FUNZOL®

DESCRIPTION

FUNZOL is the trade name of Fluconazole, a systemic azole antifungal.
Each **FUNZOL 50**, **100**, and **150** Capsule contains 50, 100, and 150 mg Fluconazole, respectively.

CHEMISTRY

Fluconazole is: 2-(2,4-Difluorophenyl)-1,3-bis(1H-1,2,4-triazol-1-yl)propan-2-ol.

CLINICAL PHARMACOLOGY

FUNZOL is fungistatic and may be fungicidal at higher concentrations. **FUNZOL** interferes with cytochrome P-450 activity, which is necessary for the demethylation of 14-alpha-methyl sterols to ergosterol, the principal sterol in the fungal cell membrane. As ergosterol becomes depleted, the cell membrane is damaged, producing alterations in membrane functions and permeability. In *Candida albicans*, **FUNZOL** inhibits transformation of blastospores into invasive mycelial form.
As compared to other azole antifungals, **FUNZOL** has a very weak, noncompetitive inhibitory effect on the liver cytochrome P-450 system, while maintaining a high affinity for fungal P-450 activity. It also has not been reported to have antiandrogenic activity at usual doses.
Fluconazole is very well-absorbed orally and is widely distributed throughout the body, with good penetration into the cerebrospinal fluid, the eye and the peritoneal fluid.

INDICATIONS

FUNZOL is indicated in the following conditions:

- ☐ Acute or recurrent vaginal candidiasis.
- ☐ Mucosal cadidiasis: Including oropharyngeal, esophageal, and non-invasive bronchopulmonary infections; candiduria; and in mucocutaneous and chronic oral atrophic candidiasis (denture sore mouth). Normal hosts and patients with compromised immune function may be treated with **FUNZOL**.
- ☐ Systemic candidiasis, including candidemia, disseminated candidiasis and other invasive candidal infections: These include infections of the peritoneum, endocardium and pulmonary and urinary tracts. **FUNZOL** may also be used in the treatment of candidal infections in patients with malignancy, in intensive care units patients, or patients receiving cytotoxic or immunosuppressive therapy.
- ☐ Cryptococcosis: Including cryptococcal meningitis and infections of other sites (e.g. pulmonary, cutaneous). Normal host and patients with acquired immune deficiency syndrome (AIDS), organ transplants or other causes of immunosuppression may be treated. **FUNZOL** can be used as maintenance therapy to prevent relapse of cryptococcal disease in patients with AIDS.

DOSAGE

Usual adult dose

- ☐ Vaginal candidiasis: One **FUNZOL 150** Capsule as a single dose.
- ☐ Mucosal candidiasis:
  - Oropharengeal candidiasis: One **FUNZOL 50** Capsule once daily for 7 to 14 days. Treatment should not normally exceed 14 days except in severely immunocompromised patients.
  - Atrophic oral candidiasis associated with denatures: One **FUNZOL 50** Capsule once daily for 14 days, administered concurrently with local antiseptic measures to dentures.
  - Other candidal infections of the mucosa (e.g. esophagitis, non-invasive bronchopulmonary infections, candiduria, mucocutaneous candidiasis, etc.): One **FUNZOL 50** Capsule once daily, given for 14 to 30 days. In unusually difficult cases of mucosal candidal infections, dose may be increased to **FUNZOL** 100mg daily.
- ☐ Candidemia, disseminated candidiasis and other invasive candidal infections: **FUNZOL** 400mg on the first day, then 200mg once a day. Depending on clinical response, dose may be increased to **FUNZOL** 400mg once daily. Duration of treatment is based on clinical response
- ☐ Cryptococcal meningitis and cryptococcal infections of other sites: **FUNZOL** 400mg on the first day followed by **FUNZOL** 200-400mg once daily. Duration of treatment will depend on the clinical and mycological response, but is usually for at least 6 to 8 weeks for cryptococcal meningitis.
- ☐ Prevention of relapse of cryptococcal meningitis in patients with AIDS, after completion of primary therapy course: **FUNZOL** is administered in a daily dose of at least 100mg, indefinitely.

Notes

- ☐ Elderly patients may receive the usual adult dose, providing that they have no evidence of renal impairment (see below).
- ☐ In patients with renal impairment, normal doses should be given on the first and second days of treatment. Subsequently, the dose regimen should be adjusted according to creatinine clearance as follows:

Creatinine clearance	Dosage interval/Daily dose
> 40	24 hours (normal dosage regimen)
21-40	48 hours or half normal daily dose
10-20	72 hours or one third normal daily dose
Patients receiving regular hemodialysis	One recommended dose after each dialysis

Usual pediatric dose
Dosage has not been established, however, a small number of children from 2 weeks to 14 years of age have been safely treated with doses of 3 to 6 mg Fluconazole per kg of body weight once a day.

ADVERSE EFFECTS

Fluconazole is generally well tolerated. The commonest side effects associated with fluconazole are symptoms associated with the gastrointestinal tract, these include abdominal discomfort, diarrhea and flatulence. Other adverse effects such as rash are rarely encountered.

