SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product

Clotri-Denk 1% Cream

2. Qualitative and quantitative composition

2.1 General description

White, homogenous cream.

2.2 Qualitative and quantitative composition

Active ingredient: clotrimazole.
1 g cream contains 0.01 g clotrimazole.
For a full list of excipients, see section 6.1.

3. Pharmaceutical form

Cream

4. Clinical particulars

4.1 Therapeutic indications

For fungal infections of the skin and mucous membrane by dermatophytes, yeasts, moulds and other fungi such as Malassezia furfur, and skin infections caused by Corynebacterium minutissimum.

The above infections may occur, for example, in the form of:
Foot mycoses (athlete's foot) between the toes and fingers; at the base of the nail (paronychia), also in combination with nail mycoses; skin diseases which are superinfected with clotrimazole-sensitive pathogens; mycoses of the skin and skin folds; superficial candidiasis; Pityriasis versicolor (skin rash due to yeast infection); infections with Corynebacterium minutissimum (erythrasma); seborrhoeic dermatitis only with microbial involvement or other pathogens.

Clotri-Denk 1% Cream can also be used for candida vulvitis and candida balanitis.
Infections of the labia and adjoining areas caused by yeasts (candida vulvitis); inflammations of the male glans and foreskin by yeasts (candida balanitis).

4.2 Posology and method of administration

The normal dose is 1-3 times a day, ½ cm of cream to cover an area about the size of the palm of the hand.

Clotri-Denk 1% Cream is applied thinly and rubbed in. For reliable clearing and depending on indication, continue to use Clotri-Denk 1% Cream for about 2 weeks after the subjective symptoms have disappeared.

The general duration of treatment is as follows:
Dermatomycoses 3-4 weeks
Erythrasma 2-4 weeks
Pityriasis versicolor 1-3 weeks
Candida vulvitis and candida balanitis 1-2 weeks

4.3 Contraindications

Hypersensitivity to the active substance, to cetylstearyl alcohol or to any of the other excipients.

4.4 Special warnings and precautions for use

Cetylstearyl alcohol may cause local skin irritations (e.g. contact dermatitis).

4.5 Interaction with other medicinal products and other forms of interaction

None known.

Note:
If Clotri-Denk 1% Cream is used at the same time as latex products (e.g. condoms, diaphragms), it may cause a decrease in function because of the excipients contained (especially stearates) and thus have an adverse effect on the reliability of these products.

4.6 Pregnancy and lactation

If used as described in the dosage instruction, the active ingredient clotrimazole is only absorbed by the body in very small quantities; a systemic effect is therefore unlikly. There are currently no prospective clinical studies on the use of clotrimazole cream during pregnancy.

As a precaution, clotrimazole may only be used during pregnancy, if applied to the vagina, after appropriate consideration of the risks/benefits by the doctor in attendance.

Because of the low level of absorption if used on the skin or mucous membrane, breast feeding probably involves no risk to the infant. During lactation, Clotri-Denk 1% Cream should not be applied directly to the breast producing milk.

4.7 Effects on ability to drive and use machines

Clotri-Denk 1% Cream has no effect on the ability to drive and use machines.

4.8 Undesirable effects

Adverse drug reactions are classified as follows:

Very common (≥1/10);
Common (≥1/100 to <1/10);
Uncommon (≥1/1,000 to <1/100);
Rare (≥1/10,000 to <1/1,000);
Very rare (<1/10,000);
Not known (cannot be assessed on the basis of the available data).

Skin and subcutaneous tissue disorders
Uncommon: Temporary irritant skin reactions, such as burning, stinging, reddening.

Hypersensitivity reactions
In the event of hypersensitivity to cetylstearyl alcohol, allergic reactions of the skin/mucous membrane may occur.

4.9 Overdose

No cases of overdose have been reported.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: topical antimycotic
ATC Code: D01AC01

Clotrimazole has a broad spectrum of antimycotic effects *in vitro* and *in vivo* covering dermatophytes, yeasts, moulds and dimorphic fungi.
Under suitable test conditions, the MIC values for these types of mould are in the range of less than 0.062–4-(–8) µg/ml substrate. In terms of effect type, clotrimazole is primarily fungistatic. The effect in vitro is limited to proliferating fungal elements; fungal spores are only barely sensitive. With fungi, the substance acts as an inhibitor of ergosterol synthesis, the inhibition of which leads to development and functional disturbances of the cytoplasma membrane. Alongside its antimycotic effect, clotrimazole in vitro inhibits the reproduction of Corynebacteria and Gram positive cocci – except for enterococci – in concentrations of 0.5 - 10 µg/ml substrate and is effective with 100 µg/ml trichomonacide.

