Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Canesten 500 mg Soft Vaginal Capsule

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each soft vaginal capsule contains 500mg Clotrimazole.

Excipients with known effect: Soya oil

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Vaginal capsule, soft
Yellow oblong soft capsule

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Canesten Soft Vaginal Capsules are recommended for the treatment of candidal vaginitis.

4.2 Posology and method of administration

Posology
Adults:
One 500mg soft vaginal capsule should be inserted at night before going to bed. A second treatment may be carried out if necessary.

Patients should be advised to consult their physician if the symptoms have not been relieved within one week of using Canesten Soft Vaginal Capsule. Canesten Soft Vaginal Capsules can be used again if the candidal infection returns after 7 days. However, if the candidal infection recurs more than twice within six months, patients should be advised to consult their physician.

Paediatric population

Not for use in children under 16.

Method of administration
The soft vaginal capsule should be inserted as high as possible into the vagina, using the applicator provided. This is best achieved when lying back with legs bent up.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Medical advice should be sought if this is the first time the patient has experienced symptoms of candidal vaginitis.

Before using Canesten Soft Vaginal Capsule, medical advice must be sought if any of the following are applicable:

- more than two infections of candidal 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 hypersensitivity to imidazoles or other vaginal antifungal products.

Canesten Soft Vaginal Capsules should not be used if the patient has any of the following symptoms where upon medical advice should be sought:

- 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
- back pain
    - associated shoulder pain

Treatment during the menstrual period should not be performed due to the risk of the soft vaginal capsule being washed out by the menstrual flow. The treatment should be finished before the onset of menstruation.

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.

Avoid contact with eyes and do not swallow.

When used in pregnancy, the soft gel pessary should be inserted without using an applicator (see "Pregnancy").

Canesten Soft Vaginal Capsule contains soya oil. If you are allergic to peanut or soya, do not use this medicinal product

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant treatment with vaginal clotrimazole and oral tacrolimus (FK-506; immunosuppressant) might lead to increased tacrolimus plasma levels and similarly with sirolimus. Patients should thus be closely monitored for signs and symptoms of tacrolimus or sirolimus overdosage, if necessary by determination of the respective plasma levels.

Laboratory tests have suggested that, when used together, this product 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 this product.

4.6 Fertility, pregnancy and lactation

Pregnancy:
There are limited data available 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 are considered unlikely. Clotrimazole can be used during pregnancy, but only under the direction of a doctor or midwife.

During pregnancy the treatment should be carried out with clotrimazole vaginal tablets, since these can be inserted without using an applicator.

Breastfeeding:
There are no data on the excretion of clotimazole into human milk. However, systemic absorption is minimal after administration and is unlikely to lead to systemic effects. Clotrimazole may be used during lactation under medical supervision.

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 (see Section 5.3).

4.7 Effects on ability to drive and use machines

The medication has no or negligible influence on the ability to drive or use machinery.

4.8 Undesirable effects

Frequency not known. The following adverse reactions have been identified during post-approval use of Clotrimazole. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency.

Immune system disorders:
Hypersensitivity, anaphylactic reactions, angioedema

Vascular disorders
Syncope, hypotension

Respiratory, thoracic and mediastinal disorders
Dyspnea

Skin and subcutaneous tissue disorders
Rash,urticaria

Reproductive system and breast disorders
Vulvovaginal discomfort, vulvovaginal burning sensation, vaginal exfoliation, ,vulvovaginal pruritus, , vulvovaginal pain, vaginal haemorrhage, vulvovaginal erythema, vaginal discharge,

Gastrointestinal disorders:
abdominal pain, nausea

General disorders and administration site conditions
Application site irritation, oedema, pain

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 HPRA Pharmacovigilance; Website: www.hpra.ie.

4.9 Overdose

In the event of accidental oral ingestion, gastric lavage is rarely required and should be considered only if clinical symptoms of overdose become apparent (e.g. dizziness, nausea or vomiting). It should be carried out only if the airway can be protected adequately.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Gynaecological antiinfectives and antiseptics – imidazole derivatives ATC Code: G01A F02

Clotrimazole is an imidazole derivative with a broad spectrum of antimycotic activity.

