| | |
|---|---|
| **BRAND NAME:** | **CLONEX – A CREAM** |
| **GENERIC NAME:** | **Betamethasone Dipropionate, Gentamicin, Idochlorhydroxyquinoline & Tolnaftate Cream** |

**1. Name of drug product**

**CLONEX – A CREAM**

**1.1 (Trade) name of product**

**CLONEX – A CREAM**

(Betamethasone Dipropionate, Gentamicin, Idochlorhydroxyquinoline & Tolnaftate Cream)

**1.2 Strength**

Betamethasone Dipropionate USP 0.643 mg

Gentamicin Sulphate BP eq. Gentamicin 1.00 mg

Iodochlorhydroxy Quinoline BP 10 mg

Tolnaftate USP 10 mg

**1.3 Pharmaceutical Dosage Form**

Cream

**2. QUALITATIVE & QUANTITATIVE COMPOSITION**

**2.1 Qualitative Declaration**

Each gram Contains:

Betamethasone Dipropionate USP……0.643 mg

Gentamicin Sulphate BP eq. Gentamicin Base… 1.0 mg

Iodochlorhydroxy Quinoline BP…….. 10 mg

Tolnaftate USP……..10 mg

Chlorocresol BP……1 mg

Cream Base ……..q.s.

| | |
|---|---|
| **BRAND NAME:** | **CLONEX – A CREAM** |
| **GENERIC NAME:** | **Betamethasone Dipropionate, Gentamicin, Idochlorhydroxyquinoline & Tolnaftate Cream** |

**Batch Formula:**

**Batch Size: 750.0 KG**

| Sr. No | Name of Raw Material | Reference | Quantity/ Batch In kg | Quantity/ g In mg |
|---|---|---|---|---|
| 1 | Betamethasone Dipropionate | USP | 0.482 | 0.643 |
| 2 | Gentamicin Sulphate BP eq. Gentamicin | BP | 0.904 | 1.205 |
| 3 | Iodochlorhydroxy Quinoline | BP | 7.500 | 10.0 |
| 4 | Tolnaftate | USP | 7.500 | 10.0 |
| 5 | Chlorocresol | BP | 0.750 | 1.0 |
| 6 | Cetostearyl Alcohol | BP | 56.250 | 75.0 |
| 7 | Cetomacragol 1000 | BP | 15.000 | 20.0 |
| 8 | Light Liquid Paraffin | BP | 30.000 | 40.0 |
| 9 | White Soft Paraffin | BP | 93.750 | 125.0 |
| 10 | B.H.T. | BP | 0.151 | 0.201 |
| 11 | Disodium EDTA | BP | 0.151 | 0.201 |
| 12 | Sodium Dihydrogen Phosphate | BP | 2.250 | 3.00 |
| 13 | Propylene Glycol | BP | 60.000 | 80.0 |
| 14 | Purified Water | BP/IH | 475.312 | 633.749 |

## 3. PHARMACEUTICAL DOSAGE FORM

Cream

White coloured Homogeneous Cream.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

CLONEX- A Cream is indicated for the relief of the inflammatory manifestations of corticosteroid responsive dermatoses when complicated by secondary infection caused by organisms sensitive to the components of this dermatologic preparation or when the possibility of such infection is suspected. Such disorders include: inguinal dermatosis, chronic dermatitis of the extremities, erythrasma, balanoposthitis, herpes zoster, eczematoid dermatitis, contact dermatitis, follicular dermatitis, dyshidrosis, paronychia, anal pruritus, seborrheic eczema, intertrigo, seborrheic dermatitis,

pustular acne, impetigo, neurodermatitis, angular stomatitis, photosensitivity dermatitis, licheni-fied inguinal dermatophytosis and tinea infections such as tinea pedis, tinea cruris and tinea corporis.

**4.2 Posology and method of administration**

A thin film of CLONEX – A Cream should be applied to cover completely the affected area two or three times daily, or as prescribed by the physician. Frequency of application should be determined according to severity of the condition.

