1. Name of the medicinal product

Tribotan cream

2. Qualitative and quantitative composition

Clotrimazole BP……. 0.5%w/w
Menthol ……..1.00% w/w
Icthammol BP ……. 0.20%w/w
Boric Acid BP …….. 1.00% w/w
Zinc oxide BP…… 5.00%w/w
Cream base …….. q.s

3. Pharmaceutical form

White cream

4. Clinical particular

4.1 Therapeutic indications

Tribotan cream is a combination of five medicines: Clotrimazole, Zinc Oxide, Menthol, Icthammol and Boric acid. Clotrimazole is an antifungal medication. It kills and stops the growth of the fungi by destroying its cell membrane, thereby treating your skin infection. Zinc Oxide creates a protective barrier and deflects UV rays off your skin (both UVA and UVB). It also soothes skin and eases inflammation. Ichthammol has anti-inflammatory, bactericidal, and fungicidal properties. It is used to treat a variety of skin disorders as e.g. eczema, psoriasis, Acne rosacea and acne, and it decreases microorganisms in the area surrounding a skin condition. **Boric acid** has mild antibiotic properties against fungal or bacterial infection. Together, they treat your infection effectively.

4.2 Posology and method of administration

Posology

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

Method of administration

The cream should be applied thinly and evenly to the affected area 2 – 3 times daily and rubbed in gently. A strip of cream (½ cm long) is enough to treat an area of about the size of the hand.

If the feet are infected, they should be thoroughly washed and dried, especially between the toes, before applying the cream.

Treatment should be continued for at least one month for dermatophyte infections, or for at least two weeks for candidal infections.

4.3 Contraindications

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

Do not use the cream to treat nail or scalp infections.

4.4 Special warnings and precautions for use

This product contains cetostearyl alcohol, which may cause local skin reactions (e.g. contact dermatitis).

4.5 Interaction with other medicinal products and other forms of interaction

Laboratory tests have suggested that, when used together, this product may cause damage to latex contraceptives. Consequently the effectiveness of such contraceptives may be reduced. Patients should be advised to use alternative precautions for at least five days after using this product.

4.6 Fertility, pregnancy and lactation

Pregnancy:

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 (see section 5.3). 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.

Lactation:

Available pharmacodynamic/toxicological data in animals have shown excretion of clotrimazole/metabolites in milk after intravenous administration (see section 5.3). A risk to the suckling child cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from clotrimazole therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Fertility:

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.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

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

Immune system disorders: allergic reaction (syncope, hypotension, dyspnoea, urticaria)

Skin and subcutaneous tissue disorders: blisters, discomfort/pain, oedema, erythema, irritation, peeling/exfoliation, pruritus, rash, stinging/burning.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Report to www.fidson.com

4.9 Overdose

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.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Clotrimazole

Clotrimazole is a broad-spectrum antifungal agent that inhibits the growth of pathogenic yeasts by changing the permeability of cell membranes. The action of clotrimazole 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. Unfortunately, resistance to clotrimazole, which was rare in the past, is now common in various patient populations.

Clotrimazole is generally considered to be a fungistatic, and not a fungicidal drug, although this contrast is not absolute, as clotrimazole shows fungicidal properties at higher concentrations.

Boric acid

Boric acid exhibits minimal bacteriostatic and antifungal activities. Boric acid is likely to mediate antifungal actions at high concentrations over prolonged exposures.

Zinc oxide
Zinc oxide has astringent, soothing and protective properties and is used in topical preparations for eczema, slight excoriations, wounds and haemorrhoids. It also reflects ultraviolet radiation and can be used as a physical sunscreen.

5.2 Pharmacokinetic properties

Mechanism of Action
Clotrimazole
Clotrimazole acts primarily by damaging the permeability barrier in the cell membrane of fungi. Clotrimazole 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*) 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 Ca2+-ATPase, depletion of intracellular calcium, and blocking of calcium-dependent potassium channels and voltage-dependent calcium channels. The action of clotrimazole on these targets accounts for other effects of this drug that are separate from its antimycotic activities.

Boric acid
Information regarding the mechanism of action of boric acid in mediating its antibacterial or antifungal actions is limited. Boric acid inhibits biofilm formation and hyphal transformation of *Candida albicans*, which are critical virulence factors. In addition, arrest of fungal growth was observed with the treatment of boric acid

Zinc oxide
It acts by providing a physical barrier to prevent skin irritation and help heal damaged skin.

5.3 Preclinical safety data

Non-clinical 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.

6. Pharmaceutical particulars

6.1 List of excipients

- Talcum BP
- Cetostearyl Alcohol
- White Petroleum jelly BP
- Liquid paraffin
- Methyl Paraben sodium