The resistance situation of clotrimazole is assessed as favourable: primarily resistant variants of sensitive fungal species are very rare; secondary resistance developments of sensitive fungi have only been observed very occasionally in therapeutic conditions.

5.2 Pharmacokinetic properties

Pharmacokinetic investigations after dermal and/or vaginal application have shown that only a small part of less than 2 and 3-10% of the clotrimazole dose is absorbed. The resultant peak plasma concentrations are less than 10 ng/ml and do not result in detectable systemic effects or side-effects.

5.3 Preclinical safety data

In studies of acute oral toxicity, clotrimazole was well tolerated. The longer-term administration of high oral doses to rats, dogs and monkeys caused a change in liver enzymes, which was reversible depending on dosage, and liver hypertrophy. Reversible thickening of the cortex of the adrenal gland was caused by increased fat deposits in the Zona reticularis and fasciculata.

With subacute dermal administration to rabbits and the vaginal administration of active ingredient doses of up to 500 mg to dogs over 3 weeks, good dermal and vaginal local

tolerance of the test samples used was determined; the active ingredient was not found to be primarily irritating to the skin or mucous membrane.

The mutagenicity tests were negative.

Investigations of chronic toxicity in rats gave no cause to believe that there was any carcinogenic potential.

Investigations into reproductive toxicology were carried out on mice, rats and rabbits with oral doses of up to 200 mg/kg body weight and rats with a vaginal application of 100 mg/kg body weight. With the oral administration of high doses (from 100 mg/kg body weight), maternal toxicity and lethal effects occurred in rats, with a secondary toxic effect on the embryo. In other animal studies and after vaginal applications in rats, no embryo-toxic or teratogenic effects occurred. Clotrimazole had no effect on fertility.

Mutagenicity, teratogenicity, embryotoxicity
Possible mutagenic properties were excluded in the dominant lethal test and in cytological investigations of spermatogonia in hamsters in receipt of doses of 100 mg/kg BW.

Teratogenicity studies were carried out on mice, rats and rabbits with oral active ingredient doses of up to 200 mg/kg body weight; there were no indications of embryotoxic or teratogenic effects. In the investigations in rats, the high dosages of 100 mg/kg body weight were only poorly tolerated by the mother animals; there was clear maternal toxicity leading to secondary embryotoxic effects. The highest dose of 200 mg/kg body weight was lethal for the females. Doses of 50 mg/kg body weight, however, were tolerated without damage as regards embryonic and lethal developments. Doses of up to 100 mg/kg body weight had no teratogenic effect. In an investigation on rats involving the intravaginal administration of doses of up to 100 mg/kg body weight, there were no indications of embryonic damage.

Data from animal experiments have so far not indicated that clotrimazole has any embryotoxic effect after vaginal or oral application.

Fertility investigations in rats involving doses of up to 50 mg/kg body weight given orally gave no cause to believe that there was any effect on fertility.

6. Pharmaceutical particulars

6.1 List of excipients

Benzyl alcohol, cetylstearyl alcohol, polysorbate 60, sorbitan stearate, octyldodecanol, hexadecyl palmitat, purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store at a temperature between 2 °C and 30 °C.
Keep the tube tightly closed.
Discard 1 year after opening.
Do not use after the expiry date.
Keep out of the reach and sight of children.

6.5 Nature and contents of container

Aluminium tubes containing 20 g cream.

6.6 Special precautions for disposal

No special requirements.

6.7 Marketing authorisation holder

DENK PHARMA GmbH & Co. KG
Prinzregentenstr. 79
81675 München
Germany

6.8 Marketing authorisation number in Ethiopia

05890/07858/REN/2021

6.9 Date of first authorisation in Ethiopia

Apr 28, 2021

6.10 Date of revision of the text

June 2010

6.11 Prescription status

In-pharmacies only medicine.