SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Timodine Cream

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient	**%w/w**
Nystatin*	3.00
Dimeticone 350	10.00
Hydrocortisone**	0.50
Benzalkonium chloride solution	0.20

(equivalent to benzalkonium chloride 0.10g)

*An overage of 15% is added at manufacture. The 3% w/w is approximate only to achieve an activity of nystatin in the final formulation of 100,000 IU/g.

**An overage of 8% is added at manufacture.

Excipients	**%w/w**
Cetostearyl alcohol	1.51
Butylated hydroxyanisole compound (containing 0.40 butylated hydroxyanisole (E320) 20%, propyl gallate 10%, citric acid 10% and 60% propylene glycol (E1520))	0.40
Methyl hydroxybenzoate (E218)	0.10
Propyl hydroxybenzoate (E216)	0.10
Sorbic acid	0.10

For a full list of excipients, see Section 6.1.

3 PHARMACEUTICAL FORM

Cream
A pale yellow cream

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of dermatoses, including intertrigo, eczema, seborrhoeic dermatitis, hand dermatitis, and pruritis ani et vulvae, in which infection with *Candida albicans* is a factor. For the treatment of severe nappy rash in which infection with *C. albicans* is a factor.

4.2 Posology and method of administration

For topical application to the skin.
Adults (including the elderly) and children
Dermatoses: Sufficient Timodine Cream should be applied to cover the lesion in a thin layer. It should then be massaged into the skin until the cream disappears.
The treatment should be repeated three times a day until the lesion has healed.
There is no indication that dosage need be modified for the elderly.

Nappy rash: After removal of the soiled nappy, the affected area should be cleaned and dried, and a thin layer of Timodine Cream applied. The treatment should be repeated after every nappy change. In infants long-term continuous topical steroid therapy should be avoided since this can lead to adrenal suppression even without occlusion. A course of treatment should not normally exceed seven days.

4.3 Contraindications

Timodine Cream is contra-indicated for use in the following conditions:

- rosacea
- perioral dermatitis
- untreated bacterial, fungal or viral skin infections
- ulcerated skin

Known hypersensitivity to nystatin, dimeticone 350, hydrocortisone or benzalkonium chloride solution, or to any of the excipients (see Section 6.1 'List of excipients').

4.4 Special warnings and precautions for use

In order to minimise the side effects of a topical corticosteroid, it is important to apply it thinly to the affected areas only. Topical corticosteroids should not be applied with an occlusive dressing to large areas of the body. Absorption is greatest on thin/raw skin, intertriginous areas, and under occlusion. Skin thinning is more likely if corticosteroids are applied under occlusion.

The label will state mild steroid.

Absorption of topical corticosteroids through the skin can rarely cause adrenal suppression and even Cushing's syndrome (see Section 4.8 'Undesirable effects' and Section 4.9 'Overdose'), depending on the area of the body being treated and the duration of treatment.

Avoid prolonged exposure on the face and keep away from the eyes. Use with caution on broken skin.

Prolonged use of compound preparations such as Timodine Cream can increase the likelihood of resistance and of sensitization. Mixing topical preparations on the skin should be avoided where possible; several minutes should elapse between application of different preparations.

Topical corticosteroids are not recommended for acne vulgaris, may worsen secondary infected lesions, and should not be used indiscriminately in pruritis.

Long term 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 advice is recommended in these cases or other treatment options should be considered.

Timodine Cream contains butylated hydroxyanisole (E320), cetostearyl alcohol, sorbic acid which may cause local skin reactions (e.g. contact dermatitis) and propylene glycol (E1520), which may cause skin irritation. Butylated hydroxyanisole (E320) may cause irritation to the eyes and mucous membranes. Timodine Cream also contains propyl hydroxybenzoate (E216) and methyl hydroxybenzoate (E218), both of which may cause allergic reactions, which may be delayed. Nystatin can rarely cause contact dermatitis, and allergic reactions can occur after use of benzalkonium chloride.

Instruct patients not to smoke or go near naked flames – risk of severe burns. Fabric (clothing, bedding, dressings etc) that has been in contact with this

product burns more easily and is a serious fire hazard. Washing clothing and bedding may reduce build-up but not totally remove it.

The elderly

The skin of the elderly is often relatively atrophic so that local and systemic side effects of hydrocortisone are more likely.

Patients with hepatic failure

The reduced metabolism of hydrocortisone in patients with hepatic failure increases the theoretical risk of adrenal suppression.

Paediatric population

Avoid prolonged use in children.

Caution is required in dermatoses of infancy including nappy rash. Care should be taken as the nappy can act as an occlusive dressing and thus allow an increase in absorption of the steroid component of the cream.

In infants, long-term continuous topical steroid therapy should be avoided since this can lead to adrenal suppression even without occlusion. A course of treatment should not normally exceed seven days.

Use of hydrocortisone should be avoided in neonates. Any proposed use of hydrocortisone in neonates should be carefully assessed, as the high body surface area:weight ratio allows a proportionate increase in percutaneous absorption. Consideration should be given to the relative fragility of neonatal skin.

4.5 Interaction with other medicinal products and other forms of interaction

None known

4.6 Fertility, pregnancy and lactation

Fertility

No data available

Pregnancy

Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established. However, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for prolonged periods.

Lactation

Although poorly absorbed, it is not known whether nystatin enters breast milk. Caution should be exercised when nystatin is prescribed for nursing mothers.

