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INSTRUCTION
for medical use

CLOFAN

Composition:
active substance: clotrimazole;
Each suppository contains 500 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, 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.
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 very 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 its 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 plasma levels and similarly with sirolimus. 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.
Avoid contact with eyes. Do not swallow.
The patient is advised to consult a physician in the following cases:
at the first manifestations of the disease;
if the symptoms persist for longer than 7 days;
if the symptoms appear again within 2 months or more than 4 times during the last 12 months;
if hypersensitivity to any antifungal agents or derivatives of imidazole is detected;
in the presence of sexually transmitted diseases in the history or burdened anamnesis of sexually transmitted diseases in a partner;
in the presence of more than two episodes of candidal vaginitis during the last 6 months;
if the patient has high body temperature (from 38 °C), pain in the lower abdomen, dysuria, back pain, purulent vaginal discharge with an unpleasant smell, vulvar ulcers and vaginal ulcers, redness, diarrhea, nausea, vomiting, vaginal bleeding that are accompanied by pain in the shoulder.
When using the drug, sexual intercourse should be avoided, as the infection can be transmitted to the partner. The effectiveness and safety of latex products (such as condoms and diaphragms) may decrease (see section “Interaction with other medicinal products and other forms of interaction”).

Since both the vagina and the external genitalia (labia and adjacent areas) are commonly affected, combined treatment of both sites should be used, including local treatment with cream for external use.
During treatment with Clofan, vaginal suppositories, the treatment of both partners with the use of a cream is recommended.
The 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.

Use during pregnancy or lactation.
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.
Animal studies with clotrimazole have not shown direct or indirect harmful effect in terms of reproductive toxicity. There are limited amount of data from the use of clotrimazole in pregnant women, therefore, it is recommended to avoid using Clofan, vaginal suppositories during the first trimester of pregnancy.
During the treatment with Clofan, vaginal suppositories, breastfeeding should be discontinued.

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.
One vaginal suppository to use at night.
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.
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 this product 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.
Immune system: allergic reactions including syncope, hypotension, dyspnea, urticaria, pruritus.

Reproductive system and breast disorders: genital peeling, pruritus, rash, oedema, erythema, discomfort, burning, irritation, pelvic pain, vaginal haemorrhage.
Digestive tract: abdominal pain.

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.
1suppository 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.