FLUCONAZOLE

Fluconazole Capsules 150 mg

Composition :

Each hard gelatin Capsule Contains :

Fluconazole USP 150 mg.

Excipients Q.S.

Approved Colours Used in Empty Capsule Shells.

Therapeutic class : Antifungal

Pharmacology :

Fluconazole is a bis-trizole antifungal structurally related to imidazole derivative antifungals. The nitrogen of the azolering triazole binds to the haem moiety of the fungal cytochrome P-450 enzyme lanosterol 14 alpha demethylase which falls conversion of lanosterol to ergosterol that to a cascade of abnormalities in membrane permeabillity, membrane bound enzyme activity and coordination of chitin synthesis.

Pharmacokinetics :

The pharmacokinetic properties of fluconazole are similar following administration by the intravenous or oral routes. In normal volunteers, the bioavailabillity of orally administered fluconazole is over 90% compared with intravenous administration. Bioequivalence was established between the 100 mg capsule and both suspension strengths when administered as a single 200 mg dose. Peak plasma concentrations (C) in fasted normal volunteers occur between 1 and 2 hours with a terminal plasma elimination half-life of approximately 30 hours (range: 20-50 hours) alter oral administration. Steady-state concentrations are reached within 5-10 days following oral dose of 50-400 mg. once given once daily administration of a loading (on day 1) of twice the usual daily dose results in plasma concentrations close to steady-state by the second day. The apparent volume of distribution of fluconazole approximates that of total body water. Plasma protein binding is low (11-12%). Following either single-or muitiple-oral doses for up to 14 days. Fluconazole penetrates into all body fluids studied (see table below). In normal volunteers, saliva concentrations of fluconazole were equal to slightly greater than plasma concentrations regardless of dose, route, or duration of dosing.

Tissue of Fluid	Ratio of Fluconazole Tissue (Fluid)/Plasma
Cerebrospinal	0.5 - 0.9
Saliva	
Sputum	
Blister fluid	
Urine	10
Normal skin	
Nails	
Blister skin	2
Vaginal tissue	
Vaginal fluid	0.4 - 0.7
. Relativa to concurrent	
.* Independent of degree of meningeol sign.	

In normal volunteers, fluconazole is cleared primarily by renal excretion, with approximately 80% of the administered dose appearing in the urine as unchanged drug. About 11% of the dose is excreted in the urine as metabolites.

Pharmcokinetic in Children :

In children, the following pharmacokinetic data {Mean(%cv)} have been reported :

Age studied	Dose (mg/kg)	Half-life	C_m. (pglmL)
9 13 years	Single - 2mg/kg	25.0	2.9 (22%) N=16
9 13 years	Single - 8mg/kg	19.5	9.8 (20%) N=15
5-15	Multiple 2mg/kg	17.4	5.5 (25%) N=5
5-15	Multiple 4mg/kg	15.2	11.4 N=6
5-15	Multiple 8mg/kg	17.6	14.1 N=8

Clearance corrected for body weight was not affected by age in these studies. Mean clearance in adults is reported to be 0.23 (17%) mL/min/kg.

Indications :

FLUCONAZOLE is indicated for mucosal candidiasis: e.g. oropharyngeal, oesophageal, mucocutaneous and chronic oral atrophic candidiasis, vaginal candidiasis etc.

Systemic candidiasis : Candidaemla, disseminated candidiasis, infection of peritoneum, endocardium, pulmonary and urinary tract.

Ctyptococcosis : Cryptococcal meningitis, primary as well as maintenance therapy.

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

Dosage and Administration :

FLUCONAZOLE may be administered either orally or by intravenous infusion at a rate of approximately 5 - 10 ml/min. On transferring the patient from the intravenous to oral route or vice versa, is no need to change the daily dose.

Adults :

Oropharyngeal candidiasis : 200 mg on the first day, followed by 100 mg once daily for 14 days.

Oesophageal candidiasis : 200 mg on the first day, followed by 100 mg once daily for 21 days.

