Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

Candid B Lotion (Clotrimazole and Anhydrous Beclometasone Dipropionate Lotion)

2. Qualitative and quantitative composition

Composition:
Clotrimazole USP 1% w/v
Anhydrous Beclometasone dipropionate BP 0.025% w/v

For full list of excipients, see section 6.1.

3. Pharmaceutical form

Lotion

4. Clinical particulars

4.1 Therapeutic indications

Fixed dose combination lotion of clotrimazole and beclometasone dipropionate is indicated for the symptomatic relief and treatment of superficial fungal infections like dermatophyte infections, candidiasis of skin and tinea versicolor when accompanied by eczematous/inflammatory symptoms. It can also be used for steroid-responsive inflammatory dermatoses, secondarily complicated by fungal infections.

This lotion is highly suited for use in hairy and intertriginous regions, extensive and large lesions and lesions of the nails. This lotion formulation entails an easier and smoother application over a larger area in an even manner.

4.2 Posology and method of administration

Posology

Adults and children over the age of 12 years:

Lotion should be thinly and evenly applied to the affected area 2 or 3 times a day and gently rubbed in. A few drops are enough to treat an area of about the size of the hand. To prevent relapse, treatment should be continued for at least two weeks after the disappearance of all signs of infection.

There is no separate dosage schedule for the elderly or the young.

Paediatric population
Clotrimazole and beclometasone dipropionate lotion is not recommended for children under the age of twelve years.

Method of administration Topical administration only.

Topical administration twice daily for two weeks (tinea cruris, tinea corporis and candidiasis) or for four weeks (tinea pedis).

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Infected skin lesions if no anti-infective agent is used simultaneously; some fungal and viral infections of the skin, including herpes simplex, vaccinia and varicella, chickenpox.

Topical corticosteroids are also contraindicated in tuberculous lesions of the skin.

If irritation or sensitisation develops with the use of lotion, treatment should be discontinued and appropriate therapy instituted.

Clotrimazole and beclometasone dipropionate lotion is contraindicated in facial rosacea, acne vulgaris, perioral dermatitis, napkin eruptions, bacterial infections, perianal and genital pruritus.

Varicose ulcers or any other stasis ulcers.

Clotrimazole and beclometasone dipropionate lotion should not be applied to the eyes.

4.4 Special warnings and precautions for use

Local and systemic toxicity is common especially following long continued use on large areas of damaged skin and in flexures. If used on the face, courses should be limited to 5 days.

CLOTRIMAZOLE AND BECLOMETASONE DIPROPIONATE LOTION SHOULD NOT BE USED WITH OCCLUSIVE DRESSING.

When topical anti-inflammatory steroids are used under occlusive dressing, over extensive areas, it is possible that sufficient absorption may take place to give rise to systemic effects. Patients should be advised to inform subsequent physicians of the prior use of corticosteroids.

Long-term continuous therapy should be avoided where possible, particularly in infants and children, as adrenal suppression can occur even without occlusion.

The face, more than other areas of the body, may exhibit atrophic changes after prolonged treatment with potent topical corticosteroids. This must be borne in mind when treating such conditions as psoriasis, discoid lupus erythematosus and severe eczema. If applied to the eyelids, care is needed to ensure that the preparation does not enter the eye, as glaucoma might result.

If used in childhood, or on the face, courses should be limited if possible to five days and occlusion should not be used.

Topical corticosteroids may be hazardous in psoriasis for a number of reasons including rebound relapses, development of tolerance, risk of generalised pustular psoriasis and development of local or systemic toxicity due to impaired barrier function of the skin. If used in psoriasis careful patient supervision is important.

Long term continuous or inappropriate use of topical steroids can result in the development of rebound flares after stopping treatment (topical steroid withdrawal syndrome). A severe form of rebound flare can develop which takes the form of a dermatitis with intense redness, stinging and burning that can spread beyond the initial treatment area. It is more likely to occur when delicate skin sites such as the face and flexures are treated. Should there be a reoccurrence of the condition within days to weeks after successful treatment a withdrawal reaction should be suspected. Reapplication should be with caution and specialist advise is recommended in these cases or other treatment options should be considered.

