Prescribing Information (Summary of Product Characteristics)

1. **Name of the medicinal Product**

Clotrimazole Vaginal Inserts USP 100 mg

2. **Qualitative and Quantitative Composition**

Qualitative declaration

Clotrimazole USP

Quantitative declaration

For full list of excipients, see section 6.1.

3. **Pharmaceutical Form**

Vaginal Insert

Distribution category: POM

White to off-white coloured, almond shaped, uncoated vaginal insert plain on both side.

4. **Clinical Particulars**

1. **Therapeutic Indications**

Clotrimazole vaginal tablets is used for the treatment of vulvovaginal candidiasis (VVC). It is used for relief of the symptoms like vaginal pruritus and burning associated with vulvovaginal candidiasis; external vulvar itching and irritation associated with vulvovaginitis, mixed vaginal infections, including bacterial and trichomonal etiologies, as an adjuvant therapy.

2. **Posology and Method of Administration**

Method of administration:

The Clotrimazole 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.

Adults:

Insert two tablet of clotrimazole 100 mg should be inserted daily (preferably at night) for three consecutive days. The applicator should be used for insert the tablet into vagina. Alternatively, insert one tablet of clotrimazole 100 mg 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.

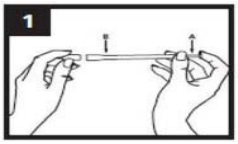
Clotrimazole vaginal tablets need moisture in the vagina in order to dissolve completely, otherwise undissolved pieces of the Clotrimazole vaginal tablets might crumble out of the vagina. Pieces of undissolved clotrimazole vaginal tablets may be noticed by women who experience vaginal dryness. To help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

Children:

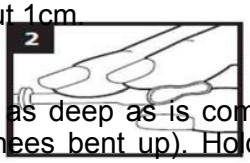
Not for use in children under age 16.

Direction for use:

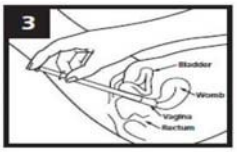
1. Remove the applicator from the packaging. Pull out the plunger A until it stops. Remove the tablet from the pack and place firmly into the applicator B.



2. To fit the tablet into the applicator, the holder of the applicator needs to be squeezed lightly at both sides. The tablet fits tightly into the applicator and needs to be squeezed into the holder to about 1cm.



3. Carefully put the applicator as deep as is comfortable into the vagina (this is easiest when lying on your back with your knees bent up). Holding the applicator in place, slowly press the plunger until it stops so that the tablet is deposited into the vagina.



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

5. After completing the treatment, dispose of the applicator in a safe place, out of the reach of children. The applicator cannot be flushed down the toilet.

3. **Contraindications**
Hypersensitivity to clotrimazole or any other ingredient in this medicine.

4. **Special Warnings and Special Precautions for Use**

Generally: Avoid contact with eyes. Do not swallow. Not for Oral Use.

Do not use tampons, intravaginal douches, spermicides or other vaginal products while using this product.
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.

Avoidance of vaginal intercourse is recommended in case of vaginal infection and while using clotrimazole vaginal tablets as the partner could become infected.

Before using clotrimazole vaginal tablets, 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. Patient's age under sixteen or over sixty years. Known hypersensitivity to imidazoles or other vaginal antifungal products.

Clotrimazole vaginal tablets 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, diarrhea, foul smelling vaginal discharge. Do not use in girls under 16 years of age.

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

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

For clotrimazole vaginal tablets containing Sodium lauryl sulfate may cause local skin reactions (such as stinging or burning sensation) or increase skin reactions caused by other products when applied on the same area.

Pregnancy: Lactation:
Excretion of Clotrimazole in breast milk is unknown. Breast-feeding should be discontinued during treatment with clotrimazole.
5. **Interaction with other medicinal products and other forms of interaction**

Clotrimazole vaginal tablets may cause damage to latex contraceptives. Consequently, the effectiveness of such latex 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), sirolimus: might lead to increased tacrolimus plasma levels. Patients should thus be closely monitored for signs and symptoms of tacrolimus or sirolimus overdosage, if necessary by determination of the respective plasma levels.

6. **Pregnancy and Lactation**

There are limited amount of data from the use of clotrimazole in pregnant women. As a precautionary measure, it is preferable to avoid the use of Clotrimazole during the first trimester of pregnancy. During pregnancy the vaginal tablets should be inserted without using an applicator.

7. **Effects on ability to Drive and use Machines**

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

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.

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 favorable 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**

1. **Pharmacodynamics Properties**

Pharmacotherapeutic group: Gynecological anti-infective 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.

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

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, embryo toxicity, 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 (Lactose Monohydrate) BP
Maize Starch BP
Pregelatinised Starch (Starch 1500) BP
Microcrystalline Cellulose (PH 102) BP
Sodium Starch Glycolate (Type A) BP
Magnesium Stearate BP
Purified Talc BP
Colloidal Anhydrous Silica (Aerosil) BP
Sodium Lauryl Sulphate BP
Purified Water BP

6.2 Incompatibilities

Not applicable

6.3 Shelf Life

36 Months

6.4 Special Precautions for Storage

Do not store above 30°C. Protect from light, moisture & crushing.

6.5 Nature and Contents of Container

6 Tablets are packed in Alu-Alu strip pack. Such a Alu-Alu strip packed in a printed carton with packing Insert.

6.6 Special precaution for disposal and other handling

No special requirements for disposal.

7.0 Marketing Authorization Holder and Manufacturing Site Addresses

7.1 Name and Address of Marketing Authorization Holder

Lincoln Pharmaceuticals Limited
Trimul Estate, Khatraj, Taluka: Kalol,
District: Gandhinagar Gujarat,
India.
Telephone no.: +91-79-41078096
Fax: +91-79-41078062
Email: hiren@lincolnpharma.com
Website: www.lincolnpharma.com

7.2 Name and Address of manufacturing site(s)
Lincoln Pharmaceuticals Limited
Trimul Estate, Khatraj, Taluka: Kalol,
District: Gandhinagar Gujarat,
India.
Telephone no.: +91-79-41078096
Fax: +91-79-41078062
Email: hiren@lincolnpharma.com
Website: www.lincolnpharma.com

8. Marketing Authorization Number
TAN 22 HM 0047

9. Date of First <Registration> / Renewal of The <Registration>
10/01/2022

10. Date of Revision of the Text