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1. NAME OF THE MEDICINE

Canesten Soft Gel Ovules, 500 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each soft gel ovule contains clotrimazole 500 mg
For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Canesten Soft Gel Ovules 500 mg is presented as a teardrop softcapsules with a yellow opaque gelatin shell.
Each ovule is contained within a colourless thermoform PVC/PVdC/PVC laminate blister with an aluminium foil lid. The blister is packaged in a folding carton with a leaflet and a disposable applicator.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Canesten Soft gel ovules are indicated for the treatment of vaginal yeast infections (vaginal candidiasis)

4.2 Posology and method of administration

Adults: One Canesten soft gel ovule should be inserted at night into the vagina as high as possible, using the applicator provided. This is best achieved when lying back with legs bent up.
A single dose treatment will be sufficient for the treatment of Candida vaginitis, however a second treatment may be carried out if necessary.

It is recommended that the treatment should be timed so as to avoid the menstrual period due to the risk of the soft gel ovule being washed out by the menstrual flow.

Paediatric population
Not for use in children under 16 years of age

4.3 Contraindications

Hypersensitivity to clotrimazole or any of the ingredients in Canesten Soft Gel Ovules

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4.4 Special warnings and precautions for use

Do not use tampons, intravaginal douches, spermicides or other vaginal products while using this product.
Vaginal intercourse should be avoided in case of vaginal infection and while using this product because the partner could become infected

Before using Canesten Soft gel ovules, medical advice should be sought if any of the following are applicable:

- More than two infections of candida vaginitis in the last 6 months.
- Previous history of sexually transmitted disease or exposure to partner with sexually transmitted disease.
- Pregnancy or suspected pregnancy.
- Aged under 16 or over 60 years.
- Known sensitivity to imidazoles or other vaginal antifungal products.

Canesten soft gel ovules should not be used if the patient has any of the following symptoms:

- Irregular vaginal bleeding.
- Abnormal vaginal bleeding or a blood-stained discharge.
- Vulval or vaginal ulcers, blisters, or sores.
- Lower abdominal pain or dysuria.
- Any adverse events such as redness, irritation or swelling associated with the treatment.
- Fever or chills.
- Nausea or vomiting.
- Diarrhoea.
- Foul smelling vaginal discharge.

Patients should consult their doctor if the symptoms have not been relieved within one week of using Canesten soft gel ovules.
Canesten Soft Gel ovules can be used again if the candida infection returns after seven days. However, if the infection reoccurs more than twice within six months, patients should consult their doctor or healthcare provider.

4.5 Interaction with other medicines and other forms of interaction

Laboratory tests have suggested that, when used together, Canesten Soft Gel Ovules may cause damage to latex contraceptives. Consequently, the effectiveness of such contraceptives may be reduced. Patients should be advised to use alternative precautions for at least five days after using Canesten Soft Gel ovules.

Concomitant use of Canesten Soft Gel Ovules and oral tacrolimus (FK-506, immunosuppressant) might lead to increased tacrolimus plasma levels. Patients should be thus be closely monitored for signs and symptoms of tacrolimus and sirolimus overdosage, if necessary by determination of the respective plasma levels.

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4.6 Fertility, pregnancy and lactation

Fertility:
No human studies of the effects of clotrimazole on fertility have been performed, however animal studies have not demonstrated any effects of the drug on fertility

Pregnancy:
There are limited amount of data from the use of clotrimazole in pregnant women. Animal studies with clotrimazole have shown reproductive toxicity at high oral doses (see section 5.3). At the low

systemic exposures of clotrimazole following vaginal treatment, harmful effects with respect to reproductive toxicity are not predicted.

Clotrimazole can be used during pregnancy, but only under the supervision of a doctor or a Healthcare professional.

During pregnancy, Canesten Soft Gel ovules should be inserted without using an applicator.

