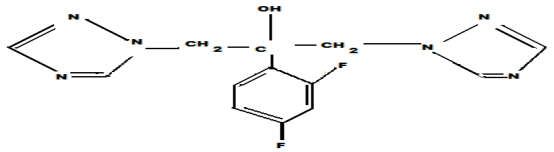
FLUTROX

For the use of a Registered Medical Practitioner, a Hospital or a Laboratory only

FLUCONAZOLE CAPSULES (FLUTROX)
Composition:
FLUTROX 50: Each capsule contains Fluconazole U.S.P.....50 mg
FLUTROX 150: Each capsule contains Fluconazole U.S.P 150mg
FLUTROX 200: Each capsule contains Fluconazole U.S.P.....200 mg

DESCRIPTION:
FLUTROX (Fluconazole) is the first of a new class of synthetic broad-spectrum bis-triazole antifungal agents. It is active against a broad spectrum of fungal pathogens and acts by inhibition of the ergosterol component of the fungal cell membrane.
Chemically Fluconazole is designated as 2,4-Difluoro-α, α-bis (1H-1,2,4 -TRIAZOL -1- ylmethyl)benzyl alcohol.



CLINICAL PHARMACOLOGY:
Mode of Action: FLUTROX (Fluconazole) is a highly selective inhibitor of fungal sterol synthesis without effect on mammalian or human steroid synthesis. It acts by inhibiting the synthesis of ergosterol, a major component of the cell membrane of yeast and fungi. Specially, the nitrogen in the azole ring is thought to bind to lanosterol-14-α-demethylase, a fungal cytochrome P450 enzyme & thereby inhibits the conversion of lanosterol to ergosterol. Inhibition of ergosterol synthesis is thought to lead to the accumulation of non-functional sterols and to the disruption of normal membrane functions including the co-ordination of chitin synthesis, the activity of membrane-bound sterols, and the preservation of normalpermeability.Spectrum: FLUTROX (Fluconazole) is active against many fungi, including yeasts and dermatophytes. Fluconazole does not appear to have any antibacterial activity.In vivo, FLUTROX (Fluconazole) is effective against strains of Candida, Cryptococcus neoformans, Blastomyces dermatidis, Histoplasma capsulatum and Coccidioides immitis.

PHARMACOKINETICS:
The drug is rapidly and almost completely absorbed from the GI tract, and there is no evidence of first-pass metabolism. Oral bioavailability of Fluconazole exceeds 90% in healthy, fasting adults: peak plasma concentrations of the drug generally are attained within 1-2 hours after oral administration. The rate and extent of GI absorption of Fluconazole are not affected by food and gastric pH.
Peak plasma Fluconazole concentrations and AUCs increase in proportion to the dose over the oral dosage range of 50-400 mg. Steady-state plasma concentrations of Fluconazole are attained within 5-10 days following oral doses of 50-400 mg given once daily.
Fluconazole is widely distributed in the body tissues and fluids following oral administration. In adult humans with normal renal function, concentrations of the drug attained in saliva, sputum, nails, blister fluid, blister skin, and vaginal secretions, are approximately equal to the concurrent plasma concentrations; concentrations attained in urine and skin may be 10 times higher than concurrent plasma concentrations.
Fluconazole, unlike some azole-derivative antifungal agents, distributes readily into CSF following oral administration; CSF concentrations of Fluconazole may be 50-94% of concurrent plasma concentrations regardless of the degree of meningeal inflammation.
Fluconazole is only 11-12% bound to plasma proteins. The plasma elimination half-life of Fluconazole in adults with normal renal function is approximately 30 hours. The elimination half-life of Fluconazole reportedly is not affected by impaired renal function.
Approximately 60-80% of a single oral dose of Fluconazole is excreted in urine unchanged, and about 11% is excreted in urine as metabolites.

INDICATIONS:
FLUTROX (Fluconazole) is indicated for:

1. Vaginal candidiasis

2. Mucosal candidiasis, e.g. oropharyngeal, oesophageal, mucocutaneous and chronic oral atrophic candidiasis, etc.

3. Systemic candidiasis: candidaemia, disseminated candidiasis, infection of peritoneum, respiratory and urinary tract.

4.Cryptococcosis: cryptococcal meningitis, primary as well as maintenance therapy.

5.Prevention of fungal infection in patients with malignancy, AIDS, in intensive care units and patients on immunosuppressive drugs.

