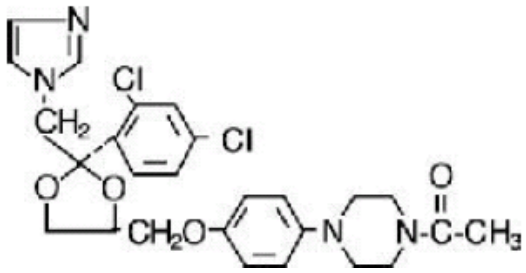
Fungicide Lotion
(Ketoconazole and Zinc Pyrithion (ZPTO) Lotion)

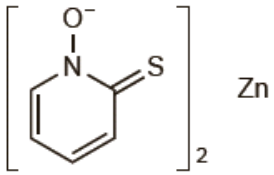
COMPOSITION
Ketoconazole I.P…….. ……2% w/v
Zinc Pyrithion (ZPTO)… 1% w/v
Base..... Q.S.
Colour: Brilliant Blue FCF

DESCRIPTION
Ketoconazole
Ketoconazole is a synthetic broad-spectrum antifungal agent available in scored white to off-white tablets. Each tablet, for oral administration contains 200 mg ketoconazole. In addition, each tablet also contains the following inactive ingredients: colloidal silicon dioxide, croscarmellose sodium, magnesium stearate and methylcellulose. Ketoconazole is cis-1- acetyl-4-[4-[[2-(2,4-dichlorophenyl)-2-(1H-imidazol-1-ylmethyl)-1,3-dioxolan–4-yl]methoxyl] phenyl] piperazine and has the following structural formula:

Ketoconazole is a white to almost white, odorless powder, soluble in acids, with a molecular weight of 531.44.



Zinc Pyrithione (ZPTO)
Pyrithione zinc has bacteriostatic and fungistatic properties. It is used similarly to selenium sulfide in usual concentrations of 1 to 2% in the control of seborrhoeic dermatitis and dandruff. It has also been used in the treatment of pityriasis versicolor.



Effects on the nervous system

Peripheral neuritis with paraesthesia and muscle weakness in a patient was associated with the prolonged use of containing pyrithione zinc 2%. The muscle weakness had disappeared 3 months after stopping the shampoo and 2 years later the paraesthesia had improved by about 75%.

Studies in animals had found signs of neurotoxicity after oral doses of pyrithione zinc but whereas absorption after topical application was found to be 13% for pyrithione sodium it was less than 1% for pyrithione zinc.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

Ketoconazole has a potent antimycotic action against dermatophytes and yeasts. Ketoconazole acts rapidly on the pruritus, which is commonly seen in dermatophyte and yeast infections. This symptomatic improvement often occurs before the first signs of healing are observed.

A study in 250 patients has shown that application twice daily for 7 days of ketoconazole 2% vs clotrimazole 1% for 4 weeks on both feet demonstrated efficacy in patients with tinea pedis (athlete's foot) presenting lesions between the toes. The primary efficacy endpoint was negative microscopic KOH examination at 4 weeks. Ketoconazole 2% treatment showed equivalent efficacy to 4 weeks clotrimazole 1% treatment. There was no evidence of relapse following treatment with ketoconazole at 8 weeks.

Pharmacokinetic properties

Plasma concentrations of ketoconazole were not detectable after topical administration of ketoconazole 2% in adults on the skin. In one study in infants with seborrhoeic dermatitis (n = 19), where approximately 40 g of ketoconazole 2% was applied daily on 40% of the body surface area, plasma levels of ketoconazole were detected in 5 infants, ranging from 32 to 133 ng/mL.

PRECLINICAL SAFETY DATA

Effects in non-clinical studies were observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use.

THERAPEUTIC INDICATIONS

For the treatment of pityriasis and dandruff of the scalp.

POSOLOGY AND METHOD OF ADMINISTRATION

Tinea pedis:

Ketoconazole 2% should be applied to the affected areas twice daily. The usual duration of treatment for mild infections is 1 week. For more severe or extensive infections (eg involving the sole or sides of the feet) treatment should be continued until a few days after all signs and symptoms have disappeared in order to prevent relapse.

For other infections:
Ketoconazole 2% should be applied to the affected areas once or twice daily, depending on the severity of the infection.

The treatment should be continued until a few days after the disappearance of all signs and symptoms. The usual duration of treatment is: tinea versicolor 2–3 weeks, tinea corporis 3–4 weeks.

The diagnosis should be reconsidered if no clinical improvement is noted after 4 weeks. General measures in regard to hygiene should be observed to control sources of infection or reinfection.

Seborrhoeic dermatitis is a chronic condition and relapse is highly likely.
Method of administration: Cutaneous administration.

CONTRAINDICATIONS
Ketoconazole 2% is contra-indicated in patients with a known hypersensitivity to any of the ingredients or to ketoconazole itself.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE
Ketoconazole 2% is not for ophthalmic use.
To prevent a rebound effect after stopping a prolonged treatment with topical corticosteroids it is recommended to continue applying a mild topical corticosteroid in the morning and to apply Ketoconazole 2% in the evening, and to subsequently and gradually withdraw the steroid therapy over a period of 2-3 weeks.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION
No interaction studies have been performed.

FERTILITY, PREGNANCY AND LACTATION
There are no adequate and well-controlled studies in pregnant or lactating women. Data on a limited number of exposed pregnancies indicate no adverse effects of topical ketoconazole on pregnancy or on the health of the foetus/newborn child. Animal studies have shown reproductive toxicity at doses that are not relevant to the topical administration of ketoconazole.

Plasma concentrations of ketoconazole are not detectable after topical application of Ketoconazole 2% to the skin of non-pregnant humans.

UNDESIRABLE EFFECTS

The safety of ketoconazole was evaluated in 1079 subjects who participated in 30 clinical trials. Ketoconazole was applied topically to the skin. Based on pooled safety data from these clinical trials, the most commonly reported (≥1% incidence) ADRs were (with % incidence): application site pruritus (2%), skin burning sensation (1.9%), and application site erythema (1%).

Including the above-mentioned adverse drug reactions (ADRs), the following table displays ADRs that have been reported with the use of ketoconazole from either clinical trial or postmarketing experiences. The displayed frequency categories use the following convention:

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)

System Organ Class	**Adverse Drug Reactions**		
	Frequency Category		
	Common (≥1/100 to <1/10)	**Uncommon** (≥1/1,000 to <1/100)	**Not Known**
Immune System Disorders		Hypersensitivity	
Skin and Subcutaneous Tissue Disorders	Skin burning sensation	Bullous eruption Dermatitis contact Rash Skin exfoliation Sticky skin	Urticaria
General Disorders and Administration Site Conditions	Application site erythema Application site pruritus	Application site bleeding Application site discomfort Application site dryness Application site inflammation	

OVERDOSE

Topical Application

Excessive topical application may lead to erythema, oedema and a burning sensation, which will disappear upon discontinuation of the treatment.

Ingestion

In the event of accidental ingestion, supportive and symptomatic measures should be carried out.

Expiry date
Do not use later than the date of expiry.

Storage
Store in cool and dry place. Protect from heat and light.

Presentation
90 ml

MARKETED BY:

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