USE IN PREGNANCY

There are no adequate or well controlled studies on the use of Fluconazole in pregnant women. When used in animals in high toxic doses (20 - 60 times the recommended human dose/kg), Fluconazole has been reported to be teratogenic and fetotoxic. Accordingly, Fluconazole should not be used during pregnancy or in women likely to become pregnant. FDA Pregnancy Category C.

USE IN LACTATION

Fluconazole is distributed into human milk at concentrations similar to those achieved in plasma. Accordingly, Fluconazole should not be used in nursing women.

INTERFERENCE WITH CLINICAL AND LABORATORY TESTS

Serum values of alanine and aspartate aminotransferase, alkaline phosphatase, and bilirubin may be elevated with Fluconazole.

DRUG INTERACTIONS

- ☐ Tolbutamide, glyburide or glipizide: Fluconazole has increased the plasma concentration of theses drugs. Blood glucose concentrations should be monitored and oral hypoglycemic dose may need to be reduced.
- ☐ High doses of Fluconazole have been reported to inhibit the metabolism of cyclosporine, and this may increase the plasma concentration of cyclosporine to potentially toxic levels. Plasma cyclosporine concentrations should be carefully monitored in patients receiving Fluconazole.
- ☐ Rifampin may increase the metabolism of Fluconazole, thus lowering its plasma concentration, leading possibly to clinical failure or relapse.
- ☐ Fluconazole may decrease the metabolism of phenytoin resulting in increased plasma concentrations and area under the curve (AUC); concurrent use has also been reported to decrease the plasma concentration of Fluconazole. Accordingly, response to both medications should be closely monitored.
- ☐ The anticoagulant effects of warfarin may be increased when used with Fluconazole, resulting in an increase in prothrombin time. Prothrombin time must be carefully monitored in patients receiving warfarin and Fluconazole.
- ☐ Azole antifungals other than Fluconazole have been reported to elevate plasma levels of terfenadine and astemizole leading to serious cardiac effects. Even though Fluconazole has not been found to cause a change in cardiac repolarization or accumulation of terfenadine, neither astemizole nor terfenadine should be used in patients receiving Fluconazole, pending further accumulation of data.
- ☐ Hydrochlorothiazide results in increased peak plasma concentrations and area under the curve of Fluconazole, possibly due to decreased clearance.

CONTRAINDICATIONS

Fluconazole is contraindicated in patients with known hypersensitivity to the drug or to azole antifungals.

WARNINGS

- ☐ In some patients, particularly those with serious underlying disease such as AIDS and cancer, abnormalities of hepatic, renal, hematological and other biochemical function tests have been observed during treatment with Fluconazole, but the clinical significance and relationship to treatment is uncertain. Very rarely patients, who died with severe underlying disease and who have received multiple dose of Fluconazole, had post-mortem findings which included hepatic necrosis. These patients were receiving multiple concomitant medications, some known to be potentially hepatotoxic, and/or had underlying diseases which could have caused the hepatic necrosis. Patients with AIDS are more prone to the development of severe cutaneous reactions to many drugs. A small number of AIDS patients have developed such reactions usually while receiving Fluconazole concomitantly with other agents known to be associated with severe exfoliation. If rash develops which is considered attributable to fluconazole, therapy with this agent should be discontinued.
- ☐ A reduction in dosage, or increase in dosing interval, is recommended in patients with renal function impairment, because Fluconazole is excreted through the kidneys.

OVERDOSE

Limited information is available on the acute toxicity of Fluconazole in humans. Hallucinations and paranoid behavior developed in a patient with human immunodeficiency virus (HIV) infection who reportedly ingested 8.2g of Fluconazole. In case of overdose, supportive and symptomatic treatment should be initiated. The stomach should be emptied by gastric lavage if indicated. Elimination of Fluconazole can be facilitated by hemodialysis which decreases plasma concentrations by about 50% over 3 hours.

PRECAUTIONS

- ☐ The overall incidence of side effects with Fluconazole has been reported to be higher in HIV-infected patients, however, many of the HIV patients in these studies were also receiving other medications.
- ☐ No information is available on the relationship of age to the effects of Fluconazole.
- ☐ Liver function test should be monitored periodically during treatment. Fluconazole should be discontinued if abnormal enzyme values persist or worsen, or if they are accompanied by symptoms of toxicity.

HOW SUPPLIED

- ☐ Boxes of 7 blistered capsules of **FUNZOL 50** Capsules.
- ☐ Boxes of 7 blistered capsules of **FUNZOL 100** Capsules.
- ☐ Boxes of one blistered capsule of **FUNZOL 150** Capsules.
- ☐ Hospital packs of different presentations.

Store according to conditions specified on the package.

Do not use after the expiry date shown on the package.

THIS IS A MEDICAMENT

- ☐ A medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.
- ☐ Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who dispensed the medicament.
- ☐ The doctor and the pharmacist are experts in medicine.
- ☐ Do not by yourself interrupt the period of treatment prescribed for you.
- ☐ Do not repeat the same prescription without consulting your doctor.
- ☐ Keep medicaments out of the reach of children.

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COUNCIL OF ARAB HEALTH MINISTERS
UNION OF ARAB PHARMACISTS

Prescribing Information Available Upon Request

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