# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Canesten Duopak

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each pessary contains Clotrimazole 100mg.

Each gram of cream contains 10mg clotrimazole (equivalent to 1% w/w).

Excipients with known effect:
Cetostearyl alcohol 100mg in each gram of cream
Benzyl alcohol 20mg in each gram of cream

For the full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Pessaries and cream
White biconvex, oblong pessaries with the name "Bayer" engraved on one side and the letters "P3" on the other.
A white oil-in-water type cream.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Canesten 100mg pessaries are recommended for the treatment of candidal vaginitis.

The cream is recommended for associated vulvitis and treatment of the sexual partner to prevent re-infection.

### 4.2 Posology and method of administration

Canesten 100mg Pessaries should be inserted intravaginally, as high as possible, using the applicator supplied.

The cream is for topical application to the vulva and surrounding area.

**Adults and children of 12 years of age and older:**
Insert one pessary daily, preferably at night, before going to bed, for six consecutive days. Alternatively, two pessaries can be inserted for three consecutive days. The cream should be applied two or three times daily.

If symptoms persist for more than 7 days the patient may have a medical condition that requires treatment by a doctor.

The treatment can be repeated if necessary, however, recurrent infections may indicate an underlying medical cause. Patient should seek medical advice if symptoms return within 2 months.

Canesten pessaries need moisture in the vagina in order to dissolve completely, otherwise undissolved pieces of the pessary might crumble out of the vagina. Pieces of undissolved pessary may be noticed by women who experience vaginal dryness. To help prevent this it is important that the pessary is inserted as deeply as possible into the vagina at bedtime.

**Children under 12 years of age:**
As the pessaries are used with an applicator, paediatric usage is not recommended.

1. Pull out plunger until it stops. Place a pessary into the applicator.
2. Insert applicator containing the pessary carefully as deeply as is comfortable into the vagina. (This is best done with the patient lying on her back with the knees bent up.)
3. Push plunger until it stops, thereby depositing the pessary into the vagina. Remove the applicator.

4. After use, remove plunger completely by pulling it out of the applicator. Then wash it in warm (not boiling) soapy water, rinse and dry carefully.

**4.3 Contraindications**

Hypersensitivity to the active substance clotrimazole 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 100mg Pessaries, 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 a sexually transmitted disease or exposure to partner with a sexually transmitted disease.
- Pregnancy or suspected pregnancy.
- Aged under 12 or over 60 years.
- Known hypersensitivity to imidazoles or other vaginal antifungal products.

Canesten 100mg Pessaries should not be used if the patient has any of the following symptoms whereupon medical advice should be sought:

- Irregular vaginal bleeding
- Abnormal vaginal bleeding (vaginal haemorrhage) 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 (temperature of 38°C or above) 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 pessary 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.

Avoidance of vaginal intercourse is recommended in case of vaginal infection while using this product because your partner could become infected.

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

Avoid contact with eyes and do not swallow.

All possible infected areas should be treated at the same time.

The cream contains cetostearyl alcohol, which may cause local skin reactions (e.g. contact dermatitis). The product also contains benzyl alcohol which may cause allergic reactions and mild local irritation.

**4.5 Interaction with other medicinal products and other forms of interaction**

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.

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 thoroughly monitored for symptoms of tacromilus or sirolimus overdosage, if necessary by determination of the respective plasma levels.

**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 may 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.

Breast-feeding:
There are no data on the excretion of clotrimazole into human milk. However, systemic absorption is minimal after administration and it 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
Allergic reaction (ME) with symptoms such as dyspnea (PT), hypotension (PT), syncope (PT), and urticaria (ME),

**Skin and subcutaneous tissue disorders**
Rash

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

**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, routine measures such as gastric lavage should be performed only if clinical symptoms of overdose become apparent (e.g. dizziness, nausea or vomiting).

**5 PHARMACOLOGICAL PROPERTIES**

**5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: Gynaecological antiinfectives and antiseptics – imidazole derivatives.
ATC Code: G01AF02

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 microgram/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 microgram/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.

**5.2 Pharmacokinetic properties**

Pharmacokinetic investigations after vaginal application have shown that only a small amount of clotrimazole (3-10% of the dose) is absorbed. Due to the rapid hepatic metabolism of absorbed clotrimazole into pharmacologically inactive metabolites the resulting peak plasma concentrations of clotrimazole after vaginal applications 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.

Pharmacokinetic investigations after dermal application have shown that clotrimazole is practically not absorbed from the intact or inflamed skin into the human blood circulation. The resulting peak serum concentrations of clotrimazole were below the detection limit of 0.001 micrograms/ml, reflecting that clotrimazole applied topically 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

Pessaries:
Calcium Lactate Pentahydrate
Maize Starch
Crospovidone
Colloidal Anhydrous Silica
Lactic Acid
Lactose Monohydrate
Magnesium Stearate
Hypromellose
Microcrystalline Cellulose

Cream:
Sorbitan stearate
Polysorbate 60
Cetyl Palmitate
Cetostearyl Alcohol
Octyldodecanol
Benzyl Alcohol
Purified Water

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf life

3 years.

**6.4 Special precautions for storage**

Do not store above 25°C.

**6.5 Nature and contents of container**

Six pessaries are packed into a blister consisting of 25 micrometre PA/ 45 micrometre soft aluminium/ 60 micrometre PVC and 20 micrometre hard aluminium/ 7 g/$m^2$ heat seal lacquer. An applicator is also provided.

20g of a smooth, white, oil-in-water type cream is packed in an aluminium tube with internal lacquer coating, tamper evident seal and HDPE screw on cap.

The pessaries, cream and applicator are enclosed in a cardboard carton.

**6.6 Special precautions for disposal and other handling**

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**

PA1410/039/005

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

Date of first authorisation: 01 April 1977

Date of last renewal: 01 April 2007

**10 DATE OF REVISION OF THE TEXT**

November 2022