SUMMARY OF PRODUCT CHARACTERISTICS

Candid (clotrimazole) 1% w/w Cream

1. NAME OF THE MEDICINAL PRODUCT

Candid (clotrimazole 1% w/w Cream)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Clotrimazole USP 1% w/w

In Water miscible base q.s.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

A white cream for topical use

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Clotrimazole cream is indicated for the topical treatment of candidiasis due to *Candida albicans* and tinea versicolor due to *Malassezia furfur*.

Clotrimazole is also available as a nonprescription item which is indicated for the topical treatment of the following dermal infections: tinea pedis, tinea cruris, and tinea corporis due to *Trichophyton rubrum, Trichophyton mentagrophytes, Epidermophyton floccosum,* and *Microsporum canis*.

4.2. Posology and Method of Administration

Gently massage sufficient Clotrimazole 1% Cream into the affected and surrounding skin areas twice a day, in the morning and evening.

Clinical improvement, with relief of pruritus, usually occurs within the first week of treatment with Clotrimazole Cream. If the patient shows no clinical improvement after four weeks of treatment with Clotrimazole Cream, the diagnosis should be reviewed.

Pediatric Use

Safety and effectiveness in children have been established for clotrimazole when used as indicated and in the recommended dosage.

4.3. Contraindications

Clotrimazole Cream is contraindicated in individuals sensitive to its components.

4.4. Special Warnings and Precautions for Use

Warnings

Clotrimazole Cream is not for ophthalmic use.

Precautions

General

If irritation or sensitivity develops with the use of Clotrimazole Cream, treatment should be discontinued and appropriate therapy instituted.

Information for Patients

The patient should be advised to:

1. Use the medication for the full treatment time even though the symptoms may have improved. Notify the physician if there is no improvement after four weeks of treatment.
2. Inform the physician if the area of application shows signs of increased irritation (redness, itching, burning, blistering, swelling, oozing) indicative of possible sensitization.
3. Avoid the use of occlusive wrappings or dressings.
4. Avoid sources of infection or reinfection.

Laboratory Tests

If there is lack of response to Clotrimazole Cream, appropriate microbiological studies should be repeated to confirm the diagnosis and rule out other pathogens before instituting another course of antimycotic therapy.

CAUTION:

FOR EXTERNAL USE ONLY.

NOT FOR OPHTHALMIC USE.

Keep this and all medication out of the reach of children.

4.5. Interaction with other medicinal products and other forms of interaction

Synergism or antagonism between clotrimazole and nystatin, or amphotericin B, or flucytosine against strains of *C. albicans* has not been reported.

4.6. Pregnancy and lactation

Pregnancy

Pregnancy Category B

The disposition of ^{14}C-clotrimazole has been studied in humans and animals. Clotrimazole is very poorly absorbed following dermal application or intravaginal administration to humans. (see section 5.1)

In clinical trials, use of vaginally applied clotrimazole in pregnant women in their second and third trimesters has not been associated with ill effects. There are, however, no adequate and well-controlled studies in pregnant women during the first trimester of pregnancy.

Studies in pregnant rats with intravaginal doses up to 100 mg/kg have revealed no evidence of harm to the fetus due to clotrimazole.

High oral doses of clotrimazole in rats and mice ranging from 50 to 120 mg/kg resulted in embryotoxicity (possibly secondary to maternal toxicity), impairment of mating, decreased litter size and number of viable young and decreased pup survival to weaning. However, clotrimazole was not teratogenic in mice, rabbits and rats at oral doses up to 200, 180 and 100 mg/kg, respectively. Oral absorption in the rat amounts to approximately 90% of the administered dose.

Because animal reproduction studies are not always predictive of human response

Nursing Mothers

It is not known whether this drug is excreted in human milk, caution should be exercised when clotrimazole is used by a nursing woman.

4.7. Effects on ability to drive and use machines

Clotrimazole cream has no or negligible influence on the ability to drive or use machines.

4.8. Undesirable effects

The following adverse reactions have been reported in connection with the use of this product: erythema, stinging, blistering, peeling, edema, pruritus, urticaria, burning, contact allergic dermatitis and general irritation of the skin.