Lactation:
Available pharmacodynamic/toxicological data in animals have shown excretion of clotrimazole/metabolites in milk after intravenous administration (see section 5.3). A risk to the suckling child cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from clotrimazole therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the Woman

4.7 Effects on ability to drive and use machines

Canesten Soft Gel ovules has no or negligible influence on the ability to drive or use machinery

4.8 Undesirable effects

The following side effects have been reported and the frequency is unknown

Immune system disorders	Allergic reaction (Syncope, hypotension, dyspnoea, urticaria, pruritus)
Gastrointestinal disorders	Abdominal pain
Reproductive system and breast disorder	Genital peeling, pruritus, rash, oedema, discomfort, burning, irritation, pelvic pain, vaginal haemorrhage
General disorders and administrative site conditions	Irritation, burning, contact dermatitis

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4.9 Overdose

No risk of acute intoxication is seen as it is unlikely to occur following a single vaginal or dermal application of an overdose (application over a large area under conditions favourable to absorption) or inadvertent oral ingestion. There is no specific antidote. However, in the event of accidental oral ingestion, only supportive care is recommended if clinical symptoms of overdose become apparent (e.g. dizziness, nausea or vomiting).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A.20.2.2 fungicides
Pharmacotherapeutic group: Gynaecological anti-infectives and antiseptics-
imidazole derivatives

ATC code: G01A F02

Mechanism of action:
Clotrimazole acts against fungi by inhibiting ergosterol synthesis. Inhibition of ergosterol synthesis leads to structural and functional impairment of the fungal cytoplasmic membrane.

Clotrimazole has a broad antimycotic spectrum of action in vitro and in vivo, which includes dermatophytes, yeasts, moulds, etc.

Under appropriate test conditions, the MIC values for these types of fungi are in the region of less than 0,062 – 8,0 µg/ml substrate. The mode of action of clotrimazole is fungistatic or fungicidal depending on the concentration of clotrimazole at the site of infection. In-vitro activity is limited to proliferating fungal elements; fungal spores are only slightly sensitive.

Primarily resistant variants of sensitive fungal species are very rare; the development of secondary resistance by sensitive fungi has so far only been observed in very isolated cases under therapeutic conditions.

5.2 Pharmacokinetic properties

Pharmacokinetic investigations after vaginal application have shown that only a small amount of clotrimazole (3 – 10%) is absorbed. Due to the rapid hepatic metabolism of absorbed clotrimazole into pharmacologically inactive metabolites the resulting peak plasma concentrations of clotrimazole after vaginal application of a 500 mg dose were less than 10 ng/ml, reflecting that clotrimazole applied intravaginally does not lead to measurable systemic effects or side effects.

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5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on studies of repeated dose toxicity, genotoxicity and carcinogenicity.
Clotrimazole was not teratogenic in reproductive toxicity studies in mice, rats and rabbits. In rats high oral doses were associated with maternal toxicity, embryotoxicity, reduced fetal weights and decreased pup survival.

In rats clotrimazole and/or its metabolites were secreted into milk at levels higher than in plasma by a factor of 10 to 20 at 4 hrs after administration, followed by a decline to a factor of 0,4 by 24 hrs.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

White soft paraffin
Liquid paraffin
Gelatine
Glycerol
Water
Titanium dioxide (E171)
Quinoline yellow (E104)
Sunset yellow (E110)
Lecithin
Medium-chain triglycerides.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store in the original carton in a dry place in order to protect it from moisture.
Store at or below 30 °C

6.5 Nature and contents of the container

Each soft gel Ovule is packed into a blister consisting of formed clear triplex laminate film PVC/PVdC/PVC (Total PVC 250µm; PVdC 120g/m2) sealed with 20 µm hard tempered aluminium lidding foil). The blister and an applicator are enclosed in a cardboard carton.

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6.6 Special precautions for disposal and other handling

No special requirements

7. MANUFACTURERS.

Bulk Manufactured by:
Berlimed S.A
Francisco Alonso, 7
28806 Alcalá de Henares, Madrid
SPAIN

Packaged and released by:
GP Grenzach Produktions GmbH
Emil-Barell-Strasse 7
79639 Grenzach-Wyhlen
Germany