SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Pevaryl 1% Topical cream

2. Qualitative and Quantitative Composition

Econazole nitrate - 1.0% w/w.

Each gram of cream contains 10 mg econazole nitrate.

Excipients of known effect:

Benzoic acid (E210)	2 mg/g
Butylhydroxyanisole (E320)	0.052 mg/g

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Cream.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of cutaneous candidiasis, dermatophytosis and pityriasis versicolor.

4.2 Posology and method of administration

For cutaneous administration.

Dosage

The dosage regimen is the same for all patients.

Apply twice daily to the affected part and rub into the skin gently with the finger.

The usual treatment duration is 2 to 4 weeks.

If no improvement in symptoms is experienced after 4 weeks, the treatment should be reassessed.

4.3 Contraindications

Pevaryl Topical Cream is contraindicated in individuals who have shown hypersensitivity to any of its ingredients.

4.4 Special warnings and precautions for use

For external use only. Care should be taken not to get Pevaryl Topical Cream in the eyes or mouth. If the product is accidently applied to the eyes the patient should wash with clean water or saline and seek medical attention if symptoms persist.

If a reaction suggesting sensitivity or chemical irritation should occur, use of the medication should be discontinued.

Care should be taken in the presence of eczematous dermatitis.

Excipients

This medicine contains 30 mg benzoic acid in each tube of 15 g which is equivalent to 2 mg/g cream.
This medicine contains 60 mg benzoic acid in each tube of 30 g which is equivalent to 2 mg/g cream.
Benzoic acid may cause local irritation.
Benzoic acid may increase jaundice (yellowing of the skin and eyes) in newborn babies (up to 4 weeks old).

Butylhydroxyanisole (E320): May cause local skin reactions (e.g. contact dermatitis) or irritation to the eyes and mucous membranes.

4.5 Interaction with other medicinal products and other forms of interaction

Econazole administered systemically is known to inhibit CYP3A4/2C9. Due to the limited systemic availability after topical application, clinically relevant interactions are rare. However, in patients on oral anticoagulants, such as

warfarin and acenocoumarol, caution should be exercised and anticoagulant effect should be monitored more frequently.

Adjustment of the oral anticoagulant dosage may be necessary during the treatment with econazole and after its termination

4.6 Fertility, pregnancy and lactation

Pregnancy

Systemic absorption of econazole is low (< 10%) after topical application to the intact skin in humans. There are no adequate and well-controlled studies on adverse effects from the use of Pevaryl Topical cream in pregnant women, and no other relevant epidemiological data are available.

Animal studies have shown reproductive toxicity (see section 5.3).

Because there is systemic absorption, use of Pevaryl Topical Cream is not recommended during pregnancy.

Breast-feeding

It is not known whether cutaneous administration of Pevaryl Topical cream results in sufficient systemic absorption of econazole nitrate to produce detectable quantities in breast milk in humans (see section 5.3).

A risk to the breast-fed child cannot be excluded.

A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Pevaryl Topical Cream therapy taking into account the benefit of breast-feeding for the child and benefit of therapy for the woman.

If Pevaryl Topical Cream is used while breast-feeding, care should be taken to ensure the cream is not applied to the nipple or surrounding area.

Fertility

Results of econazole animal reproduction studies showed no effects on fertility.

4.7 Effects on ability to drive and use machines

None known

4.8 Undesirable effects

The safety of econazole nitrate cream (1%) and econazole nitrate emulsion (1%) was evaluated in 470 subjects who participated in 12 clinical trials and received at least one administration of either formulation. Based on pooled safety data from these clinical trials, the most commonly reported (≥1% incidence) adverse reactions were (with % incidence): pruritus (1.3%), skin burning sensation (1.3%), and pain (1.1%).
Including the above-mentioned adverse reactions, the following table displays adverse reactions that have been reported with the use of PEVARYL Dermatological Formulations from either clinical trial or post-marketing experiences. The displayed frequency categories use the following convention:

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); and not known (cannot be estimated from the available clinical trial data).
In the PEVARYL Dermatological Formulations adverse reaction table below, all adverse reactions with a known incidence (common or uncommon) are from clinical trial data and all adverse reactions with an unknown incidence are from post-marketing data.

Table 1: Adverse Reactions

System Organ Class	**Adverse Reactions**		
	Frequency Category		
	Common (≥1/100 to <1/10)	**Uncommon** (≥1/1,000 to <1/100)	**Not Known**
Immune System Disorder			Hypersensitivity
Skin and Subcutaneous Tissue Disorders	Pruritus Skin burning sensation	Erythema	Angioedema Contact dermatitis Rash Urticaria Blister Skin exfoliation
General Disorders and Administration Site Conditions	Pain	Discomfort Swelling	

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at:

www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Pevaryl Topical Cream is for cutaneous application only. In the event of accidental ingestion, treat symptomatically.

If large amounts have been taken by mouth or swallowed, use appropriate supportive care.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antifungals For Topical Use, Imidazole and triazole derivatives, econazole; ATC code: D01AC03.

Econazole nitrate is a broad spectrum antimycotic with activity against dermatophytes, yeasts and moulds. A clinically relevant action against Gram positive bacteria has also been found

5.2 Pharmacokinetic properties

Econazole nitrate is only slightly absorbed from the skin. No active drug has been detected in the serum. Radio labelling shows that less than 0.1% of an oral dose is absorbed. Peak serum levels are achieved after 2 hours and 90% binds to plasma proteins. Metabolism is limited but occurs primarily in the liver with excretion of metabolites in the urine.

5.3 Preclinical safety data

Low neonatal survival and fetal toxicity was associated only with maternal toxicity. In animal studies, econazole nitrate has shown no teratogenic effects but was foetotoxic in rodents at maternal subcutaneous doses of 20 mg/kg/day and at maternal oral doses of 10 mg/kg/day. The significance of this in humans is unknown.

Following oral administration of econazole nitrate to lactating rats, econazole and/or metabolites were excreted in milk and were found in nursing pups.

6. Pharmaceutical Particulars

6.1 List of excipients

Macrogols (PEG-6 and PEG-32) / glycol stearate
Oleoyl macrogolglycerides
Liquid paraffin
Butylhydroxyanisole (E320)
Benzoic acid (E210)
Purified water

6.2 Incompatibilities

None stated.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Do not store above 25° C.

6.5 Nature and contents of container

Resin lined, aluminium tubes containing 15g or 30g of cream.

6.6 Special precautions for disposal

No special requirements.

Any unused product or waste material should be disposed of in accordance with local requirements

7 MARKETING AUTHORISATION HOLDER

Karo Pharma AB
Box 16184
103 24 Stockholm
Sweden

8 MARKETING AUTHORISATION NUMBER(S)

PL 50567/0007

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

01/07/1995 / 04/10/2010

10 DATE OF REVISION OF THE TEXT

16/11/2022