Duration of therapy should be determined by patient response. In cases of tinea pedis, longer therapy (2-4 weeks) may be necessary.

**Method of Administration**

Topical Use only

**4.3 Contraindications**

CLONEX – A Cream is contraindicated in those patients with a history of sensitivity reactions to any of its components.

**4.4 Special warnings and precautions for use**

Any of the side effects that are reported following systemic use of corticosteroids, including adrenal suppression, may also occur with topical corticosteroids, especially in infants and children.

Systemic absorption of topical corticosteroids will be increased if extensive body surface areas are treated or if the occlusive technique is used. Suitable precautions should be taken under these conditions or when long-term use is anticipated, particularly in infants and children.

Systemic absorption of topically applied gentamicin may be increased if extensive body surface areas are treated, especially over prolonged time periods or in the presence of dermal disruption.

In these cases, the undesirable effects which occur following systemic use of gentamicin may potentially occur.

Cautious use is recommended under these conditions, particularly in infants and children.

Prolonged use of topical antibiotics occasionally may result in overgrowth of non-susceptible organisms. If this occurs or if irritation, sensitization or superinfection develops, treatment with Clonex- A cream Cream should be discontinued and appropriate therapy instituted. Systemic absorption of Iodochlorhydroxyquinolin may interfere with thyroid function tests. Therapy should be discontinued one month before these tests are conducted. The ferric chloride test for phenylketonuria can yield a false

positive result if Iodochlorhydroxyquinolin is present in the urine. Slight staining of linens or clothing due to Iodochlorhydroxyquinolin may occur. CLONEX - A Cream is not for ophthalmic use.

**Pediatric Use:** Pediatric patients may demonstrate greater susceptibility to topical corticosteroidinduced hypothalamic-pituitary-adrenal (HPA) axis suppression and to exogenous corticosteroid effects than mature patients because of greater absorption due to a large skin surface area to body weight ratio.

HPA axis suppression, Cushing's syndrome, linear growth retardation, delayed weight gain, and intracranial hypertension have been reported in children receiving topical corticosteroids.

Manifestations of adrenal suppression in children include low plasma cortisol levels and absence of response to ACTH stimulation. Manifestations of intracranial hypertension include a bulging fontanelle, headaches and bilateral papilledema.

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

CYP3A4 inhibitors

Co-administered drugs that can inhibit CYP3A4 (e.g. ritonavir and itraconazole) have been shown to inhibit the metabolism of corticosteroids leading to increased systemic exposure. The extent to which this interaction is clinically relevant depends on the dose and route of administration of the corticosteroids and the potency of the CYP3A4 inhibitor.

Systemic aminoglycoside therapy

Possibility of cumulative toxicity should be considered when gentamicin sulphate is applied topically in combination with systemic aminoglycoside therapy.

**4.6 Fertility, pregnancy and lactation**

Since safety of topical corticosteroid use in pregnant women has not been established, drugs of this class should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Drugs of this class should not be used extensively in large amounts or for prolonged periods of time in pregnant patients.

Since it is not known whether topical administration of corticosteroids can result in sufficient systemic absorption to produce detectable quantities in breast milk, a decision should be made to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

**4.7 Effects on ability to drive and use machines**

There have been no studies to investigate the effect of Betamethasone Dipropionate with gentamicin, Tolnaftate and Iodochlorhydroxyquinolin on driving performance or the ability to operate machinery. A detrimental effect on such activities would not be anticipated from the adverse reaction profile of CLONEX - A Cream.

**4.8 Undesirable effects**

Local adverse reactions reported with the use of topical corticosteroids, especially under occlusive dressings, include: burning, itching, irritation, dryness, folliculitis, hypertrichosis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, maceration of the skin, secondary infection, skin atrophy, striae and miliaria.

