HOVID-KETOCONAZOLE TABLET 200 MG

VIKET27-1var (MY)

DESCRIPTION
Round, white uncoated tablet, bevel-edged, shallow convex faces, "HD" and break-bar embossed on one face.

COMPOSITION
Each tablet contains: Ketoconazole 200 mg/tablet.

PHARMACODYNAMICS
Fungistatic; may be fungicidal, depending on concentration; inhibits biosynthesis of ergosterol or other sterols, damaging the fungal cell membrane and altering its permeability; as a result, loss of essential intracellular elements may occur; also inhibits biosynthesis of triglycerides and phospholipids by fungi; in addition, inhibits oxidative and peroxidative enzyme activity, resulting in intracellular buildup of toxic concentrations of hydrogen peroxide, which may contribute to deterioration of subcellular organelles and cellular necrosis. In Candida albicans, inhibits transformation of blastospores into invasive mycelial form.

PHARMACOKINETICS
Readily absorbed orally in normal patients and it is excreted as metabolites and unchanged drug chiefly in the faeces; some is excreted in the urine.

INDICATIONS
- hovid-Ketoconazole 200 Tablet should be used only when other effective antifungal therapy is not available or tolerated and the potential benefits are considered to outweight the potential risks.
- hovid-Ketoconazole 200 Tablet are indicated for the treatment of the following systemic fungal infections in patients who have failed or who are intolerant to other therapies: blastomycosis, coccidioidomycosis, histoplasmosis, chromomycosis, and paracoccidioidomycosis.
- hovid-Ketoconazole 200 Tablet should not be used for fungal meningitis because it penetrates poorly into the cerebrospinal fluid.

CONTRAINDICATIONS
- It is contraindicated in patients with acute or chronic liver disease or with a known hypersensitivity to the drug.
- It is also contraindicated when co-administered with terfenadine, astemizole and cisapride.

WARNING AND PRECAUTIONS
- Ketoconazole was considered to be unsafe in patients with acute porphyria because it has been shown to be porphyrinogenic in animals or in vitro systems.
- Patients allergic to other azole antifungals (itraconazole, fluconazole, miconazole) may also be allergic to ketoconazole.
- Taking histamine H2-receptor antagonists at least 2 hours after ketoconazole.
- Avoiding alcoholic beverages while taking ketoconazole.
- Caution if dizziness or drowsiness occurs.
- Caution use in children since hepatitis has been reported in children.
- Ketoconazole has been shown to be teratogenic in animal studies and its use is generally not recommended during pregnancy.
- Ketoconazole is excreted in breast milk and may increase the possibility of kernicterus in the nursing infant. Therefore, nursing mothers should stop breast-feeding when beginning and throughout treatment with ketoconazole and for 24 to 48 hour thereafter.
- Ketoconazole Tablets have not been systematically studied in children of any age, and essentially no information is available on children under 2 years. Ketoconazole 200 Tablet should not be used in pediatric patients unless the potential benefit outweighs the risks.

Because of the risk of serious hepatotoxicity, hovid-Ketoconazole 200 Tablet 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.

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.

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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.

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.

MAIN SIDE / ADVERSE EFFECTS

Hepatitis, hypersensitivity, skin rash, pruritus, diarrhoea, nausea, vomiting, constipation, abdominal pain, dizziness, drowsiness, headache, gynaecomastia, impotence, menstrual irregularities, photophobia, somnolence and thrombocytopenia has been reported rarely.

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 warnings and precautions)

DRUG INTERACTIONS

- Concurrent use with alcohol or other hepatotoxic medications may result in an increased incidence of hepatotoxicity; patients, especially those on prolonged administration or those with a history of liver disease, should be carefully monitored and should be advised to avoid alcoholic beverages and other hepatotoxins; with concurrent use of dantrolene, females over 35 years of age may be especially at risk.
- Concurrent use with antacids, anticholinergics, antispasmodics, histamine H2-receptor antagonists or omeprazole may cause increased gastrointestinal pH and may result in a marked reduction in absorption of ketoconazole.
- Anticoagulant effects may be increased when these agents are used concurrently with ketoconazole; patients should be closely monitored, and dosage adjustments may be necessary during and after ketoconazole therapy.
- Ketoconazole has been reported to increase plasma concentrations of cyclosporine by inhibiting its metabolism; this may increase the risk of nephrotoxicity; concurrent use is recommended only with great caution; serum concentrations of cyclosporine should be monitored and the dose of cyclosporine may need to be reduced.
- Concurrent administration of ketoconazole with dideoxyinosine (ddI) may decrease the absorption of ketoconazole; ddI must be given with a buffer to neutralize stomach acidity in order to increase its absorption, and ketoconazole requires an acidic environment for optimal absorption; ketoconazole should be administered at least 2 hours before or 2 hours after ddI is given.
- Concurrent use of isoniazid or rifampin either separately or together with ketoconazole may result in significantly decreased serum concentrations of ketoconazole; therefore, isoniazid or rifampin, alone or in combination, should be used with caution when given concurrently with ketoconazole.
- Concurrent use with phenytoin may result in altered metabolism of either or both medications; serum concentrations of phenytoin have been reported to be increased by miconazole, another imidazole derivative; in addition, time to peak ketoconazole serum concentrations may be delayed; response to both medications should be closely monitored.
- Concurrent use with terfenadine has been reported to increase plasma levels of terfenadine because of inhibition of the P450 metabolic pathways by ketoconazole; the increased plasma level of terfenadine has resulted in cardiotoxicity (torsades de pointes).

OVERDOSAGE

Clinical features: High dose ketoconazole therapy has been shown to suppress corticosteroid and testosterone secretion.

Treatment for overdosage: Treat overdosage by gastric lavage with sodium bicarbonate solution to help reduce absorption of ketoconazole.

DOSAGE AND ADMINISTRATION

For oral use.
There should be laboratory as well as clinical documentation of infection prior to starting ketoconazole therapy. The usual duration of therapy for systemic infection is 6 months. Treatment should be continued until active fungal infection has subsided.

Adults: The recommended starting dose of Ketoconazole 200 Tablet is a single daily administration of 200 mg (one tablet). If clinical responsiveness is insufficient within the expected time, the dose of Ketoconazole 200 Tablet may be increased to 400 mg (two tablets) once daily.

Children: In small numbers of children over 2 years of age, a single daily dose of 3.3 to 6.6 mg/kg has been used.

Ketoconazole 200 Tablet have not been studied in children under 2 years of age.

Storage: Store below 30°C. Protect from moisture.

Presentation/Packing: Blister of 3 x 10's, 10 x 10's.

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