4.9. Overdose

Acute overdosage with topical application of clotrimazole is unlikely and would not be expected to lead to a life-threatening situation.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Clotrimazole is a broad-spectrum antifungal agent that is used for the treatment of dermal infections caused by various species of pathogenic dermatophytes, yeasts, and *Malassezia furfur*. The primary action of clotrimazole is against dividing and growing organisms.

In vitro, clotrimazole exhibits fungistatic and fungicidal activity against isolates of *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Epidermophyton floccosum*, *Microsporum canis* and *Candida* species including *Candida albicans*. In general, the *in vitro* activity of clotrimazole corresponds to that of tolnaftate and griseofulvin against the mycelia of dermatophytes (*Trichophyton*, *Microsporum* and *Epidermophyton*), and to that of the polyenes (amphotericin B and nystatin) against budding fungi (*Candida*). Using an *in vivo* (mouse) and an *in vitro* (mouse kidney homogenate) testing system, clotrimazole and miconazole were equally effective in preventing the growth of the pseudomycelia and mycelia of *Candida albicans*.

Strains of fungi having a natural resistance to clotrimazole are rare. Only a single isolate of *Candida guilliermondi* has been reported to have primary resistance to clotrimazole.

No single-step or multiple-step resistance to clotrimazole has developed during successive passages of *Candida albicans* and *Trichophyton mentagrophytes*. No appreciable change in sensitivity was detected after successive passage of isolates of *C. albicans*, *C. krusei*, or *C. pseudotropicalis* in liquid or solid media containing clotrimazole. Also, resistance could not be developed in chemically induced mutant strains of polyene-resistant isolates of *C. albicans*. Slight, reversible resistance was noted in three isolates of *C. albicans* tested by one investigator. There is a single report that records the clinical emergence of *C. albicans* strain with considerable resistance to flucytosine and miconazole, and with cross-resistance to clotrimazole, the strain remained sensitive to nystatin and amphotericin B.

5.2. Pharmacokinetic properties

In studies of the mechanism of action, the minimum fungicidal concentration of clotrimazole caused leakage of intracellular phosphorus compounds into the ambient medium with concomitant breakdown of cellular nucleic acids and accelerated potassium efflux. Both these events began rapidly and extensively after addition of the drug.

Clotrimazole appears to be well absorbed in humans following oral administration and is eliminated mainly as inactive metabolites. Following topical and vaginal administration, however, clotrimazole appears to be minimally absorbed.

Six hours after the application of radioactive clotrimazole 1% cream and 1% solution onto intact and acutely inflamed skin, the concentration of clotrimazole varied from 100 $\mu g/cm^3$ in the stratum corneum to 0.5 to 1 $\mu g/cm^3$ in the stratum reticulare, and 0.1 $\mu g/cm^3$ in the subcutis. No measurable amount of radioactivity ($\leq$0.001 µg/mL) was found in the serum within 48 hours after application under occlusive dressing of 0.5 mL of the solution or 0.8 g of the cream. Only 0.5% or less of the applied radioactivity was excreted in the urine.

Following intravaginal administration of 100 mg C-clotrimazole vaginal tablets to nine adult females, an average peak serum level, corresponding to only 0.03 µg equivalents/mL of clotrimazole, was reached one to two days after application. After intravaginal administration of 5 g of 1% C-clotrimazole vaginal cream containing 50 mg active drug, to five subjects (one with candidal colpitis), serum levels corresponding to approximately 0.01 µg equivalents/mL were reached between 8 and 24 hours after application.

5.3. Preclinical safety data

Carcinogenicity

An 18-month oral dosing study with clotrimazole in rats has not revealed any carcinogenic effect.

Mutagenicity

In tests for mutagenesis, chromosomes of the spermatophores of Chinese hamsters which had been exposed to clotrimazole were examined for structural changes during the metaphase. Prior to testing, the hamsters had received five oral clotrimazole doses of 100 mg/kg body weight. The results of this study showed that clotrimazole had no mutagenic effect.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Propylene glycol, White petrolatum, Mineral oil, Cetomacrogol Emulsifying Wax, Benzyl Alcohol, Methyl Paraben, Propyl Paraben, Butylated Hydroxytoluene (BHT), Monobasic Sodium Phosphate (Dihydrate), Dibasic Sodium Phosphate (Anhydrous), Purified Water.