Rash, irritation and hypersensitivity have been reported with the topical usage of gentamicin sulfate, Iodochlorhydroxyquinolin and rarely with tolnaftate

**4.9 Overdose**

Symptoms Excessive or prolonged use of topical corticosteroids can suppress pituitary-adrenal function, resulting in secondary adrenal insufficiency, and produce manifestations of hypercorticism, including Cushing's disease. A single overdose of gentamicin would not be expected to produce symptoms. Excessive or prolonged use of topical antibiotics may lead to over-growth of lesions by nonsusceptible organisms. Systemically, tolnaftate is pharmacologically inactive. Iodochlorhydroxyquinolin rarely produces iodism. Treatment Appropriate symptomatic treatment is indicated. Acute hypercorticoid symptoms are usually reversible. Treat electrolyte imbalance, if necessary. In case of chronic toxicity, slow withdrawal of corticosteroids is advised. If overgrowth by nonsusceptible organisms occurs, stop treatment with CLONEX - A CREAM and institute appropriate therapy.

**5.0 Pharmacological properties**

**5.1 Pharmacodynamics properties**

CLONEX - A CREAM combines the anti-inflammatory, antipruritic and vasoconstrictive agent betamethasone dipropioate, the wide-spectrum antibiotic gentamicin sulfate, the fungicidal agent tolnaftate and Iodochlorhydroxyquinolin, an antibacterial and antifungal agent. The corticosteroids are a class of compounds comprising steroid hormones, secreted by the adrenal cortex and their synthetic analogs. In pharmacologic doses corticosteroids are used primarily for their anti-inflammatory and/or

immunosuppressive effects. Topical corticosteroids, such as betamethasone dipropionate, are effective in the treatment of corticosteroid-responsive dermatoses primarily because of their anti-inflammatory, antipruritic, and vasoconstrictive actions. However, while the physiologic, pharmacologic, and clinical effects of the corticosteroids are well known, the exact mechanisms of their actions in each disease are uncertain. Betamethasone dipropionate, a corticosteroid, has been shown to have topical (dermatologic) and systemic pharmacologic and metabolic effects characteristic of this class of drugs. Gentamicin sulphate is mixture of antibiotic substances produced by the growth of micromonospora purpurea. It is a bactericidal antibiotic which acts by inhibiting protein synthesis. It has greater antibacterial activity than streptomycin, neomycin or kanamycin. Gentamicin exerts a number of effects on cells of susceptible bacteria. It affects the integrity of the plasma membrane and the metabolism of RNA, but it's most important effect is inhibition of protein synthesis at the level of the 30s ribosomal subunit. Iodochlorhydroxyquinolin is a broad spectrum anti-bacterial and anti-fungal agent. Its precise mechanism of action is unknown. Tolnaftate is a potent fungicidal agent against Trichophyton mentagrophytes, Trichophyton rubrum, Microsporum canis, Epidermophyton floccosum and Malassezia furfur. Clinical studies have shown the excellent fungicidal effect of tolnaftate in a large number of patients with superficial fungal infections.1 Therapy with tolnaftate has been notable for lack of recurrence. Each component of CLONEX - A CREAM makes a significant contribution to the efficacy of the product in treating infections of mixed etiology.

**5.2 Pharmacokinetic properties**

The extent of percutaneous absorption of topical corticosteroids 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. Once absorbed through the skin, topical corticosteroids are handled through pharmacokinetic pathways similar to systemically administered corticosteroids. Corticosteroids are bound to plasma proteins in varying degrees. Corticosteroids are metabolized primarily in the liver and are then excreted by the kidneys. Some of the topical corticosteroids and their metabolites are also excreted into the bile.

Sixty-three pediatric patients' ages 1 to 12 years, with atopic dermatitis, were enrolled in an open-label,

hypothalamic-pituitary-adrenal (HPA) axis safety study. Betamethasone dipropionate cream was applied twice daily for 2 to 3 weeks over a mean body surface area of 40% (range 35% to 90%). In 10 of 43 (23%) evaluable patients, adrenal suppression was indicated by either a less than or equal to 5 mcg/dL pre-stimulation cortisol, or a cosyntropin post-stimulation cortisol less than or equal to 18 mcg/dL and/or an increase of less than 7 mcg/dL from the baseline cortisol.

