SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

AMAZABACT-T CREAM

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1. NAME OF THE MEDICINAL PRODUCT

AMAZABACT-T CREAM

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram contains:

Clobetasol Propionate	USP 0.05%	
Neomycin Sulphate	USP 0.05%	
Clotrimazole	USP 1.00%	
Cream Base	Q.s.	(For full list of excipients, see section 6.1)

3. PHARMACEUTICAL FORM

White or almost white, odorless cream.
Presentation: Aluminium Tube of 25g.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Amazabact-t cream is indicated for the topical treatment of the fungal and bacterial infections sustained by acute inflammatory reactions including: Tinea infections of the skin, dermatitis, allergic reactions such as eczema.

4.2 Posology and method of administration

Amazabact-t cream is a Prescription Only Medicine for dermatological use.
It is to be used as directed by the physician.

Use in pediatric patients under 12 years of age is not recommended.

Method of administration

For EXTERNAL USE ONLY.
Apply with a gentle rub to the affected area as directed by the physician.
The treated skin area should not be bandaged, otherwise covered or wrapped, so as to be occlusive unless directed by the physician.
Treatment beyond 2 consecutive weeks is not recommended and the total dosage

If no improvement is seen within 2 weeks, reassessment of the diagnosis may be necessary.

4.3 Contraindications:

Amazabact-t cream is contraindicated in those patients with a history of hypersensitivity to any of the components of the preparations.
Amazabact-t cream should not be used in the treatment of rosacea or perioral dermatitis and it should not be used on the face, groin, or axillae.

4.4 Special warnings and precautions for use

Long-term continuous topical therapy should be avoided where possible, particularly in infants and children, as adrenal suppression, with or without clinical features of Cushing`s syndrome, can occur even without occlusion. In this situation, topical steroids should be discontinued gradually under medical supervision because of the risk of adrenal insufficiency. If infection persists, systemic chemotherapy is required. Withdraw topical corticosteroid if there is a spread of infection.

Bacterial infection is encouraged by the warm, moist conditions included by occlusive dressings, and skin should be cleansed before a fresh dressing is applied. Extended or recurrent application may increase the risk of contact sensitization. Extended of infection may occur due to the masking effect of the steroid. Following significant systemic absorption, aminoglycosides such as neomycin can cause irreversible ototoxicity; and neomycin has nephrotoxic potential. In renal impairment the plasma clearance of neomycin is reduced.

4.5 Interactions with other medicinal products and other forms of interaction

When used together, this product may cause damage to latex contraceptives the effectiveness of such contraceptives may be reduced. Patients should be advised to use alterative precautions for at least 5 days after using the product. Following significant systemic absorption, neomycin sulphate can intensify and prolong the respiratory depressant effects of neuromuscular blocking agents.

The risk of topical corticosteroids interacting with other drugs is low, however the use of Amazabact-t cream might interact with other topical medications that contain steroids and any drug that affects the immune system. The Doctor or Pharmacist is to be informed if using any of the above class of drugs.

4.6 Pregnancy and lactation

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

There is little information to demonstrate the possible effect of topically applied Neomycin in pregnancy and lactation. However, neomycin present in maternal blood can cross the placenta and may give rise to a theoretical risk of fetal toxicity. To date, no other relevant epidemiological data available.

There are no adequate and well controlled studies of the teratogenic potential of topically applied Clobetasol Propionate in pregnant women. Therefore, Amazabact-t should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

It is unknown whether topical administration of the cream is excreted in breast milk but because many drugs are excreted in human milk, caution should be exercised when Amazabact-t cream is administered to a nursing woman.

4.7 Effect on ability to drive and use machines

None known.

4.8 Undesirable effects

Amazabact-t cream is generally well tolerated and has little or no side effects when used properly but if signs of hypersensitivity appear, application should be stopped immediately. Some of the rarely reported side effects are burning sensation, itching, irritation, dryness, folliculitis, acneiform eruptions, hypopigmentation, maceration of the skin, secondary infection, skin atrophy etc.

4.9 Overdose

Acute over-dosage is very unlikely to occur. However, in the case of chronic over-dosage or misuse, the features of Cushing syndrome may appear and in this situation topical steroids should be discontinued gradually under medical supervision. Consideration should be given to significant systemic absorption of neomycin sulphate. If this is suspected, use of the product should be stopped and the patient's general status, hearing ability, renal and neuromuscular functions should be monitored. Blood levels of neomycin sulphate should also be determined. Haemodialysis may reduce the serum level of neomycin sulphate. In the event of accidental oral ingestion, gastric lavage is rarely required and should be considered only only if the airway can be protected adequately and if a life-threatening amount of clotrimazole has been ingested within the preceding hour or if clinical symptoms of overdose become apparent (e.g. dizziness, nausea or vomiting).

Treatment in case of over-dosage

Product should be discontinued. See above.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

Clobetasol Propionate is a potent corticosteroid. The pharmacodynamics of corticosteroids is well known and described in the scientific literature.

