SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF DRUG

UNIVAGIL LP 150 mg sustained release ovum

2. Qualitative and quantitative composition

Econazole nitrate ..... 150 mg

For a sustained release ovum.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Sustained release ovum

Ovum with a white to cream white color

4. CLINICAL

4.1. Therapeutic indications

Local treatment of vulvovaginal mycoses secondarily infected or not by Gram+ bacteria.

4.2. Dosage and administration

Dosage

- In the majority of cases: one ovum at bedtime in a single administration, introduce deep into the vagina, preferably lying down.
- In the case of recurrent or rebel mycoses, assuming predisposing factors, one ovum at night before sleep and one the next morning

Administration mode

Toilet with a soap at neutral or alkaline pH.

The treatment will be accompanied by advice on hygiene (wearing cotton underwear, avoid vaginal douches, avoid wearing tamons during the treatment...) and removal of predisposing factors if possible

Do not interrupt treatment during menstruation.

Partner treatment is discussed according to each case.

To treat vulvar or perianal fungus extensions, it is recommended to add an antifungal with applications to the ovum

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

4.3. Cons-indications

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

4.4. Special warnings and precautions

Reserved for vaginal use only. UNIVAGIL LP is not intended for oral administration.

Special warnings

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

When candidiasis confirmed, look carefully for ecological factors that promote the development of candida.

To prevent relapse, eradication and the integration of predisposing factors is essential.

It is desirable to simultaneously process any associated candida home and recognized pathogen.

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

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 have also shown sensitivity to econazole nitrate.

Precautions

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

It is not recommended to use an acid pH soap (pH favoring the proliferation of candida): see section 4.2, practical advice.

4.5. Interactions with other drugs and other forms of interaction

Contra-indicated combinations

- **Male latex condoms / latex diaphragms**

Risk of rupture of the diaphragm or condom latex.

Non recommended combinations

- **spermicides**

All local vaginal treatment may inactivate local spermicidal contraception.

Combinations requiring precautions for use

- **Oral anticoagulants**

Econazole is a known inhibitor of CYP3A4 / 2C9. Despite limited systemic exposure after vaginal application, clinically relevant interactions may 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, caution should be taken and the INR should be monitored more frequently.

The dose adjustment of the oral anticoagulant may be necessary during treatment with econazole and after its arrest.

4.6. Fertility, pregnancy and lactation

Pregnancy

Studies in animals have shown no evidence of teratogenic effects but have shown fetotoxicity at high doses (see section 5.3). It is not known whether these findings are relevant to humans.

In the absence of teratogenic effects in animals, a malformative effect in humans is not expected. Indeed, to date, the substances responsible for malformations in humans have proved to be teratogenic in animals during well-conducted studies in two species.

Clinically, no malformative or foetotoxic particular has appeared to date. However, monitoring of pregnancies exposed to econazole is insufficient to exclude any risk.

Due to absorption through the vaginal mucosa using UNIVAGIL LP should not be considered during the first trimester of pregnancy unless the doctor considers 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

The absorption of econazole nitrate by the vaginal mucosa is low.

It is not known whether econazole nitrate is excreted in breast milk in humans.

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

4.7. Effects on ability to drive and use machines

Not applicable.

4.8. Side effects

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

In the table below side effects with the use of vaginal econazole in clinical trials (including side effects listed above) and adverse reactions from post-marketing data (notifications spontaneous) are reported.

For adverse reactions reported in clinical trials, the frequency categories in the table are defined as follows: very common (≥1 / 10); common (≥1 / 100 to <1/10); uncommon (≥1 / 1000 to <1/100); rare (≥1 / 10,000 to <1/1 000); very rare (<1/10 000).

For side effects from spontaneous reports, their frequency is not known (can not be estimated from the available data).

