SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

UNIVAGIL LP 150 mg, sustained release ovule

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Econazole nitrate ..... 150 mg

For a sustained release ovule.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Sustained release ovule.

Ovule white to creamy white.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Local treatment of vulvovaginal mycoses, whether or not surinfected by Gram+ bacteria.

4.2. Posology and method of administration

Posology

- In most cases: 1 ovule in the evening at bedtime as a single administration to be inserted deep into the vagina, preferably while lying down.
- In the case of recurrent or stubborn fungal infection suggesting predisposing factors, one ovule in the evening at bedtime and one ovule the following morning.

Method of administration

Wash with a pH-neutral or alkaline soap.

The treatment will be accompanied by hygiene advice (wearing cotton underwear, avoiding vaginal douches, avoiding the use of internal tampons during treatment…) and, where possible, the elimination of contributing factors.

Do not interrupt treatment during menstruation.

The treatment of the partner will be discussed on a case-by-case basis.

To treat vulvar or perianal extensions of the fungal infection, it is recommended to combine gynecological suppositories with a local antifungal application.

Pregnant women should wash their hands thoroughly before administering UNIVAGIL LP (see section 4.6 Pregnancy and breastfeeding for further recommendations).

4.3. Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1 (or cross-sensitivity with other members of the imidazole group);
- in association with latex condoms or diaphragms, due to the risk of rupture of the diaphragms or latex condoms.

4.4. Special warnings and precautions for use

For vaginal use only. UNIVAGIL LP is not for oral use.

Special warnings

In the absence of suggestive clinical symptoms, the mere observation of candida on the skin or mucous membranes cannot in itself constitute an indication.

Once candidiasis is confirmed, it is necessary to carefully investigate the ecological factors that allow and promote the development of candida .

To avoid relapses, eradication and consideration of contributing factors is essential.

It is advisable to treat simultaneously any associated and known pathogenic candida infection.

The use of latex condoms or diaphragms with an anti-infective vaginal preparation may decrease their contraceptive effectiveness.

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

Patients with sensitivity to imidazoles also showed sensitivity to econazole nitrate .

Precautions for use

In case of local intolerance, significant irritation or allergic reaction, treatment should be discontinued.

It is not recommended to use a soap with an acidic pH (pH which promotes the growth of candida): see section 4.2, practical advice.

4.5. Interactions with other medicinal products and other forms of interaction

Contraindicated combinations

- **Male latex condoms / Latex diaphragms**

Risk of rupture of the diaphragm or latex condom.

Associations not recommended

- **Spermicides**

Any local vaginal treatment is likely to inactivate a spermicidal local contraceptive.

Associations requiring precautions for use

- **Oral anticoagulants**

Econazole is a known inhibitor of CYP3A4/2C9. Despite limited systemic absorption after vaginal application, clinically significant interactions can occur and have been reported in patients taking oral anticoagulants such as warfarin and acenocoumarol (increased effect of the oral anticoagulant and risk of bleeding).

In these patients, precautions must be taken and the INR must be monitored more frequently.

Dosage adjustment of the oral anticoagulant may be necessary during treatment with econazole and after its discontinuation.

4.6. Fertility, pregnancy and breastfeeding

Pregnancy

Animal studies have not shown any teratogenic effects but have demonstrated fetotoxicity at high doses (see section 5.3). It is unknown whether these results are relevant to humans.

In the absence of teratogenic effects in animals, malformations in humans are not expected. Indeed, to date, substances responsible for malformations in humans have been shown to be teratogenic in animals in well-conducted studies on two species.

In clinical practice, no specific malformative or fetotoxic effects have been observed to date. However, the follow-up of pregnancies exposed to econazole is insufficient to rule out all risks.

Due to absorption through the vaginal mucosa, the use of UNIVAGIL LP should not be considered during the 1st trimester of pregnancy unless the doctor considers it necessary.

UNIVAGIL LP can be used during the 2nd and 3rd trimesters of pregnancy if the potential benefit to the mother outweighs the potential risk to the fetus.

Breastfeeding

Absorption of econazole nitrate through the vaginal mucosa is low.

econazole nitrate passes into human breast milk.

Breastfeeding is possible but caution is advised when UNIVAGIL LP is used in a breastfeeding patient.

4.7. Effects on the ability to drive vehicles and use machinery

Not applicable.

4.8. Undesirable effects

The tolerability of econazole was evaluated in 3630 patients participating in 32 clinical trials. Based on pooled tolerability data from these clinical trials, the most frequently reported adverse reactions (in % incidence) were skin and subcutaneous tissue disorders, such as pruritus (1.2%) and skin burning sensation (1.2%).

The table below presents the adverse reactions reported during the use of vaginal econazole in clinical trials (including the adverse reactions mentioned above) as well as adverse reactions from post-marketing data (spontaneous reports).

