KETOCONAZOLE TABLETS USP 200 mg
Phytoral

COMPOSITION:
Each tablet contains Ketoconazole USP 200 mg.

Description of appearance of the product : White, flat, circular, bevel edged uncoated tablets with a break line on one surface and plain on the other surface.

INDICATIONS:
Because of the risk for serious hepatic toxicity, ketoconazole tablets should be used only when the potential benefits are considered to outweigh the potential risks, taking into consideration the availability of other effective antifungal therapy.
Ketoconazole tablets are indicated for:

- Infections of the skin, hair, and mucosa, induced by dermatophytes and/or yeasts that cannot be treated topically because of the site or extent of the lesion or deep infection of the skin, in patients who have failed or who are intolerant to other therapies.
  - Dermatophytosis
  - Pityriasis versicolor
  - Malassezia folliculitis
  - Chronic mucocutaneous candidosis
  - Chronic, recurrent vaginal candidosis

- Systemic fungal infections in patients who have failed or who are intolerant to other therapies.
  - Paracoccidioidomycosis
  - Histoplasmosis
  - Coccidioidomycosis
  - Blastomycosis

Ketoconazole does not penetrate well in the CNS. Therefore, fungal meningitis should not be treated with oral ketoconazole.

ADVERSE EFFECTS:
Gastro- intestinal disturbances including nausea and vomiting, rash, pruritus, headache, dizziness, somnolence and thrombocytopenia have been reported after the administration of Ketoconazole by mouth.
Hepatitis has also been reported; it is usually reversible on discontinuation of Ketoconazole but fatalities have occurred.

CONTRAINDICATIONS:
Since Ketoconazole has been reported to cause hepatotoxicity it should not be administered to patients with pre-existing liver disease.
Patients with acute or chronic liver disease

STATEMENT ON USAGE DURING PREGNANCY:
Ketoconazole has been shown to be teratogenic in animal studies and its use is generally not recommended during pregnancy.

DOSAGE & ADMINISTRATION:
The usual dose for treatment and prophylaxis of fungal infections is 200 mg once daily taken with food. This may be increased to 400 mg daily if an adequate response is not obtained. A dose of 400 mg once daily for 5 days is used for the treatment of chronic vaginal candidiasis. The duration of treatment has not been established for most fungal infections, although it is considered that Ketoconazole should be given for at least 6 months for systemic infections. Treatment should usually be continued for at least one week after symptoms have cleared and cultures have become negative. However, maintenance treatment may be required for some infections to prevent relapse.
The type of organism responsible for the infection should be identified; however therapy may be initiated prior to obtaining these results, when clinically warranted.

Ketoconazole tablets should be taken during meals for maximal absorption.

Ketoconazole tablets are indicated for patients who have failed or who are intolerant to other therapies (see Indications).

INCOMPATIBILITIES:
There are no known incompatibilities to the use of Ketoconazole.

DRUG INTERACTIONS:
Concomitant administration of drugs that reduce stomach acidity such as anticholinergic agents, antacids and H_2 receptor antagonists, may reduce the absorption of Ketoconazole. If indicated, these drugs should be taken not less than 2 hours after Ketoconazole. Ketoconazole has been shown to increase plasma concentration of cyclosporin in patients receiving both drugs. Symptomatic, life Threatening ventricular arrhythmias have been reported from concomitant use of Terfenadine and Ketoconazole. Ketoconazole Interferes with the normal metabolism of Terfenadine and can be associated with a prolongation of the QT interval in healthy individuals on Terfenadine. Both drugs should not be administered concomitantly.
Ritonavir increases the bioavailability of ketoconazole. Therefore, when ritonavir is to be given concomitantly, higher doses (>200 mg/day) of ketoconazole tablets should not be used.

PRECAUTIONS & WARNING:
Hepatotoxicity
Serious hepatotoxicity, including cases with a fatal outcome or requiring liver transplantation, has occurred with the use of oral ketoconazole. Some patients had no obvious risk factors for liver disease. Serious hepatotoxicity was reported both by patients receiving high doses for short treatment durations and by patients receiving low doses for long durations. Cases have been reported that occurred within the first month of treatment, including some within the first week.

The hepatic injury has usually, but not always, been reversible upon discontinuation of oral ketoconazole treatment. Cases of hepatitis have been reported in children.

The cumulative dose of the treatment is a risk factor for serious hepatotoxicity. Monitor liver function in all patients receiving treatment with ketoconazole tablets (see Monitoring of hepatic function).

Patients should be advised against alcohol consumption while on treatment. If possible, use of other potentially hepatotoxic drugs should be avoided in patients receiving ketoconazole tablets. Patients should be instructed to promptly report to their physician signs and symptoms suggestive of hepatitis such as anorexia, nausea, vomiting, fatigue, jaundice, abdominal pain or dark urine. In these patients, treatment should be stopped immediately and liver function testing should be conducted.

Monitoring of hepatic function
Monitor liver function in all patients receiving treatment with ketoconazole tablets. Monitor liver function prior to treatment to rule out acute or chronic liver disease (see Contraindications), at frequent and regular intervals during treatment, and at the first signs or symptoms of possible hepatic toxicity

During the course of treatment, serum ALT should be monitored weekly for the duration of treatment. If ALT values increase to a level above the upper limit of normal or 30 percent above baseline, or if the patient develops symptoms, ketoconazole treatment should be interrupted and a full set of liver tests should be obtained. Liver tests should be repeated to ensure normalisation of values.

In patients with elevated liver enzymes, or who have experienced liver toxicity with other drugs, treatment should not be started unless the expected benefit exceeds the risk of hepatic injury. In such cases close monitoring of the liver enzymes is necessary.

Hepatotoxicity has been reported with restarting oral ketoconazole (challenge). If it is decided to restart oral ketoconazole, monitor the patient frequently to detect any recurring liver injury from the drug.

List of excipients:
Lactose Monohydrate, Starch (Dried), Microcrystalline Cellulose, Povidone, Silicone Dioxide, Magnesium Stearate.

PRESENTATION: Blister pack of 10's.

STORAGE:
Store at or below 30°C. Store in a cool dry place protected from light.

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Manufactured by:
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