APPROVED
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INSTRUCTION
for medical use

CLOFAN

Composition:
active substance: clotrimazole;
each suppository contains 100 mg of clotrimazole;
excipients: hard fat.

Pharmaceutical form. Vaginal suppository.
Basic physico-chemical properties: white to light yellow colour torpedo shaped suppositories.

Pharmacotherapeutic group. Gynaecological antimycotics and antiseptics, excluding combinations with corticosteroids. Clotrimazole.
ATC code G01A F02.

Pharmacological properties.
Pharmacodynamics.
The mechanism of antimycotic action of clotrimazole is connected with inhibition of ergosterol synthesis leading 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, and dimorphic fungi.
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 of 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 antimycotic activity, clotrimazole also acts on gram-positive microorganisms (*streptococci, staphylococci, Gardnerella vaginalis*) and gram-negative microorganisms (*Bacteroids*).
In vitro clotrimazole inhibits the proliferation of *Corynebacteria* and gram-positive cocci (excluding *Enterococci*) at a concentration of 0.5–10 μg/ml of substrate. Primarily resistant variants of sensitive fungal species are rare. The development of secondary resistance by sensitive fungi has so far only been observed in very isolated cases under therapeutic conditions.
Preclinical studies conducted with volunteers using a single and repeated toxic dose did not reveal any toxic, genotoxic and reproductive effects.
Pharmacokinetics.
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. This means that clotrimazole applied intravaginally does not lead to measurable systemic effects or side effects.

Clinical characteristics.

Indications.

Infections in the genital area (vaginitis) caused by fungi (usually of the *Candida* genus) and superinfections caused by bacteria susceptible to clotrimazole.

Contraindications.

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

Interaction with other medicinal products and other forms of interaction.

Concomitant medication with vaginal clotrimazole and oral tacrolimus (FK-506; immunosuppressant) might lead to increased tacrolimus/sirolimus 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.

Concomitant use of vaginal suppositories with latex contraceptives (such as a condom and a diaphragm) can damage the latter, so the effectiveness of these contraceptives may be reduced. The indicated effect is temporary and can occur only during treatment. Patients should be advised to use alternative precautions for at least five days after using this product.

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 Clofan suppositories, 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.

Clofan suppositories 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 (38°C or above) 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 suppository 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 while using Clofan because the partner could become infected.
Patients should be advised to consult their physician if the symptoms have not been relieved within 7 days of using Clofan suppositories. The suppositories 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.

Use during pregnancy or lactation.
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. At the low systemic exposures of clotrimazole following vaginal treatment, harmful effects with respect to reproductive toxicity are not predicted.
It is recommended to avoid using Clofan, vaginal suppositories during the first trimester of pregnancy.
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. Clofan, vaginal suppositories may be used during 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.

Effects on ability to drive a car or use machines.
The medication has no or negligible influence on the ability to drive or use machinery.

Dosage and administration.
The suppository should be inserted into the vagina as high as possible at bedtime. It is most convenient to introduce a suppository lying on a back with slightly bent legs.
One treatment course: 2 suppositories for three days or 1 suppository for six days.
A second treatment course may be performed if necessary.
Treatment should not be continued during menstruation. 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 while using Clofan because the partner could become infected.

Children.
Not for use in children under 12. Children under 12 years of age could be treated after consulting a physician.

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.

Adverse reactions.
The frequency of adverse reactions cannot be determined because they have been reported during the post-marketing period. The frequency of adverse reactions listed below is indicated as "frequency not known".
Immune system disorders
Frequency not known: anaphylactic reaction, angioedema, hypersensitivity, allergic reactions.
Vascular disorders
Frequency not known: syncope, hypotension.
Respiratory, thoracic and mediastinal disorders
Frequency not known: dyspnoea.
Skin and subcutaneous tissue disorders
Frequency not known: rash, urticaria, pruritus.
Reproductive system and breast disorders
Frequency not known: vulvovaginal disorders (skin exfoliation, discomfort, erythema, burning sensation, pruritus, pain), vaginal discharge, vaginal haemorrhage.
Gastrointestinal disorders
Frequency not known: abdominal pain, nausea.
General disorders and administration site conditions
Frequency not known: irritation at the site of application, edema, 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. Medical and pharmaceutical workers, as well as patients or their legal representatives are asked to report any suspected adverse reactions and lack of effectiveness of the medicinal product through the Pharmacovigilance Automated Information System at: https://aisf.dec.gov.ua.

Shelf life.
3 years.

Storage conditions.
Store in the original package at the temperature not exceeding 25°C.
Keep out of reach of children.

Package.
6 suppositories in a strip. 1 strip in a carton package.

Condition of supply.
Without prescription.

Manufacturer.
KUSUM HEALTHCARE PVT LTD.

Manufacturer's location and address of the place of business.
SP-289 (A), RIICO Industrial area, Chopanki, Bhiwadi, Dist. Alwar (Rajasthan), India.

Date of last revision.