For adverse reactions reported during clinical trials, the frequency categories presented in the table are defined as follows: 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).

For adverse effects reported from spontaneous notifications, their frequency is undetermined (cannot be estimated from the available data).

Organ system classes	**Side effects**			
	Frequency categories			
	Frequent (≥1/100 to < 1/10)	**Uncommon (≥1/1000 to <1/100)**	**Rare (≥1/10,000 to <1/1,000)**	**Undetermined**
Immune system disorders				Hypersensitivity
Skin and subcutaneous tissue disorders	Itching, burning sensation on the skin	Rash	Erythema	Angioedema , urticaria, contact dermatitis, skin exfoliation
Disease of the reproductive organs and breast		Vulvovaginal burning sensation		
General disorders and administration site abnormalities				Pain at the application site, Irritation at the application site, Swelling at the application site

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals report any suspected adverse reactions via the national reporting system: French National Agency for Medicines and Health Products Safety (ANSM) and the network of Regional Pharmacovigilance Centers - Website : www.ansm.sante.fr .

4.9. Overdose

In case of overdose with UNIVAGIL LP, the expected adverse events are similar to the adverse effects listed in section 4.8 “Undesirable effects”.

In case of accidental ingestion, nausea, vomiting, or diarrhea may occur. Symptomatic treatment should be administered, if necessary.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic class : ANTI-INFECTIVES AND ANTISEPTICS FOR GYNECOLOGICAL USE (G: genitourinary system and sex hormones), ATC code: G01AF05.

Econazole nitrate is an imidazole derivative with antifungal and antibacterial activity.

The activity has been demonstrated *in vitro and is exerted on the agents responsible for* cutaneous and mucosal mycoses :

- Candida and other yeasts (causes of vaginal yeast infections),
- bacteria are sometimes responsible for a superinfection.

In vitro , attempts to select strains of *Candida albicans* resistant to econazole have not revealed acquired resistance; *in vivo* , this risk is minimal.

Mechanism of action

Unlike that of antibiotics, it is located at several levels: membrane (increased permeability), cytoplasmic (inhibition of oxidative processes at the level of mitochondria), nuclear (inhibition of RNA synthesis).

This dosage is suitable for short-term treatment.

5.2. Pharmacokinetic properties

In humans, econazole is poorly absorbed after vaginal administration.

The maximum concentrations of econazole and/or its metabolites in plasma or serum observed 1 to 2 days after administration are approximately 65 ng /ml for a 150 mg ovule. Approximately 5% of the econazole dose is absorbed from a 150 mg ovule .

In systemic circulation, econazole and /or its metabolites are highly bound (>98%) to plasma proteins. Econazole is extensively metabolized by oxidation, deamination, and/or O- dealkylation , and the metabolites are eliminated via the kidneys and feces.

Upon contact with the vaginal mucosa, the excipient in UNIVAGIL LP forms a bioadhesive gel containing econazole nitrate . This gel adheres to the vaginal mucosa, thus maintaining an effective concentration of the active ingredient in the vagina for several days.

5.3. Preclinical safety data

Sub -chronic toxicity

The liver has been identified as the target organ. The safety margin associated with this effect is significant.

Functions of reproduction

Studies have not shown any impairment of fertility or teratogenicity , but fetotoxicity at high doses.

Breastfeeding

After oral administration of econazole nitrate to lactating rats, econazole and /or its metabolites were excreted in the milk and found in breastfed pups.

Genotoxicity

Studies suggest the induction of aneuploidy, and some indicate a mutagenic effect. However, all of these studies indicate that the genotoxic effects are limited.

Local tolerance

Studies conducted have revealed no mucosal or vaginal irritation, no phototoxicity or sensitization.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Galactomannan , anhydrous colloidal silica, solid semi-synthetic glycerides (type WI H 15 and WE FS), stearyl enanthate .

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

3 years.

6.4. Special precautions for storage

Store at a temperature below 25°C.

6.5. Nature and contents of container

1 ovule in a thermoformed blister pack (PVC/PE).

6.6. Special precautions for disposal and handling

No special requirements. Any unused medicinal product or waste material should be disposed of in accordance with local regulations.

7. OPERATORS AND MANUFACTURERS

Holder and operator of the export marketing authorization
FRILAB SA
17, rue des Pierres du Niton
1207 Geneva

Manufacturer
UNITHER industries
Malcourlet Industrial Zone
03800 Gannat , FRANCE

8. DATE OF REVISION OF THE TEXT

2 August 2022

9. DOSIMETRY

Not applicable.

CONDITIONS FOR PRESCRIPTION AND DISPENSING

This medication is not subject to medical prescription.