**Gentamicin sulphate**

**Absorption:** Topical application of gentamicin can result in some systemic absorption. Treatment of large areas can result in plasma concentrations of up to 1µg/ml.

Gentamicin is 70-85% bound to plasma albumin following administration.

Effective plasma concentration is 4 - 8ug/ml.

The volume of distribution (VD) is 0.31/kg.

Elimination

> 90% Gentamicin is excreted unchanged in the urine by glomerular filtration.

T½ = 2 - 3 hours in individuals with normal kidney function, but can be increased in cases of renal insufficiency. The elimination rate constant is;

0.02 Hr-1 for anuric patients*

0.30 Hr-1 normal

*Therefore, in those with anuria, care must be exercised.

Up to 4% Iodochlorhydroxyquinolin applied to the skin may be absorbed. Excretion is mainly as conjugated metabolites in the urine.

**5.3 Preclinical safety data**

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

| | |
|---|---|
| **BRAND NAME:** | **CLONEX – A CREAM** |
| **GENERIC NAME:** | **Betamethasone Dipropionate, Gentamicin, Idochlorhydroxyquinoline & Tolnaftate Cream** |

## 6. Pharmaceutical Particulars

### 6.1. List of excipients

Chlorocresol

Cetostearyl Alcohol

Cetomacragol 1000

Light Liquid Paraffin

White Soft Paraffin

B.H.T.

Disodium EDTA

Sodium Dihydrogen Phosphate

Propylene Glycol

Purified water

### 6.2. Incompatibilities

None

### 6.3. Shelf life

36 Months.

### 6.4. Special precautions for storage

Keep below $30^0$ C.

Protect from light.

Keep out of reach of children.

For External use only.

### 6.5. Nature and contents of container

30 gm lami tube

### 6.6. Instruction for use and handling

No special requirement

| | |
|---|---|
| **BRAND NAME:** | **CLONEX – A CREAM** |
| **GENERIC NAME:** | **Betamethasone Dipropionate, Gentamicin, Idochlorhydroxyquinoline & Tolnaftate Cream** |

**7. Marketing Authorization Holder**

**MAXHEAL PHARMACEUTICALS (INDIA) LTD.**

J-7, M.I.D.C, TARAPUR INDUSTRIAL AREA,

BOISAR-401506, DIST. PALGHAR, INDIA

**8. Marketing Authorization Number**

Not Applicable.