Appropriate antimicrobial therapy should be used whenever treating inflammatory lesions which have become infected. Any spread of infection requires withdrawal of topical corticosteroid therapy and systemic administration of antimicrobial agents.

Bacterial infection is encouraged by the warm, moist conditions induced by occlusive dressings, and so the skin should be cleansed before a fresh dressing is applied.
Any of the side effects that are reported following systemic use of corticosteroids, including adrenal suppression, manifestation of Cushing's syndrome, hyperglycemia, and glycosuria may also occur with topical steroids, especially in infants and children.

Visual disturbance may be reported with systemic and topical (including, intranasal, inhaled and intraocular) corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for

evaluation of possible causes of visual disturbances which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

Paediatric population

- Long term continuous therapy should be avoided in all children irrespective of age.
- Clotrimazole and beclometasone dipropionate lotion should not be used with adhesive dressing.
- The safety and effectiveness of Clotrimazole and beclometasone dipropionate lotion has not been established in children below the age of 12 years.
- If used on children, courses should be limited to 5 days.

Hypothalamic-pituitary adrenal axis suppression, Cushing's syndrome and intracranial hypertension have been reported in children receiving topical corticosteroids. Manifestation of adrenal suppression in children include linear growth retardation, delayed weight gain, low plasma cortisol levels, and absence of response to ACTH stimulation.

Manifestation of intracranial hypertension include bulging fontanelles, headaches, and bilateral papilloedema.

4.5 Interaction with other medicinal products and other forms of interaction

There are no known interactions with the clotrimazole and beclometasone dipropionate lotion.

However, there have been reports of a heat reaction when clotrimazole is used concomitantly with Framycetin sulfate + Gramicidin + Dexamethasone drops in the ear.

4.6 Pregnancy and Lactation

Clotrimazole and Beclometasone dipropionate lotion should only be used in pregnancy or lactation if the benefit justifies the potential risk to the foetus and such use should not be extensive i.e. in large amounts or for long periods.

Fertility:
Clotrimazole
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.

Beclometasone dipropionate None stated.

Pregnancy:
Clotrimazole
There is a 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 topical treatment, harmful effects with respect to reproductive toxicity are not predicted.

Clotrimazole can be used during pregnancy, but only under the supervision of a physician or midwife.

Beclometasone dipropionate
There is inadequate evidence of safety in human pregnancy. Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development including cleft palate and intrauterine growth retardation. There may therefore be a very small risk of such effects in the human foetus.

Lactation:
Clotrimazole
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. Clotrimazole may be used during lactation. If used topically on the nipple area, wash breasts before feeding child.

Beclometasone dipropionate
None stated.

4.7 Effects on ability to drive and use machines

4.8 Undesirable effects

Clotrimazole and beclometasone dipropionate lotion has no or negligible influence on the ability to drive or use machines.

4.8 Undesirable effects

Clotrimazole

As the listed undesirable effects are based on spontaneous reports, assigning an accurate frequency of occurrence for each is not possible.

Immune system disorders: anaphylactic reaction, angioedema, hypersensitivity.

Vascular disorders: syncope, hypotension.

Respiratory, thoracic and mediastinal disorders: dyspnoea.

Skin and subcutaneous tissue disorders: blisters, dermatitis contact, erythema, paraesthesia, skin exfoliation, pruritus, rash, urticaria, stinging skin/burning sensation skin.

General disorders and administration site conditions: application site irritation, application site reaction, oedema, pain.

Beclometasone dipropionate

Skin and Subcutaneous Tissue Disorders

Not known (cannot be estimated from available data): Withdrawal reactions - redness of the skin which may extend to areas beyond the initial affected area, burning or stinging sensation, itch, skin peeling, oozing pustules.

Prolonged and intensive treatment with highly active corticosteroid preparations may cause local atrophic changes in the skin such as thinning, striae, and dilatation of the superficial blood vessels, particularly when occlusive dressings are used or when skin folds are involved.

As with other topical corticosteroids, prolonged used of large amounts, or treatment of extensive areas, can result in sufficient systemic absorption to produce the features of hypercorticism. The effect is more likely to occur in infants and children, and if occlusive dressings are used. In infants, the napkin may act as an occlusive dressing.

