

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Gyno-Pevaryl Cream.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 100 g of cream contains 1 g econazole nitrate (1% w/w).

Excipients of known effect:

Benzoic acid (E210)	2 mg/g
Butylated hydroxyanisole (E320)	0.052 mg/g

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Vaginal cream

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of mycotic vulvovaginitis and mycotic balanitis.

4.2 Posology and method of administration

Route of Administration

For vaginal/penile administration.

Females: One applicator full (approximately 5 g) intravaginally once daily at night for not less than 14 days. The cream should also be applied to the vulva. The full 14 days treatment should be carried out even if the symptoms of vaginal itching or discharge have disappeared.

In pregnant women, it is recommended that administration takes place without the use of an applicator, or is performed by a physician. Pregnant women should thoroughly wash their hands before self-administering Gyno-Pevaryl cream.

Males: Apply the cream to the penis, including under the foreskin, once daily for not less than 14 days.

The sexual partner should also be treated.

4.3 Contraindications

Hypersensitivity to any imidazole preparation, other vaginal antifungal products or to any ingredients of Gyno- Pevaryl cream.

4.4 Special warnings and precautions for use

Not for ophthalmic or oral use.

Hypersensitivity has rarely been recorded; if it should occur administration should be discontinued.

Contact between contraceptive diaphragms or condoms and this product must be avoided since the rubber may be damaged by the preparation.

Patients using spermicidal contraceptives should consult their physician since any local vaginal treatment may inactivate the spermicidal contraceptive (see section 4.5).

Gyno-Pevaryl Cream should not be used in conjunction with other internal or external treatment of the genitalia.

Gyno-Pevaryl Cream is not indicated for use in children under the age of 16 years.

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.

Butylated hydroxyanisole (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 is a known inhibitor of CYP3A4/2C9. Due to the limited systemic availability after vaginal application (see Section 5.2. Pharmacokinetic Properties), clinically relevant interactions are unlikely to occur but have been reported with oral anticoagulants. In patients taking oral anticoagulants, such as warfarin or acenocoumarol, caution should be exercised and the anticoagulant effect should be monitored more frequently.

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

Contact between latex products such as contraceptive diaphragms or condoms and this product must be avoided since the constituents of the product may damage the latex. Patients using spermicidal contraceptives should consult their physician since any local vaginal treatment may inactivate the spermicidal contraceptive (see section 4.4).

4.6 Fertility, pregnancy and lactation

Pregnancy

In animals, econazole nitrate has shown no teratogenic effects but is foetotoxic at high doses. The significance of this to man is unknown as there is no evidence of an increased risk when taken in human pregnancy. However, animal studies have shown reproductive toxicity (see section 5.3). Because there is vaginal absorption, as with other imidazoles, econazole should be used in pregnancy only if the practitioner considers it to be necessary.

Breast-feeding

Following oral administration of econazole nitrate to lactating rats, econazole and/or metabolites were excreted in milk and were found in nursing pups. It is not known whether econazole nitrate is excreted in human milk. Caution should be exercised when using Gyno-Pevaryl Cream if the patient is breast-feeding.

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 Gyno-Pevaryl Vaginal Cream and Vaginal Pessaries was evaluated in 3630 patients who participated in 32 clinical trials.

Based on pooled safety data from these clinical trials, the most commonly reported adverse reactions were (with % incidence) pruritus (1.2%) and skin burning sensation (1.2%).

Including the above mentioned adverse reactions, the following table displays adverse reactions that have been reported with the use of Gyno-Pevaryl Vaginal Cream and Vaginal Pessaries from either clinical trial or postmarketing experiences. The displayed frequency categories use the following convention:

Very common ($\geq 1/10$); common ($\geq 1/100$ to $< 1/10$); uncommon ($\geq 1/1,000$ to $< 1/100$); rare ($\geq 1/10,000$ to $< 1/1,000$); very rare ($< 1/10,000$); and not known (cannot be estimated from the available clinical trial data).

Adverse reactions

System Organ Class	Adverse Reactions			
	Frequency Category			
	Common ($\geq 1/100$ to $< 1/10$)	Uncommon ($\geq 1/1,000$ to $< 1/100$)	Rare ($\geq 1/10,000$ to $< 1/1,000$)	Not known
Immune System Disorders				Hypersensitivity
Skin and Subcutaneous Tissue Disorders	Pruritus, Skin burning sensation	Rash	Erythema	Angioedema, Urticaria, Contact dermatitis, Skin exfoliation
Reproductive System and Breast Disorders		Vulvovaginal burning sensation		
General Disorders and Administrati on Site Conditions				Application site pain, Application site irritation, Application site 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

4.9 Overdose

Adverse events associated with overdose or misuse of Gyno-Pevaryl Cream are expected to be consistent with adverse drug reactions already listed in Section 4.8. (Undesirable effects)

In the event of accidental ingestion, nausea, vomiting and diarrhoea may occur. If necessary treat symptomatically.

If the product is accidentally applied to the eyes, wash with clean water or saline and seek medical attention if symptoms persist.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic classification: (Antiinfectives and antiseptics, excl. combinations with corticosteroids, imidazole derivatives)

ATC code: G01A F05

Econazole nitrate has no anti-inflammatory action, no effect on circulation, no central or autonomic nervous effects, no effects on respiration, no effect on α or β receptors, no anticholinergic or antiserotonergic reactions.

A broad spectrum of antimycotic activity has been demonstrated against dermatophytes, yeasts and moulds. A clinically relevant action against Gram positive bacteria has also been found.

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

5.2 Pharmacokinetic properties

Econazole nitrate is poorly absorbed from the vagina and skin. If given orally, peak plasma levels occur six hours after dosing. About 90% of the absorbed dose is bound to plasma proteins. Metabolism is limited, but primarily occurs in the liver, the metabolites excreted in the urine.

Five major and two minor metabolites have been identified.

5.3 Preclinical safety data

Low neonatal survival and foetal toxicity was associated with high doses. 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. In repeat dose toxicity studies in rats, at high subcutaneous doses (50 mg/kg/day, 300 mg/m²/day) the liver was identified as a target organ with minimal toxicity and full recovery. The human to animal safety margin for liver toxicity (based on Human Equivalent Dose taking into account normalisation of body surface area) is 32 to 126x for a 50 to 70 kg human based on 2.5 to 7% absorption in humans and 83% bioavailability in rats. No significant topical toxicity, phototoxicity, local dermal irritation, vaginal irritation or sensitization was noted. Only mild ocular irritation was noted with a cream formulation.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tefose 63
Labrafil M 1944 CS
Mineral oil
Butylated hydroxyanisole (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

Aluminium lacquered tubes

Pack sizes: 78g, 30g, 15g

6.6 Special precautions for disposal

None stated.

7 MARKETING AUTHORISATION HOLDER

Karo Pharma AB
Box 16184
103 24 Stockholm
Sweden

8 MARKETING AUTHORISATION NUMBER(S)

PL 50567/0008

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE
AUTHORISATION**

22/09/1995 / 04/10/2010

10 DATE OF REVISION OF THE TEXT

15/06/2021