**9. Date of First Authorization /Renewal of the Authorization**

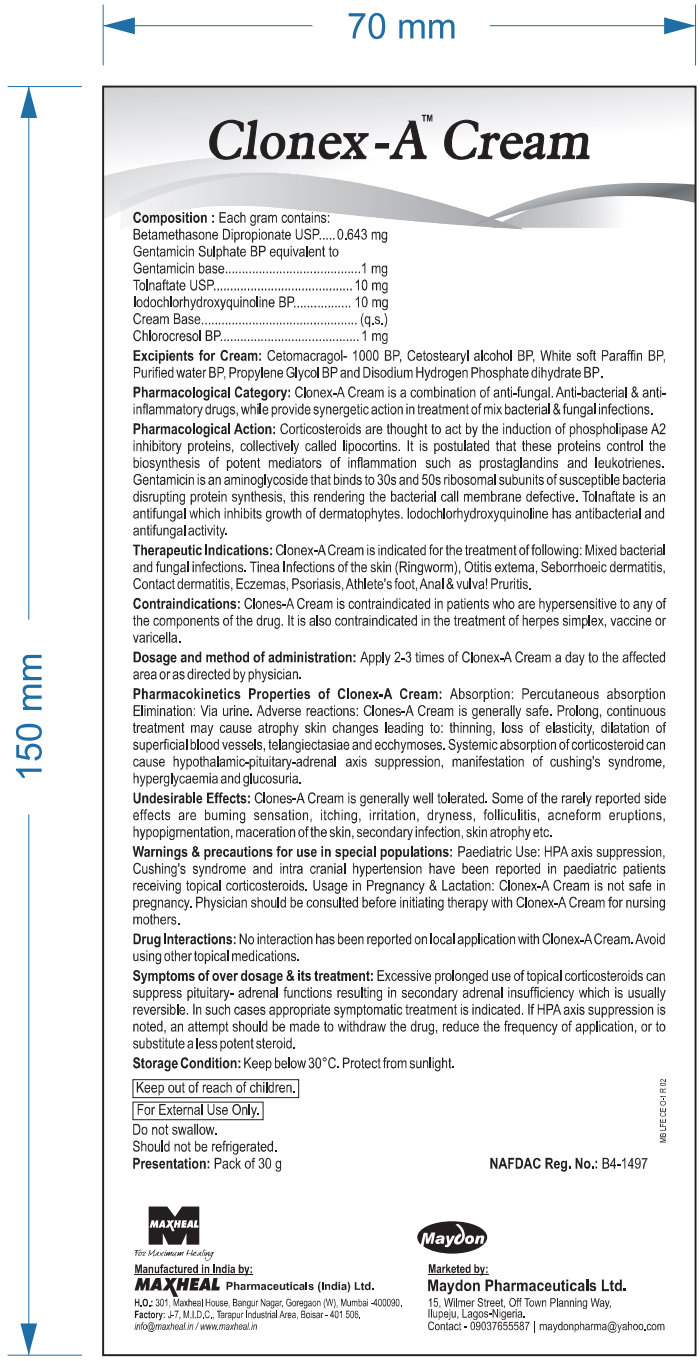
Not Applicable.

**10. Date of Revision of the**

Not Applicable.

| MAXHEAL For Maximum Healing | MARKETING | DESIGNER | QA DEPT | QC DEPT | PRODUCTION | |
|---|---|---|---|---|---|---|

| | | |
|---|---|---|
| GENERIC NAME: | Betamethasone + Gentamycin + Tolnaftate + Iodochlorhydroxyquinoline | A/W COLOR |
| BRAND NAME: | Clonex-A Cream | |
| PARTY NAME: | Maydon Pharmaceuticals Ltd. | |
| COMPONENT: | Leaflet | |
| PACKING STYLE: | Lami Tube | ■ K |
| PACK SIZE: | 30 g | |
| DIMENSION: | L: 70 mm x H: 150 mm | |
| ARTWORK CODE: | MB LFE CE O-1 R 02 | |




# Clonex-A™ Cream

**Composition :** Each gram contains:
Betamethasone Dipropionate USP..... 0.643 mg
Gentamicin Sulphate BP equivalent to
Gentamicin base..... 1 mg
Tolnaftate USP..... 10 mg
Iodochlorhydroxyquinoline BP..... 10 mg
Cream Base..... (q.s.)
Chlorocresol BP..... 1 mg

**Excipients for Cream:** Cetomacragol- 1000 BP, Cetostearyl alcohol BP, White soft Paraffin BP, Purified water BP, Propylene Glycol BP and Disodium Hydrogen Phosphate dihydrate BP.

**Pharmacological Category:** Clonex-A Cream is a combination of anti-fungal. Anti-bacterial & anti-inflammatory drugs, while provide synergetic action in treatment of mix bacterial & fungal infections.

**Pharmacological Action:** Corticosteroids are thought to act by the induction of phospholipase A2 inhibitory proteins, collectively called lipocortins. It is postulated that these proteins control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes. Gentamicin is an aminoglycoside that binds to 30s and 50s ribosomal subunits of susceptible bacteria disrupting protein synthesis, this rendering the bacterial call membrane defective. Tolnaftate is an antifungal which inhibits growth of dermatophytes. Iodochlorhydroxyquinoline has antibacterial and antifungal activity.

