# SUMMARY OF PRODUCT CHARACTERISTICS

## 1 NAME OF THE MEDICINAL PRODUCT

Gyno-Pevaryl Once 150mg vaginal pessary

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each pessary contains econazole nitrate 150 mg

For a full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Light beige torpedo-shaped pessary

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Vaginitis due to Candida Albicans and other yeasts.

### 4.2 Posology and method of administration

*For vaginal administration.*

Adults:

Insert one pessary high into the vagina at night prior to retiring. Pregnant women should thoroughly wash their hands before self-administering Gyno-Pevaryl Once pessary.

Children:

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

Elderly:

No specific dosage recommendations or precautions apply.

## 4.3 Contraindications

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

## 4.4 Special warnings and precautions for use

For intravaginal use only. This preparation is not for 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 once vaginal pessary should not be used in conjunction with other internal or external treatment of the genitalia.

## 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 Once vaginal pessaries 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 (≥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).

**Adverse reactions**

| System Organ Class | Adverse Reactions | | | |
|---|---|---|---|---|
| | Frequency Category | | | |
| | **Common** (≥1/100 to <1/10) | **Uncommon** (≥1/1,000 to <1/100) | **Rare** (≥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 Administration 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 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

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic classification: (Antiinfectives and antiseptics, excl.

combinations with corticosteroids, imidazole derivatives)

*ATC code:* G0lA F05

Econazole is an imidazole derivative. The compound acts by damaging the membranes of bacterial and fungal cells; both the cellular and subcellular membranes are affected. Econazole apparently disturbs the permeability characteristics of the membrane which allow leakage of potassium and sodium ions and other intra cellular components. Macro-molecular synthesis may also be inhibited. Econazole is active against dermatophytes, yeast, moulds and Gram positive bacteria. Gram negative bacteria are generally resistant to econazole.

### 5.2 Pharmacokinetic properties

Econazole nitrate is poorly absorbed after vaginal application. Using radiolabelled techniques, it has been determined that between 2.5% and 7% of vaginally applied econazole nitrate is absorbed. However, no antimycotic activity could be detected in the serum after vaginal application of 5 g or 1% econazole nitrate cream or a suppository containing 50 mg econazole nitrate.

### 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/$m^2$/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

Polygel

Colloidal silicon dioxide
Witepsol H19
Wecobee FS
Stearyl heptanoate

## 6.2 Incompatibilities

None stated.

## 6.3 Shelf life

3 years.

## 6.4 Special precautions for storage

Do not store above 30º C

## 6.5 Nature and contents of container

Multi-plast strip or PVC/PE moulds, containing one pessary.

1 applicator

## 6.6 Special precautions for disposal

Not applicable.

# 7 MARKETING AUTHORISATION HOLDER

Karo Pharma AB
Box 16184
103 24 Stockholm
Sweden

## 8 MARKETING AUTHORISATION NUMBER(S)

PL 50567/0009

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

01/10/1995 / 04/10/2010

## 10 DATE OF REVISION OF THE TEXT

21/06/2021