6. Fungal infections of the skin and nails.

DOSAGE AND ADMINISTRATION:
FLUTROX (Fluconazole) is used as once daily dose for the following indications:

Vaginal candidiasis: 150 mg single oral dose

Oropharyngeal candidiasis: 50 mg once daily for 7 to 14 days

Atrophic oral candidiasis associated with dentures: 50 mg once daily for 14 days.

For other candidial infections: 50 mg daily for 14 to 30 days.

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Indications	Loading Dose	Daily Dose	Duration
Oropharyngeal Candidiasis (acute)	200 mg	50-100 mg	15 days
Oesophageal Candidiasis (acute)	200 mg	50-100 mg	21 days
Systemic Candidiasis	400 mg	200 mg	28 days
Cryptococcal Meningitis (acute) negative	400 mg*	200 mg	10-12 weeks after CSF becomes culture negative
Cryptococcal Meningitis (maintenance dose to prevent relapse)	200 mg	--	
Tinea corporis		150 mg Once a week	upto 4 weeks
Tinea cruris		150 mg Once a week	upto 4 weeks
Tinea pedis		150 mg Once a week	upto 4 weeks
Cutaneous candidiasis		150 mg Once a week	upto 4 weeks
Onychomycosis		150 mg once a week	6-12 months
Tinea versicolor (Pityriasis versicolor)	400mg	–	single oral dose

*Doses of up to 400 mg/day may be used based on medical judgment of the patient's response to therapy.

Use in renal impairment: Fluconazole is excreted predominantly in urine as unchanged drug. Hence in patients with impaired renal function, dosage of Fluconazole must be modified in response to the degree of impairment and should be based on the patient's measured or estimated creatinine clearance.
The recommended dosages are:

Creatinine clearance (ml/min.)	Dosage interval/ % of daily dose
>50	24 hrs / 100%
21-50	48 hrs/50%
10-20	72 hrs/25%
Patients receiving regular Haemodialysis	100% dose after dialysis

CONTRAINDICATIONS:
Hypersensitivity to Fluconazole or related azole compounds.
WARNING AND PRECAUTIONS:
Patients who develop abnormal liver function should be monitored. Immunocompromised patients who develop rash during Fluconazole therapy should be monitored and the drug discontinued if lesion progresses.
Use in pregnancy, nursing mothers and children
There are no adequate and well controlled studies in pregnant women. FLUTROX should be used in pregnancy only if the benefits outweigh the risks. Since it is secreted in human milk, it should not be used in lactating women.
FLUTROX is not recommended for children below 16 years as limited data is available. A small number of patients from age 3 to 13 years have been treated safely with Fluconazole using doses of 3-6 mg per kg daily.
DRUG INTERACTIONS:
Fluconazole has shown to prolong prothrombin time of coumarin drugs hence requires careful monitoring.
Concomitant administration of Fluconazole and cyclosporine may result in an increase in cyclosporine levels. Fluconazole significantly increases phenytoin levels and AUC resulting in phenytoin toxicity. Concomitant administration of Fluconazole and oral hypoglycaemics such as sulphonylurea in diabetic patients results in increased plasma concentration and reduced metabolism of anti-diabetic agents. Concomitant administration of Fluconazole and rifampicin decreases AUC for Fluconazole by 20 per cent.
SIDE EFFECTS:
Fluconazole is generally well tolerated. Commonly reported side effects are nausea, vomiting, abdominal pain, headache, skin rash and diarrhoea. Mild transient, reversible increase in liver enzymes like ALT, AST, alkaline phosphatase and serum bilirubin, etc. may be seen. Serious hepatotoxicity is rarely seen. Clinical adverse reactions have been more frequently reported in HIV patients than in non-HIV infected patients, however, the patterns were similar. In rare cases, anaphylaxis has been reported.
OVERDOSAGE:
In the event of overdosage, supportive measures and symptomatic treatment with gastric lavage if necessary, may be adequate. As Fluconazole is excreted largely in urine, forced diuresis would probably increase the elimination rate. A three hour session of haemodialysis decreases plasma levels by approximately 50 per cent.
PRESENTATION:
FLUTROX-50 Capsules - 10's in blister packs.
FLUTROX-150 Capsules - 1 strip x 1 capsule
FLUTROX-200 Capsules - 10's in blister packs
FLUTROX-200 Capsules-10 X 10's in blister pack.
STORAGE: D0 not store above 30°C.Store in a dry place. Protect from direct sunlight. Keep all medicines out of reach of children.

Manufactured by:

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