**Therapeutic Indications:** Clonex-A Cream is indicated for the treatment of following: Mixed bacterial and fungal infections. Tinea Infections of the skin (Ringworm), Otitis extema, Seborrhoeic dermatitis, Contact dermatitis, Eczemas, Psoriasis, Athlete's foot, Anal & vulva! Pruritis.

**Contraindications:** Clones-A Cream is contraindicated in patients who are hypersensitive to any of the components of the drug. It is also contraindicated in the treatment of herpes simplex, vaccine or varicella.

**Dosage and method of administration:** Apply 2-3 times of Clonex-A Cream a day to the affected area or as directed by physician.

**Pharmacokinetics Properties of Clonex-A Cream:** Absorption: Percutaneous absorption Elimination: Via urine. Adverse reactions: Clones-A Cream is generally safe. Prolong, continuous treatment may cause atrophy skin changes leading to: thinning, loss of elasticity, dilatation of superficial blood vessels, telangiectasiae and ecchymoses. Systemic absorption of corticosteroid can cause hypothalamic-pituitary-adrenal axis suppression, manifestation of cushing's syndrome, hyperglycaemia and glucosuria.

**Undesirable Effects:** Clones-A Cream is generally well tolerated. Some of the rarely reported side effects are buming sensation, itching, irritation, dryness, folliculitis, acneform eruptions, hypopigmentation, maceration of the skin, secondary infection, skin atrophy etc.

**Warnings & precautions for use in special populations:** Paediatric Use: HPA axis suppression, Cushing's syndrome and intra cranial hypertension have been reported in paediatric patients receiving topical corticosteroids. Usage in Pregnancy & Lactation: Clonex-A Cream is not safe in pregnancy. Physician should be consulted before initiating therapy with Clonex-A Cream for nursing mothers.

**Drug Interactions:** No interaction has been reported on local application with Clonex-A Cream. Avoid using other topical medications.

**Symptoms of over dosage & its treatment:** Excessive prolonged use of topical corticosteroids can suppress pituitary- adrenal functions resulting in secondary adrenal insufficiency which is usually reversible. In such cases appropriate symptomatic treatment is indicated. If HPA axis suppression is noted, an attempt should be made to withdraw the drug, reduce the frequency of application, or to substitute a less potent steroid.

**Storage Condition:** Keep below 30°C. Protect from sunlight.

Keep out of reach of children.

For External Use Only.

Do not swallow.

Should not be refrigerated.

**Presentation:** Pack of 30 g

**NAFDAC Reg. No.:** B4-1497

MB LFE CE O-1 R 02

MAXHEAL For Maximum Healing

Manufactured in India by:
**MAXHEAL Pharmaceuticals (India) Ltd.**
H.O.: 301, Maxheal House, Bangur Nagar, Goregaon (W), Mumbai -400090.
Factory: J-7, M.I.D.C., Tarapur Industrial Area, Boisar - 401 506.
info@maxheal.in / www.maxheal.in

Maydon

Marketed by:
**Maydon Pharmaceuticals Ltd.**
15, Wilmer Street, Off Town Planning Way,
Ilupeju, Lagos-Nigeria.
Contact - 09037655587 | maydonpharma@yahoo.com

MAYDON PHARMACEUTICALS LTD.
15, Wilmer Street,
Off Town Planning Way,
Ilupeju Lagos.
Phone: 08074150577,
09037655687
e mail: maydonpharma@yahoo.com

6th December, 2023

The Deputy Director
Drug R&R
NAFDAC
Isolo,
Lagos.

Dear sir/ma,

## SUBMISSION OF LAB SAMPLES

We hereby submit the samples of our products below for laboratory analysis.

- **CLONEX A CREAM**
- **DIADON CAPSULES**
- **WORMTAC**
- **DIFLAZON 50MG**
- **FANMET CAPSULES**
- **TENZELTOL 200MG TABLET**

Please find attached all the necessary supporting documents for your perusal

Yours faithfully

Pharm Ayobambo f
Managing Director