 clinical trial. Adverse reactions that occurred in ≥ 1 % of adults and children treated with PEVISONE CREAM in these studies are listed below in Table 1.

b. Tabulated list of adverse reactions
Table 1: Adverse reactions reported by ≥ 1 % of adults and children treated with PEVISONE CREAM in 4 clinical trials and 1 clinical trial, respectively.

System Organ Class Adverse reaction	**Frequency**
Skin and subcutaneous tissue disorder Skin burning sensation Skin irritation Erythema	Common

No adverse reactions were reported in < 1 % of adults and children treated with PEVISONE CREAM in the 4 clinical trials and the 1 clinical trial, respectively.

Post-marketing experience
Adverse reactions first identified during post-marketing experience with PEVISONE CREAM are included in Table 2.

Table 2: Adverse reactions identified during post-marketing experience with PEVISONE CREAM

Immune system disorders Hypersensitivity
General disorders and administration site conditions Application site pain, application site swelling.
Skin and subcutaneous tissue disorders Angioedema, contact dermatitis, skin atrophy, pruritus, skin exfoliation, skin striae, telangiectasia, erythema. Frequency not known (cannot be estimated from available data) 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).

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.
Reporting can also be done directly to Adcock Ingram Limited at:
E-mail: Adcock.aereports@adcock.com
Tel: 011 635 0134

4.9 Overdose
PEVISONE CREAM is for cutaneous application only. PEVISONE CREAM, can be absorbed in sufficient amounts to produce systemic events.

In the event of accidental ingestion, treat symptomatically. If PEVISONE CREAM is accidentally applied to the eyes, wash with clean water or 0,9 % sodium chloride.

5. PHARMACOLOGICAL PROPERTIES
A 13.4.1 Dermatological preparations – Corticosteroids with or without anti-infective agents. Pharmacotherapeutic group: Imidazoles/triazoles in combination with corticosteroids; ATC code: D01AC20.

5.1 Pharmacodynamic properties
PEVISONE CREAM is a combination of econazole nitrate plus triamcinolone acetonide.

Econazole nitrate
Econazole nitrate acts by damaging fungal cell membranes, resulting in increased permeability. Sub-cellular membranes in the cytoplasm are damaged. The site of action is most probably the unsaturated fatty acid acyl moiety of membrane phospholipids.

Triamcinolone acetonide
Triamcinolone acetonide is primarily effective because of its anti-inflammatory, antipruritic and vasoconstrictive actions, characteristic of the topical corticosteroid class of medicines. The pharmacologic effects of the topical corticosteroids are well-known; however, the mechanisms of their dermatologic actions are unclear. Various laboratory methods, including vasoconstrictor assays, are used to compare and predict potencies and/or clinical

efficacies of the topical corticosteroids. There is some evidence to suggest that a recognisable correlation exists between vasoconstrictor potency and therapeutic efficacy in man.

Microbiology
Econazole possesses a broad spectrum of antimycotic activity that has been demonstrated against dermatophytes, yeasts and moulds. A clinically relevant action against gram-positive bacteria has also been found.

5.2 Pharmacokinetic properties

Econazole nitrate

Absorption
Systemic absorption of econazole is extremely low after topical application to the skin. Mean peak plasma/serum concentrations of econazole and/or its metabolites were observed 1 to 2 days after dose administration and were < 1 ng/mL for the 2 % dermal cream applied to intact skin and 20 ng/mL for the 2% dermal cream applied to stripped skin. Although most econazole remains on the skin surface (approximately 90 %) after application of a 1 % cream, concentrations of econazole that have been found in the stratum corneum exceed the minimum inhibitory concentration for dermatophytes, and inhibitory concentrations are achieved in the middermis.

Distribution
Econazole and/or its metabolites in the systemic circulation are extensively bound (> 98 %) to serum proteins.

Biotransformation
Econazole that reaches the systemic circulation is extensively metabolised by oxidation of the imidazole ring, followed by O-dealkylation and glucuronidation.

Elimination
Econazole and its metabolites are eliminated in urine and faeces in approximately equal amounts.

Triamcinolone acetonide

Absorption
The extent of percutaneous absorption of topical corticosteroids is determined by many factors including the vehicle, the integrity of the epidermal barrier, and the use of occlusive dressings.

Topical corticosteroids can be absorbed from normal intact skin. Inflammation and/or other disease processes in the skin increase percutaneous absorption. Occlusive dressings substantially increase the percutaneous absorption of topical corticosteroids. Thus, occlusive dressings may be a valuable therapeutic adjunct for treatment of resistant dermatoses (see section 4.2).

Distribution
Once absorbed through the skin, topical corticosteroids are handled through pharmacokinetic pathways similar to systemically administered corticosteroids. Corticosteroids are bound to plasma proteins in varying degrees.

Biotransformation
Corticosteroids are metabolised primarily in the liver.

Elimination
Corticosteroids are then excreted by the kidneys. Some of the topical corticosteroids and their metabolites are also excreted into the bile.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Benzoic acid
Butylated hydroxyanisole
Disodium edetate
Liquid paraffin
Oleoyl macrogolglycerides,
PEG-6 (and) PEG-32 (and) glycerol stearate
Purified water

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
24 months.

6.4 Special precautions for storage
Store at or below 25 °C.

6.5 Nature and contents of container
15 g and 30 g Aluminium tubes with a polypropylene screw cap.

6.6 Special precautions for disposal
No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION
Adcock Ingram Limited
1 New Road,
Erand Gardens
Midrand, 1685
Customer Care: 0860 ADCOCK / 232625

8. REGISTRATION NUMBER
Q/13.4.1/0220

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
06 May 1983

10. DATE OF REVISION OF THE TEXT
02 February 2024

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