Topical corticosteroids act as anti-inflammatory agents via multiple mechanisms to inhibit late phase allergic reactions including decreasing the density of mast cells, decreasing chemotaxis and activation of eosinophils, decreasing cytokine production by lymphocytes, monocytes, mast cells and eosinophils, and inhibiting the metabolism of arachidonic acid. Corticosteroids modify the functions of epidermal and dermal cells and of leukocytes participating in proliferative and inflammatory skin diseases. After passage through the cell membrane corticosteroids react with receptor proteins in the cytoplasm to form a steroid-receptor complex. This complex moves into the nucleus, where it binds to DNA. The binding process then changes the transcription of messenger RNA (mRNA). Because mRNA acts as template for protein synthesis, corticosteroids can either stimulate or inhibit the synthesis of specific proteins. Thus corticosteroids are known to stimulate the production of a glycoprotein called lipocortin. The formed lipocortin inhibits the activity of phospholipase A2, which releases arachidonic acid, the precursor of prostanoids and leukotrienes, from phospholipids. In contrast, corticosteroids inhibit mRNA responsible for interleukin-1 formation. These actions of corticosteroids on arachidonic acid metabolism and interleukin-1

formation produce anti-inflammatory, immunosuppressive and anti-mitogenic effects.

Neomycin Sulphate is a broad-spectrum aminoglycoside antibiotic drug effective against the majority of bacteria commonly associated with skin infections. Neomycin is active against both gram-positive and gram-negative organisms and mediates its pharmacological bactericidal action by binding to the 30S ribosomal subunit of susceptible bacteria and disrupting the translational machinery of bacterial protein synthesis which is crucial for the survival of bacteria.

Neomycin is a broad-spectrum that is derived from the metabolic products of Streptomyces fradiae. Neomycin is a complex comprised of three components, neomycin A, B, and C. Neomycin B, also known as framycetin, is the most active component of the complex and neomycin C is the isomer of neomycin B, making these two stereoisomers the active components of neomycin. Neomycin A, or neamine, is a moiety that conjoins two molecules of neomycin B and C together.

Clotrimazole is an imidazole derivative with a topical broad-spectrum antifungal or antimycotic action. It is a used for the treatment of a wide variety of dermatophyte infections and candidiasis. The mode of action of clotrimazole depending on the concentration of clotrimazole at the site of infection is fungistatic at concentrations of drug up to 20 mcg/mL and may be fungicidal in vitro against Candida albicans and other species of the genus Candida at higher concentrations. The minimal side effect profile of this drug and its uncomplicated metabolic profile have led it to gain widespread acceptance for the treatment of mycotic outbreaks such as vaginal yeast infections as well as athlete's foot.

Clotrimazole acts primarily by damaging the permeability barrier in the cell membrane of fungi. It causes inhibition of ergosterol biosynthesis, an essential constituent of fungal cell membranes. If ergosterol synthesis is either completely or partially inhibited, the cell is no longer able to construct an intact and functional cell membrane. Because ergosterol directly promotes the growth of fungal cells in a hormone-like fashion, rapid onset of the above events leads to dose-dependent inhibition of fungal growth. Though decreased ergosterol, due to the inhibition of lanosterol 14-demethylase (also known as CYP51) 2 is accepted to be primarily responsible for the antimycotic properties of clotrimazole, this drug also shows other pharmacological effects. These include the inhibition of sarcoplasmic reticulum Ca^{2+}-ATPase, depletion of intracellular calcium, and blocking of calcium-dependent potassium channels and voltage-dependent calcium channels 2. The action of clotrimazole on these targets accounts for other effects of this drug that are separate from its antimycotic activities.

5.2 Pharmacokinetic properties

Clobetasol Propionate can be absorbed from normal intact skin. Once absorbed through the skin, it is handled through pharmacokinetic pathways similar to systematically administered corticosteroids. The extent of percutaneous absorption of topical corticosteroids is determined by many factors, including the vehicle and the integrity of the epidermal barrier. Occlusion, inflammation and/or other disease processes in the skin may also increase percutaneous absorption.

Corticosteroids are bound to plasma proteins in varying degrees and metabolized primarily by the liver and are then excreted by the kidneys.

The metabolism of *Neomycin* is deemed to be negligible. Neomycin is either not absorbed or is absorbed only minimally through intact skin. The small fraction of neomycin which is absorbed will be rapidly excreted by the kidneys in an uncharged state while the unabsorbed portion of the drug is excreted unchanged in the feces.
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 0.001 mcg/ml, suggesting that clotrimazole applied topically is unlikely to lead to measurable systemic effects or sides effects.

5.3 Clinical data

The indications applied for are similar to the authorized therapeutic indications for medicinal products with the same active substances which are the fungal and bacterial infections sustained by acute inflammatory reactions including:
Tinea infections of the skin, contact dermatitis, allergic reactions such as eczema, psoriasis, athlete's foot, anal and vulval pruritis.

6. PHARMACEUTICAL PARTICULARS

6.1 List of ingredients

Active ingredient
Clobetasol Propionate
Clotrimazole
Neomycin Sulphate

Excipients
Propylene Glycol
Glycerol
Carbomers
Triethanolammine
Cethyl Alcohol
Stearic Acid
Paraffinum Liquid
Methyl Paraben
Propyl Paraben
Water

6.2 Incompatibilities

See section 4.4.

6.3 Shelf life

36 months from the date of production.

6.4 Special precautions for storage

Store in a cool, dry place at a temperature not exceeding 30°C. Do not freeze.
Keep medicine out of reach of children.

6.5 Nature and content of container

Aluminium tube.

Presentation: Tube of 25g packed in a paper pack with leaflet.

6.6 Special precaution for disposal

N/A

7. APPLICANT / MANUFACTURER

Name: OZAH CHEMICALS & PHARMACEUTICAL Ltd.

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