YUCOMY TABLET 200MG

Name and Strength of Active Ingredient(s):
Ketoconazole 200mg/tab

Product Description:
A slight grayish-yellow color tablet, one side with a score, and the other side impressed with the mark. "YSC 1901 —".

To update information.

Pharmacodynamics:
Ketoconazole blocks the synthesis of ergosterol, a key component of the fungal cell membrane, through the inhibition of cytochrome P-450 dependent enzyme lanosterol 14 α-demethylase responsible for the conversion of lanosterol to ergosterol in the fungal cell membrane. This results in an accumulation of methylated sterol precursors and a depletion of ergosterol within the cell membrane thus weakening the structure and function of the fungal cell membrane.

To update information.

Pharmacokinetics:
1. Mean peak plasma levels of approximately 3.5µg/ml are reached within 1-2 hours following oral administration of a single 200mg dose taken with a meal.
2. The absorption of ketoconazole from the gastrointestinal tract is variable and increases with decreasing stomach pH. Peak plasma concentrations of up to 3.5 µg/ml have been obtained 2 hours after administration of 200mg by mouth. It is extensively bound to plasma proteins. Penetration into cerebral fluid is poor following oral administration.
3. The elimination of Ketoconazole is reported to be biphasic, with a half-life of 2 hours during the first 10 hours and 8 hours thereafter. Ketoconazole is extensively metabolised in the liver to inactive metabolites. It is excreted as metabolites and unchanged drug, chiefly in the feces; some are excreted in the urine.

To update as per directive (9) dlm. BPFK/PPP/07/25.

Indication:
1. Ketoconazole Tablets should be used only when other effective antifungal therapy is not available or tolerated and the potential benefits are considered to outweigh the potential risks.
2. Ketoconazole Tablets are indicated for the treatment of the following systemic fungal infections in patients who have failed or who are intolerant to other therapies:blastomycosis, coccidioidomy cosis, histoplasmosis, chromomycosis, and paracoccidioidomycosis.
3. Ketoconazole Tablets should not be used for fungal meningitis because it penetrates poorly into the cerebrospinal fluid.

To update information.

Recommended Dose:
Adults:
The usual dosage is one tablet daily with food. If response is inadequate, increase to 2 tablets daily.
Children (over 2 years old) : 3.3-6.6 mg/kg body weight daily.
Duration of treatment :
Paracoccidioidomycosis, chromomycosis, histoplasmosis, coccidioidomycosis and blastomycosis : 3 to 6 months.
Treatment should be continued until all syndromes have subsided. To be dispensed on physician's prescription.

Mode of Administration:
To be taken orally.

To update as per directive (22) dlm. BPFK/PPP/01/03 Jilid.1.

Contraindication
a) Known hypersensitivity to this product.
b) Patient with acute or chronic liver disease.

Warning and Precautions:
1. The cortisol response to ACTH stimulation will be reduced by Ketoconazole. Therefore, patient with adrenal insufficiency should have their adrenal function monitored.
2. In case of achlorhydria, the patients should be instructed to dissolve each tablet in [illegible] aqueous solution of 0.2N HCl. To ingest the resulting mixture, the patients should [illegible] glass or plastic straw so as to avoid contact with the teeth. This administration s[illegible] be followed with a cup of drinking water.

To update as per directive (22) dlm. BPFK/PPP/01/03 Jilid.1.

3. Hepatotoxicity
   Very rare cases of serious hepatotoxicity, including cases with a fatal outcome or requiring liver transplantation have occurred with the use of oral ketoconazole. Some patients had no obvious risk factors for liver disease. Cases have been reported that occurred within the first month of treatment, including some within the first week. The cumulative dose of the treatment is a risk factor for serious hepatotoxicity. Factors which may increase the risk of hepatitis are prolonged treatment with ketoconazole tablets, females over 50 years of age, previous treatment with griseofulvin, a history of liver disease, known drug intolerance and concurrent use of medication which compromises liver function. A period of one month should be allowed between cessation of griseofulvin treatment and commencement treatment with ketoconazole tablets because of an apparent association between recent griseofulvin therapy and hepatic reactions to ketoconazole tablets. Monitor liver function in all patients receiving treatment with ketoconazole tablets (See Monitoring of hepatic function). 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 should be conducted.
4. 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), after two weeks of treatment and then on a monthly basis and at the first signs or symptoms of possible hepatic toxicity. When the liver function tests indicate liver injury, the treatment should be stopped immediately.