Should systemic corticosteroid effects arise from application of beclometasone dipropionate, topical treatment should be discontinued. If adrenal function is impaired the patient will need to be protected from any harmful effects of stress with oral corticosteroid preparations until normal adrenal function is established.

There are reports of pigmentation changes and hypertrichosis with topical steroids.

In rare instances, treatment of psoriasis with corticosteroids (or its withdrawal) is thought to have provoked the pustular form of the disease.

Beclometasone dipropionate is usually well tolerated, but if signs of hypersensitivity appear, application should stop immediately. Exacerbation of symptoms may occur.

Posterior subcapsular cataracts have been reported following the systemic use of corticosteroids.

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. Healthcare professionals are requested to report any suspected adverse reactions via national regulatory portal or systems.

4.9 Overdose

Clotrimazole
No risk of acute intoxication is seen as it is unlikely to occur following a single 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.

Beclometasone dipropionate
Should systemic corticosteroid effects arise from application of beclometasone dipropionate topical treatment should be discontinued. If adrenal function is impaired the patient will need to be protected from any harmful effects of stress with oral corticosteroid preparations until normal adrenal function is established.

Discontinuation of therapy, when the typical signs of hypercorticisim appear.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Clotrimazole and beclometasone dipropionate Lotion contains beclometasone, a glucocorticoid exhibiting the general properties of corticosteroids, and clotrimazole which is an imidazole antifungal agent.

Mechanism of Action

Clotrimazole

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 0.0628.0 µg/ml substrate. The mode of action of clotrimazole is primarily 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 its antimycotic action, clotrimazole also acts on gram-positive microorganisms (*Streptococci / Staphylococci / Gardnerella vaginalis*), and gram-negative microorganisms (*Bacteroides*).

In vitro clotrimazole inhibits the multiplication of Corynebacteria and gram-positive cocci with the exception of Enterococci in concentrations of 0.5-10 µg/ml 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.

Beclometasone dipropionate

Beclometasone dipropionate is an active corticosteroid with topical anti-inflammatory activity.

5.2 Pharmacokinetic properties

Clotrimazole

Pharmacokinetic investigations after dermal application have shown that clotrimazole is minimally absorbed from the intact or inflamed skin into the

human blood circulation. The resulting peak serum concentrations of clotrimazole were below the detection limit of 0.001 µg/ml suggesting that, clotrimazole applied topically is unlikely to lead to measurable systemic effects or side effects.

Beclometasone dipropionate
Absorption

The extent of percutaneous absorption of topical corticosteroid is determined by many factors including the vehicle, the integrity of the epidermal barrier, and the use of occlusive dressings.

Topical corticosteroids can be absorbed from normal intact skin. Inflammation and/or other disease processes in the skin increase percutaneous absorption. Occlusive dressings substantially increase the percutaneous absorption of topical corticosteroids.

Distribution
Once absorbed through the skin, topical corticosteroids are handled through pharmacokinetic pathways similar to systematically administered corticosteroids. Corticosteroids are bound to plasma proteins in varying degrees.

Biotransformation
Corticosteroids are metabolised primarily by the liver.

Elimination
Topical corticosteroids are excreted by the kidneys.

5.3 Preclinical safety data

Clotrimazole
Nonclinical 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, embryotoxicity, 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.

Beclometasone dipropionate
There are no preclinical data of relevance to the prescriber which are additional to that in other sections of the SmPC.

6. Pharmaceutical Particulars

6.1 List of Excipients

Hexylene Glycol
Medium Chain Triglycerides
Isopropyl Myristate

6.2 Incompatibilities

None

6.3 Shelf-Life

24 Months

6.4 Special Precautions for storage

Store below 30°C. Do not freeze. Protect from light.

6.5 Nature and Content of container

A printed carton containing a leaflet and a set of temper proof LDPE labeled bottle fitted with plug and green coloured cap containing a clear, colourless to pale yellow, viscous liquid.

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 Authorization Holder

Glenmark Pharmaceuticals Ltd.
B/2, Mahalaxmi Chambers, 22,
Bhulabhai Desai Road,
Mumbai – 400 026, India.

8. Marketing Authorization Number

11660

9. Date of first authorization/renewal of the authorization

29/05/1999

10. Date of revision of the text

17/06/2026