Classes organ systems	**Side effects**			
	Categories of frequency			
	Frequent **(≥1 / 100 to <1/10)**	**Rare** **(≥1 / 1000 to <1/100)**	**Rare** **(≥1 / 10 000 <1/1 000)**	**indeterminate**
Immune system disorders				hypersensitivity
Skin and subcutaneous tissue	Pruritus, skin burning sensation	rash	Erythema	Angioedema, urticaria, contact dermatitis, skin exfoliation
Affection Reproductive system and breast		vulvovaginal burning sensation		
General disorders and administration site				Pain at the application site irritation at the application site, swelling at the application site

Declaration of suspected adverse reactions

The reporting of suspected adverse reactions after drug approval is important. It allows continuous monitoring of the benefit / risk ratio of the drug. Health professionals report any suspected adverse reactions via the national reporting system: Agence française de sécurité sanitaire des produits de santé (ANSM) network of Regional Pharmacovigilance Centers - Website: www.ansm.sante.fr.

4.9. Overdose

If overdose with UNIVAGIL LP, expected adverse events are similar to the side effects listed in section 4.8 "Undesirable effects".

In case of accidental ingestion, nausea, vomiting or diarrhea may occur. A symptomatic treatment is used if necessary.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic: ANTIINFECTIVES ANTISEPTICS AND USE GYNECOLOGICAL (G: Genito-urinary system and sex hormones), ATC code: G01AF05.

Econazole nitrate is a imidazole derivative that has antifungal and antibacterial activity.

The activity has been demonstrated in vitro and acts on the agents responsible for mucocutaneous fungal infections:

- Candida and other yeasts (Agents vaginal mycoses)
- Gram + bacteria sometimes responsible for a secondary infection.

In vitro attempts of selection of Canida Albicans resisting to econazole did not show any acquired resistances. *In* vivo, the risk is minimal.

Action mechanism

Different from that of antibiotics, it is located at several levels: membrane (increase in permeability), cytoplasmic (inhibition of oxidative processes in the mitochondria), nuclear (inhibition of RNA synthesis).

This dosage is suitable for short treatment.

5.2. Pharmacokinetic properties

In humans, econazole is poorly absorbed after vaginal administration.

The highest concentrations of econazole and / or its metabolites in the plasma or serum observed 1-2 days after administration were approximately 65 ng / ml for an ovum of 150 mg. For an ovum of 150 mg, approximately 5% of the dose of econazole is absorbed.

In the systemic circulation, econazole and / or its metabolites are extensively bound (> 98%) to plasma proteins. The econazole is extensively metabolized by oxidation, deamination and / or O-dealkylation and the metabolites are excreted by renal and fecal pathways.

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

5.3. Preclinical safety data

Sub-Chronic toxicity

The liver was identified as the target organ. The safety margin associated with this effect is important.

Reproductive functions

Studies have shown no evidence of impaired fertility or teratogenicity but foetotoxicity in high doses.

Breastfeeding

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

genotoxicity

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

local tolerance

The studies revealed no mucosal or vaginal irritation, no phototoxicity or sensitization.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Galactomannan, silica colloidal anhydrous, solid semisynthetic glycerides (type H 15 WI and WE FS), enantate stearyl.

6.2. incompatibility

Not applicable.

6.3. The duration of the conversation

3 years.

6.4. Special precautions for storage

Store at a temperature not exceeding 30 ° C.

6.5. Nature and contents of container

1 ovum blister (PVC / PE).

6.6. Special precautions for disposal and handling

No special requirements.

7. HOLDER OF MARKETING AUTHORIZATION IN THE COUNTRY OF ORIGIN

KELLER PHARMA
2 RUE DU CHATEAU
67170 MITTELHAUSEN

Operator Export: FRILAB SA 17 RUE DES Pierres du Niton, 1207 Genève

Maker : UNITHER industries, ZI le Marcourlet, 03800 Gannat, FRANCE

8. NUMBER (S) AUTHORIZATION MARKETING IN THE COUNTRY OF ORIGIN

- 34009 300 086 5 2: 1 ovum blister (PVC / PE).

9. DATE OF FIRST AUTHORIZATION / RENEWAL OF THE AUTHORIZATION IN THE COUNTRY

February 20, 2015.

10. DATE OF THE TEXT

Unspecified.

11. DOSIMETRY

Not applicable.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Not applicable.

CONDITIONS OF PRESCRIPTION AND DELIVERY

Medicinal product not subject to medical prescription.