To update as per directive (22) dlm. BPFK/PPP/01/03 Jilid.1.

A risk and benefit evaluation should be made before oral ketoconazole is used in cases of non-life threatening diseases requiring long treatment periods. 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.

Because of the risk for serious hepatotoxicity, this product 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.

Assess liver function, prior to treatment to rule out acute or chronic liver disease, and monitor at frequent and regular intervals during treatment, and at the first signs or symptoms of possible hepatotoxicity.

Interaction with Other Medicaments:

a) Concurent use of alcohol and hepatotoxicity medication with Ketoconazole may result in an increased incidence of hepatotoxicity; concurrent injection of alcohol with Ketoconazole has been reported to result in a disulfiram-like reaction, characterized by facial flushing; other symptoms may includedifficult breathing, slight fever and tightness of the chest.
b) Concurent use of antacids or antihistamine H2-receptors antagonists such as Cimetidine, Ranitidine or Famotidine or Omeprazole mat result in a marked reduction on absorption of Ketoconazole, patients should be advised to take these medications at least 2 hours after Ketoconazole.
c) Anticoagulant effects may be increased when these agents are used concurrently with Ketoconazole.
d) Combination use of Isoniazid or Rifampicin either separately or together with Ketoconazole may result in significantly decreased serum concentration of Ketoconazole.
e) Ketoconazole has been reported to increase plasma levels of Terfinadine and Astemizole due to the inhibition of the P-450 metabolic pathways. This has resulted in cardiotoxicity.
f) Ketoconazole increases plasma concentration of cyslosporine by inhibiting its metabolism, and may lead to the risk of nephrotoxicity.
g) Metabolism and ctlearance of Methyl Prednisolone is reduced by Ketoconazole. The dosage of methyl Prednisolone therefore need to be reduced.
h) Ketoconazole reduces the clearance of Benzodiazepines (Midazolam and Triazolam). This may potentiate and prolong hypnotic and sedative effects, especially with repeated dosing or chronic administration of these agents.
i) Ketoconazole inhibit hepatic P-450 metabolic pathway and result in decrease elimination of cisapride and lovastatin. The increase levels of the drug will associate with increase side effects and/or prolongation of effects.

Pregnancy and Lactation:

Ketoconazole crosses the placenta and is excreted in breast milk and may cause kernicterus in the nursing infants. Therefore, ketoconazole should not be used during pregnancy and breast feeding unless the potential adventage justify outweighs the potential risk to the foetus and infant.

Side Effects:

1. Yucomy is very well tolerated. Nausea and vomiting, abdominal pain, diarrhoea, headach dizziness, somnolence, fever, chills, photophobia and pruritus have been rarely reporte Other side effects reported with low incidence are alopecia, thrombocytopenia ar parasthesia.
2. In higher doses than the recommended dose, menstrual disorder, reversible gynecomast and oligospermia have been observed in rare cases.
3. Post Marketing Experience
   Hepato-biliary Disorders: Very rare: serious hepatotoxicity, including hepatitis cholestatic, biopsy-confirmed hepatic necrosis, cirrhosis, hepatic failure including cases resulting in transplantation or death (see WARNING & PRECAUTIONS).

To update as per directive (22) dlm. BPFK/PPP/01/03 Jilid.1.

Symptoms and Treatment of Overdose:

Symptoms of overdosage include hepatitis (dark or amber urine, loss of appetite, pale stools, stomach pain, unusual tiredness or weakness, yellow eyes or skin), and hypersensitivity (skin rash or itching).
Since there is no specific antidote, treatment for ketoconazole overdose should be symptomatic and supportive. Within the first hour after ingestion, activated charcoal may be administered.

Storage Condition:

Keep in a tight container. Store at temperature below 30°C. Protect from light and moisture.

Shelf Life:

3 years from the date of manufacture.

Dosage Forms and Packaging Available:

Plastic bottle of 100's and 1500's (for export only).
Strip packaging of 10's x 1, 10's x 10 and 10's x 50.

Y. S. P.®

Manufacturer and Product Registration Holder:
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