Veginal candidiasis: 150 mg single dose

Mucosal candidiasis :50-100 mg daily for 14-30 days. *Systemic candidiasis :* 400 mg on first day, then 200400 mg once daily.

Cryptococcal meningitis : 400 mg loading dose, followed by 200 mg daily for 10-12 weeks after CSF become culture negative

Maintenance to prevent relapse of cryptococcai meningitis: 100-200 mg daily.

Prophylaxis in immunocompromised : 50-400 mg once daily started several days before onset of neutropenia and continued for-7days afterneutmphit count > 1000 cell/me.

Children :

Mucosal candidiasis:

<2 weeks3 mg/kg every 72 hrs

2-4 weeks3 mg/kg every 48 hrs

over4 weeks3 mg/kg daily

Systemic candidiasis:

<2 weeks6-12 mg/kg every 72 hrs

2-4 weeks6-12 mg/kg every 48 hrs

over4 weeks6-12 mg/kg daily

Prophylaxis in immunocompromised:
<2 weeks: 3-12 mg/kg every 72 hrs
2-4 weeks: 3-12 mg/kg every 48 hrs
over4 weeks: 3-12 mg/kg daily

In impaired renal function:
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 patients measured or estimated creatinine clearance.

The recommended dosage are :

Creatinine clearance (mL/min)	Dosage daily dose
>50	24 hrs / 100%
21-50	48 hrs / 50%?
10-20	72 hrs / 25%
Patients regular haemodialysis	100 percent dose every dialysis

Compatibility of intravenous infusion : Although further dilution is unnecessary, FLUCONAZOLE intravenous infusion is compatible with the following administration fluids :

- Dextrose 20 per cent
- Ringer's solution
- Hartmann's solution
- Potassium chloride in dextrose
- Sodium bicarbonate
- Normal saline (0.9 percent)

Mixing with any other drug prior to infusion is not recommended.

Contraindications :
Hypersensitivity to FLUCONAZOLE or any of its excipients of related azole compounds.

Warnings and Precautions :
DRUG INTERACTIONS :
Anticoagulants: Fluconazole has been shown to prolong prothrombin times of coumarin drugs, hence requires careful monitoring.
Cyclosporin : Concomitant administration of fluconazole and cyclosporin may result in increase in cyclosporin level.
Phenytoin : FLUCONAZOLE significantly increases phenytoin levels and AUC resulting in phenytoin toxicity.
Oral Hypoglycaemics : Concomitant administration of FLUCONAZOLE and oral hypoglycaemics such as sulphonylurea in diabetic patients results in increased plasma concentration and reduced metabolism of antidiabetic agents.
Rifampicin : Concomitant administration of FLUCONAZOLE and rifampicin decrease AUC for FLUCONAZOLE by 20 percent.
Theophylline : FLUCONAZOLE may increase serum concentrations of theophlline. Careful monitoring is recommended if the two drugs are coadministered.

PREGNANCY
There are no adequate and wellcontrolled studies in pregnant women FLUCONAZOLE should be used in pregnancy only if the benefits outweigh risks.

NURSING MOTHERS
Since the drug is secreted in breast milk, it should not be used in lactating women.

PAEDIATRIC USE

See Dosage and Administration.

IN IMPAIRED RENAL FUNCTION See Dosage and Administration.

IN IMPAIRED HEPATIC FUNCTION

Patients who develop abnormal liver function should be monitored. Immuno compromised patients who develop rash during FLUCONAZOLE therapy should be monitored and the drug discontinued if lesions progress.

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 infected 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.

FLUCONAZOLE is excreted largely in the urine, forced diuresis would probably increase the elimination rate. A three hour session of haemodialysis decreases plasma levels by approximately 50 percent

Storage : Store in a cool & dry place. Protect from light.

Keep medicines out of
Reach of Children.

Dosage :

As directed by the physicians.

Presentation :

FLUCONAZOLE Strip of 1*1 capsules.