6.2. Incompatibilities

Not applicable

6.3. Shelf life

4 years

6.4. Special precautions for storage

Store at temperature not exceeding 25°C. Protect from light.

6.5. Nature and contents of container

A printed carton containing a leaflet and a printed aluminium collapsible tube.

6.6. Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements

7. MARKETING AUTHORISATION HOLDER

Glenmark Pharmaceuticals Limited
B/2, Mahalaxmi Chambers,
22, Bhulabhai Desai road, Mumbai – 400 026

8. MARKETING AUTHORISATION NUMBER(S)

FDA/SD.203-04164

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

12.09.2003

10. DATE OF REVISION OF THE TEXT

May 2017

INFORMATION PATIENTS LEAFLET

Candid (clotrimazole) 1% cream

Read all of this leaflet carefully because it contains important information for you.

This medicine is available without prescription. However, you still need to use Candid Cream carefully to get the best results from it.

- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- You must contact a doctor if your symptoms worsen or do not improve.
- If you have any unusual effects after using this product, tell your doctor or pharmacist.

IN THIS LEAFLET

1. WHAT IS CANDID CREAM AND WHAT IS IT USED FOR?

Candid Cream is used to treat fungal skin infections such as ringworm, athlete's foot, fungal nappy rash and fungal sweat rash. It is also used to relieve irritation of the vulva (external thrush) or the end of the penis, which may be associated with thrush.

If you are unsure whether you (or your baby if treating nappy rash) have one of these fungal skin infections, seek the advice of your doctor or pharmacist.

The active substance in Candid Cream is clotrimazole. Clotrimazole belongs to a group of medicines called imidazoles and is an antifungal agent which fights the cause of fungal skin infections.

2. BEFORE YOU USE CANDID CREAM

Do not use Candid Cream:

- If you (or your baby if treating nappy rash) are allergic (hypersensitive) to clotrimazole or any of the other ingredients of Candid Cream.
- To treat nail or scalp infections.

Special precautions:

As with other creams, Candid Cream may reduce the effectiveness of rubber contraceptives, such as condoms or diaphragms. Consequently, if you are using this cream on the vulva or penis, you should use alternative precautions for at least five days after using this product.

Pregnancy and breast-feeding:

If you are pregnant, breast-feeding or trying for a baby, tell your doctor or midwife before using Candid Cream. If you have informed your doctor or midwife already, follow his/her instructions carefully.

3. HOW TO USE CANDID CREAM?

If Candid Cream has been prescribed for you by your doctor, follow any instructions he/she may have given you. If you purchased this product without a prescription, follow these directions closely:

- Before use, pierce the tube seal by inverting the cap over the end of the tube and press.
- If the feet are infected, they should be washed and dried thoroughly, especially between the toes, before applying the cream.
- Candid Cream should be applied thinly and evenly to the affected areas two or three times daily and rubbed in gently.
- A strip of cream (1/2 cm long) is enough to treat an area of about the size of the hand.
- The duration of the treatment depends upon the type of infection. Generally a minimum of two weeks is required, although up to four weeks may be necessary.
- If you have athlete's foot, it may help to use an antifungal dusting powder as well. Ask your doctor or pharmacist to recommend one.

The symptoms of skin infection, such as itching or soreness, should improve within a few days of treatment although signs such as redness and scaling may take longer to disappear. If symptoms persist, consult your doctor.

Candid Cream is for external use only: Do not put the cream in your mouth or swallow it.

If the cream is swallowed accidentally, tell your doctor straight away or contact the Accident and Emergency Department of your nearest hospital.

If you accidentally get cream in your eyes or mouth, wash immediately with water and contact your doctor.

If you forget to use Candid Cream:

Apply the cream as soon as possible and then continue the rest of your treatment as usual.

You can help the treatment to work if you follow these simple self-help tips:

- Although the infected area will itch, try not to scratch. Scratching will damage the surface of the skin and cause the infection to spread further.
- Keep the affected skin areas clean.
- Pay particular attention to drying the skin, but avoid excessive rubbing.
- Do not share towels, bath mats, etc. with other people as you could spread the infection to them.
- Always wash your hands after treating the infection to prevent it from spreading.

