

Summary of product characteristics

1. Name of the medicinal product

Canesten V

2. Qualitative and quantitative composition

Clotrimazole 200mg

For excipients, see 6.1

3. Pharmaceutical form

Vaginal tablets

4. Clinical particulars

4.1 Therapeutic indications

Infections in external female genital organs and vagina caused by clotrimazole-sensitive microorganisms such as fungi (*Candida albicans*) and *Trichomonas*.

During treatment of vaginitis caused by *Trichomonas*, Canesten V must be combined with an oral trichomonacide (e.g. metronidazole).

4.2 Posology and method of administration

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

There is no separate dosage schedule for the elderly.

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

One vaginal tablet should be inserted daily (preferably at night) for three consecutive days. A second treatment may be carried out if necessary.

Generally:

- If symptoms persist for more than 7 days the patient may have a medical condition that requires treatment by a doctor.
- The treatments can be repeated if necessary however recurrent infections may indicate an underlying medical cause, including diabetes or HIV infections. Patients should seek medical advice if symptoms return within 2 months.
- Since the vagina and vulva are usually both affected, a combination treatment (treatment of both of these areas) should be performed.
- Treatment during the menstrual period should not be performed due to the risk of the vaginal tablet being washed out by the menstrual flow. The treatment should be finished before the onset of menstruation.
- If the labia and adjacent areas are simultaneously infected, local treatment with an external cream should also be given. The sexual partner should also undergo local treatment if symptoms, e.g. pruritus, inflammation, etc. are present.
- 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 and the effectiveness and safety of latex products such as condoms and diaphragms may be reduced.

Paediatric population:

Intended for use by adults and children 12 years of age and older.

4.3 Contraindications

- Hypersensitivity to clotrimazole or any of the excipients in this product 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 V, medical advice must be sought if any of the following are applicable:

- more than two infections of candidal vaginitis in the last six months.

- previous history of a 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 anti-fungal products.

Canesten V 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 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.

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.

Vaginal intercourse should be avoided in case of vaginal infection and while using this product because the partner could become infected.

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

Patients should be advised to consult their physician if the symptoms have not been relieved within one week of using Canesten V. The vaginal tablets 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.

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 closely monitored for signs and symptoms of tacrolimus or sirolimus overdose, if necessary, by determination of the respective plasma levels.

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 physician.

During pregnancy the vaginal tablet should be inserted without using an applicator.

Lactation:

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

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. As the listed undesirable effects are based on spontaneous reports, assigning accurate frequency of occurrence for each is not possible.

Immune system disorders: anaphylactic reaction, angioedema, hypersensitivity.

Vascular disorder: syncope, hypotension.

Respiratory, thoracic and mediastinal disorders: dyspnoea.

Gastrointestinal disorders: abdominal pain.

Skin and Subcutaneous Tissue Disorders: rash, urticaria, pruritus.

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

Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form: <https://sideeffects.health.gov.il/>

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, routine measures such as gastric lavage should be performed only if clinical symptoms of overdose become apparent (e.g. dizziness, nausea or vomiting). Gastric lavage should be carried out only if the airway can be protected adequately.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Gynaecological anti-infectives and antiseptics – imidazole derivatives

ATC Code: G01A F02

Mechanism of Action:

Azoles (e.g. clotrimazole) are usually recommended for the local treatment of vulvovaginal candidosis that is characterized by vulvovaginal symptoms such as itching, burning, discharge, redness, swelling and soreness.

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% 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 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 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

Lactose monohydrate, microcrystalline cellulose, maize starch, croscopovidone, lactic acid, magnesium stearate, calcium lactate pentahydrate, silica, colloidal anhydrous, hypromellose 15 cP.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Three pessaries are packed in a blister pack (foil 25µm PA / 45µm Al soft / 60µm PVC) sealed with aluminium backing foil (foil 20µm Al hard / sealable to PVC/PVDC). An applicator is also provided.

The vaginal tablets and applicator are enclosed in a cardboard carton.

6.6 Special precautions for disposal and other handling

No special requirements.

6.7 MANUFACTURER

GP Grenzach Produktions GmbH, Grenzach-Wyhlen, Germany.

7. Marketing authorisation holder

Bayer Israel Ltd, 36 Hacharash St., Hod Hasharon 45240

8. Marketing authorisation number(s)

149-92-33642-02

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