Corticosteroids cross the placenta to varying degrees and may be distributed in small amounts in breast milk. Any topically applied hydrocortisone should be wiped off thoroughly prior to nursing if it is being applied to the breast or nipple area.

4.7 Effects on ability to drive and use machines

None known

4.8 Undesirable effects

Tabulated list of adverse reactions

Undesirable effects are listed by MedDRA System Organ Classes.

Assessment of undesirable effects is based on the following frequency groupings:

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 estimated from the available data

System Organ Class	Frequency	Undesirable Effect
Endocrine disorders	Not known	• adrenal suppression (see Section 4.4 'Special warnings and precautions for use')
Immune system disorders	Not known	• hypersensitivity reactions*
Infections and infestations	Not known	• spread and worsening of untreated infection (see Section 4.4 'Special warnings and precautions for use')
Metabolism and nutrition disorders	Not known	• Cushing's syndrome (see Section 4.4 'Special warnings and precautions for use')
Skin and subcutaneous tissue disorder	Not known	• thinning of the skin* (see Section 4.4 'Special warnings and precautions for use' and Section 4.9 'Overdose') • irreversible striae atrophicae (see Section 4.9 'Overdose') • telangiectasia (see Section 4.9 'Overdose') • contact dermatitis (see Section 4.4 'Special warnings and precautions for use') • perioral dermatitis • acne or worsening of acne • rosacea • mild depigmentation* • hypertrichosis

		• contact sensitisation • purpura • loss of skin collagen and subcutaneous atrophy • 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 (see section 4.4).

*see section 'Description of selected adverse reactions'.

Description of selected adverse reactions

If signs of hypersensitivity appear, application should stop immediately.

Thinning of the skin may be restored over a period after stopping treatment but the original structure may never return.

Mild depigmentation may be reversible.

Exacerbation of symptoms may occur.

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 asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Prolonged administration of hydrocortisone, especially to sensitive areas, such as the face and flexures, may result in irreversible adverse effects such as epidermal thinning, telangiectasia and striae. Chronic administration of hydrocortisone may lead to systemic absorption and thereby suppression of the pituitary-adrenal axis. High doses of corticosteroids can cause Cushing's syndrome.

It is possible that nausea and vomiting or diarrhoea may occur after ingestion of this product. Treat symptomatically. A small glass of milk or water may be helpful.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antifungals for topical use
ATC code: D01A

Nystatin

Nystatin is a polyene antifungal antibiotic that interferes with the permeability of the cell membrane of sensitive fungi by binding to sterols, chiefly ergosterol. Nystatin is used for the prophylaxis and treatment of candidiasis of the skin and mucous membranes. It is both fungistatic and fungicidal against a wide range of yeasts and yeast-like fungi.

Dimeticone 350
Dimeticones and other silicones are water-repellent and have a low surface tension. They are used in topical barrier preparations for protecting the skin against water-soluble irritants.

Hydrocortisone
Hydrocortisone is a mild corticosteroid and an effective anti-inflammatory agent.

Benzalkonium chloride solution

Benzalkonium chloride is a quaternary ammonium antiseptic with a broad spectrum of antibacterial activity.

5.2 Pharmacokinetic properties

Nystatin

Nystatin is poorly absorbed.

Dimeticone 350

Dimeticone is a silicone polymer that is not absorbed.

Hydrocortisone

Hydrocortisone is absorbed through the skin, metabolised in the liver, kidneys and most other body tissues. It is metabolised to hydrogenated and degraded forms such as tetrahydrocortisone and tetrahydrocortisol, which are excreted in the urine mainly conjugated as glucuronides, together with a small proportion of unchanged hydrocortisone (<1%).

Hydrocortisone is extensively bound to plasma proteins, >90%, and has a small volume of distribution, $0.31.kg^{-1}$. It has a short biological half-life of about 100 minutes and elimination is rapid, with about 90% of the absorbed dose excreted within 24 hours.

Absorption through the skin is greatest where the skin is thin or raw, and from intertriginous areas; it is increased by occlusion.

Benzalkonium chloride solution

Quaternary ammonium salts, such as benzalkonium chloride, are poorly absorbed through the skin.

5.3 Preclinical safety data

No preclinical findings of relevance to the prescriber have been reported.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Dibutyl phthalate
PEG 100 Stearate
Glycerol Stearate
Purified water
Stearic acid
Sodium metabisulphite
Cellulose nitrate
Cetostearyl alcohol
Butylated hydroxyanisole compound (containing butylated hydroxyanisole (E320), propyl gallate, citric acid and propylene glycol (E1520))
Methyl hydroxybenzoate (E218)
Propyl hydroxybenzoate (E216)
Sorbic acid

6.2 Incompatibilities

None known

6.3 Shelf life

2 years

6.4 Special precautions for storage

Store below 15ºC

6.5 Nature and contents of container

Collapsible aluminium tubes with diaphragm and an internal lacquer coating of epoxy phenolic resin.

Pack sizes: 5.5 g, 7.5 g and 30 g.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Timodine Cream may cause yellow staining on terry cotton nappies. This will disappear after soaking in bleach or nappy solution followed by rinsing and normal washing.

7 MARKETING AUTHORISATION HOLDER

Chemidex Pharma Limited
8A Crabtree Road
Egham, Surrey
TW20 8RN
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 17736/0152

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

17/06/2003

10 DATE OF REVISION OF THE TEXT

11/06/2026