If you have athlete's foot:

- Remember to dry the skin between the toes thoroughly.

- Wash your socks, stockings and tights thoroughly in hot water to remove any shed skin or fungal spores.
- Change your footwear daily if possible.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Candid Cream can cause side effects, although not everybody gets them.

As with all medicines, some people may be allergic to the cream. If you or your baby are allergic, a reaction will occur soon after you start using it. If you or your baby experience an allergic reaction, stop using Candid Cream and tell your doctor straight away or contact the Accident and Emergency Department of your nearest hospital. Signs of an allergic reaction may include:

- Rash.
- Swallowing or breathing problems.
- Swelling of your lips, face, throat or tongue.
- Weakness, feeling dizzy or faint.
- Nausea.

After you apply the cream you might experience:

- Itching, rash, blisters, burning, discomfort, swelling, irritation, redness or peeling of skin.

If you or your baby experiences any of the above effects or react badly to the cream in any other way not listed in this leaflet, tell your doctor or pharmacist immediately.

5. HOW TO STORE CANDID CREAM?

Keep out of the reach and sight of children.

This product should be stored in the original carton.

Store at temperature not exceeding 25°. Protect from light.Do not use Candid Cream after the expiry date which is stated at one end of the carton and on the end of the tube of cream. The expiry date refers to the last day of that month.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Candid Cream contains:

The active substance is clotrimazole at a strength of 1% w/w.

The other ingredients are Propylene glycol, White petrolatum, Mineral oil, Cetomacrogol Emulsifying Wax, Benzyl Alcohol, Methyl Paraben, Propyl Paraben, Butylated Hydroxytoluene (BHT), Monobasic Sodium Phosphate (Dihydrate), Dibasic Sodium Phosphate (Anhydrous), Purified Water.

See Section 2 ‘Do not use’.

What Candid Cream looks like and contents of the pack:

Candid Cream is available in tubes containing 20g of white cream. Not all pack sizes may be marketed.

Marketing authorisation holder:

Glenmark Pharmaceuticals Limited
B/2, Mahalaxmi Chambers,
22, Bhulabhai Desai road, Mumbai – 400 026

Manufacturer:

Glenmark Pharmaceuticals Limited
Plot No. E-37,39, D-Road, MIDC, Satpur,
Nashik – 422 007, Maharashtra State, India.

Remember: If you have any doubts about using Candid Cream correctly, seek the advice of your doctor or pharmacist.

Further information about fungal infections:

Fungal infections are very common and affect many people. Some of the most common fungal skin infections include athlete's foot, nappy rash, sweat rash and ringworm.

There are two main types of fungal infection:

- The tinea group, also known as dermatophytes.
- The candida group, also known as yeasts.

The tinea group includes athlete's foot and ringworm, both of which are easily spread by contact. The fungus that causes athlete's foot usually lives harmlessly on our skin and in our environment. The natural balance that normally keeps it under control can be upset by factors such as damp moist conditions. This could happen, for example, through regularly wearing training shoes that keep the feet hot and sweaty. Since this fungus is contagious, it can also often be picked up in changing rooms. Ringworm is usually passed on from animals to children. Ringworm is not actually a worm, its name comes from the circular wormlike shape that it forms on the skin. The main symptom for both is an itchy, scaly and irritating rash.

The candida group can be responsible for conditions such as sweat rash and thrush. Sweat rash can appear anywhere on the body, but is more likely to occur where folds of skin rub against each other, such as: under the breasts, under arms, around the groin and on the back. Candida is a yeast-like fungus that usually lives harmlessly on our skin. However, the natural balance that normally keeps it under control can be upset by factors such as sweating, tight or synthetic clothing and cosmetic preparations such as bath additives. When levels of the yeast increase, the skin can develop the following symptoms: persistent burning and itching, soreness and a variety of patches or blemishes as well as a softened and soggy appearance.

The candida group can also be responsible for nappy rash. Most babies develop nappy rash at some stage. Although this is rarely a serious condition, the rash can be extremely distressing

for both you and your baby. Nappy rash which lasts longer than three days may be fungal in origin and will require an antifungal treatment. The symptoms of fungal nappy rash include red patches on the baby's bottom and genitals, burning and itching.