SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Candigo 100/500 mg Pessaries

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each pessary contains:
Clotrimazole BP.....100/500 mg

For full list of excipients, see section 6l.

3. PHARMACEUTICAL FORM

White to light yellow colour torpedo shaped pessaries.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Candigo pessaries are recommended for the treatment of candidal vaginitis.

4.2 Posology and method of administration

The pessary should be inserted into the vagina, as high as possible. This is best achieved when lying back with legs bent up. A second treatment may be carried out if necessary.

Adults:
Candigo Pessaries 100 mg
Two 100 mg pessaries should be inserted daily (preferably at night) for three consecutive days. Alternatively, one pessary may be inserted daily for six days, preferably at night. A second treatment may be carried out if necessary. There is no separate dosage schedule for the elderly.

Candigo Pessary 500 mg
One 500 mg pessary should be inserted at night; the pessary should be inserted as high as possible into the vagina.
Candigo Pessary 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 high as possible into the vagina at bedtime.

Generally:
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. Children: Paediatric usage is not recommended.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients.

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 Candigo suppositories, 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. Candigo pessary 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.

Patients should be advised to consult their physician if the symptoms have not been relieved within one week of using Candigo pessaries. Candigo prssaries 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 medication 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 over dosage, 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.

<u>Pregnancy</u>
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 or midwife

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

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

4.8 Undesirable effects

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

Immune system disorders:
Allergic reaction (syncope, hypotension, dyspnea, urticaria, pruritus)

Reproductive system and breast disorders:
Genital peeling, pruritus, rash, oedema, erythema, discomfort, burning, irritation, pelvic pain, vaginal haemorrhage

Gastrointestinal disorders:
Abdominal pain

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:
Gynecological anti-infective and antiseptics - imidazole derivatives
ATC Code: G01AF02

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

Hard fat (Suppocire NAI 25 A)

6.2 Incompatibilities

None known

6.3 Shelf life

3 Years

6.4 Special precautions for storage

Store in dry place, temperature below 30°C. Do not freeze.
Keep medicine out of reach of children.

6.5 Nature and contents of container

Clotrimazole Pessaries l00 mg: 6 pessaries are packed in PVC/PE strip, such 1 strip is packed along with instruction for medical use in a carton pack.

Clotrimazole Pessary 500 mg: 1 pessary is packed in PVC/PE strip, such 1 strip is packed in with instruction for medical use in a carton pack.

6.6 Special precautions for disposal and other handling

None

7. MARKETING AUTHORISATION HOLDER

Kusum Healthcare Pvt. Ltd.
SP-289(A), RIICO Industrial Area, Chopanki, Bhiwadi, Dist. Alwar (Rajasthan) India

8. MARKETING AUTHORISATION NUMBER(S)

For 100mg: 08317/08418/NMR/2020

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORIZATION

For 100mg: 30 December 2022

10. DATE OF REVISION OF THE TEXT

08/2023

11. REFERENCES

SmPC published on electronic medicines compendium
https://www.medicines.org.uk/emc#gref

The MHRA published product information
https://products.mhra.gov.uk/

Human medicine European public assessment report
https://www.ema.europa.eu/en/medicines