Mechanism of Action

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

Pharmacodynamic Effects
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 micrograms/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.

In addition to its antimycotic action, clotrimazole also acts on gram-positive microorganisms (Streptococci/Staphylococci/ Gardnerella vagiinalis) and gram-negative microorganisms (Bacteroides). It has no effect on lactobacilli.

In vitro, clotrimazole inhibits the multiplication of Corynebacteria and gram-positive cocci – with the exception of Enterococci – in concentrations of 0.5 – 10 micrograms/ml substrate.

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.

Clotrimazole 500 mg vaginal capsule is non-inferior to a single dose of Clotrimazole 500 mg vaginal tablet in terms of overall response defined as clinical and mycological cure at 14 days after treatment.

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 500mg dose were less than 10 ng/ml, reflecting that clotrimazole applied intravaginally does not lead to measurable systemic effects or side effects.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential and toxicity to reproduction and development.

The local and systemic tolerance of clotrimazole in different dosage forms was assessed in intravaginal studies in dogs and monkeys and in subacute dermal studies in rabbits. There was no evidence of treatment-related local or systemic adverse effects in any of these studies.

The oral toxicity of clotrimazole has been well-studied.

Following a single oral administration, clotrimazole was slightly-to-moderately toxic in experimental animals, with LD50 values of 761 to 923 mg/kg bw for mice, 95 to 114 mg/kg bw for newborn rats and 114 to 718 mg/kg bw for adult rats, > 1000 mg/kg bw for rabbits, and > 2000 mg/kg bw for dogs and cats.

In repeated dose oral studies conducted in rats and dogs, the liver was found to be the primary target organ for toxicity. This was evidenced by an increase in serum transaminase activities and the appearance of liver vacuolation and fatty deposits starting at 50 mg/kg in the chronic (78-week) rat study and at 100 mg/kg in the subchronic (13-week) dog study.

Clotrimazole has been extensively studied in in vitro and in vivo mutagenicity assays, and no evidence of mutagenic potential was found. A 78-week oral dosing study of clotrimazole in rats did not show any carcinogenic effect.

In a rat fertility study, groups of FB30 rats received oral doses of clotrimazole up to 50 mg/kg bw, for 10 weeks prior to mating and either throughout a 3-week mating period (for males only) or, for females, until day 13 of gestation or 4-week postpartum. Neonatal survival was reduced in 50 mg/kg bw group. Clotrimazole at doses up to 25 mg/kg bw did not impair the development of the pups. Clotrimazole at all doses did not affect fertility.

No teratogenicity effects were demonstrated in studies in mice, rabbits, and rats, given oral doses of up to 200, 180, and 100 mg/kg, respectively.

A study with 3 lactating rats administered 30 mg/kg clotrimazole intravenously showed that the drug was 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.

Given the limited absorption of clotrimazole after vaginal application (estimated to be 3%-10%), no hazard is expected from the use of vaginal clotrimazole.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

White soft paraffin
Liquid paraffin
Gelatine
Glycerol

Titanium dioxide (E171)
Quinoline yellow (E104)
Sunset yellow (E110)
Lecithin (source of soya oil)
Medium-chain triglycerides.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

This medicinal product does not require any special temperature storage precautions.

6.5 Nature and contents of container

Each pack contains 1 soft vaginal capsule, which is packed into a blister consisting of formed clear triplex laminate film PVC/PVdC/PVC (Total PVC 250µm; PVdC 120g/m^2) sealed with 20 µm hard tempered aluminium lidding foil). The blister and a white disposable PP applicator, which is wrapped separately, are enclosed in a cardboard carton.

6.6 Special precautions for disposal and other handling

Each applicator is for single use only. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Bayer Limited
1st Floor, The Grange Offices
The Grange
Brewery Road
Stillorgan
Co Dublin
A94 H2K7
Ireland

8 MARKETING AUTHORISATION NUMBER

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 12th December 2014
Date of latest renewal: 11th December 2019

10 DATE OF REVISION OF THE TEXT

March 2026