SUMMARY OF PRODUCT CHARACTERISTICS (SmPC) TEMPLATE

National Agency for Food & Drug Administration & Control (NAFDAC)

Registration & Regulatory Affairs (R & R) Directorate

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC) TEMPLATE

Summary Product Characteristics

1. Name of drug product

Fluconazole tablet USP 200 mg

1.2 Strength

Each uncoated tablet contains:

Fluconazole USP ……..200 mg

Excipients……Q.S.

1.3 Pharmaceutical Dosage Form

Tablets for oral administration

2. QUALITATIVE & QUANTITATIVE COMPOSITION

2.1 Qualitative Declaration

Each uncoated tablet contains:

Fluconazole USP ……..200 mg

Excipients……Q.S.

3. PHARMACEUTICAL DOSAGE FORM

Tablets for oral administration

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

4.1 Therapeutic indications

Fluconazole is indicated for the treatment of:

1. Vaginal candidiasis (vaginal yeast infections due to Candida).

2. Oropharyngeal and esophageal candidiasis, Candida urinary tract infections, peritonitis, and systemic Candida infections including candidemia, disseminated candidiasis, and pneumonia.

3. Cryptococcal meningitis.

4.2 Posology and method of administration

Single Dose

Vaginal candidiasis: The recommended dosage of fluconazole for vaginal candidiasis is 150 mg as a single oral dose. Multiple Dose
In general, a loading dose of twice the daily dose is recommended on the first day of therapy to result in plasma concentrations close to steady-state by the second day of therapy. Treatment should be continued until clinical parameters or laboratory tests indicate that active fungal infection has subsided.

Oropharyngeal candidiasis: The recommended dosage of fluconazole for oropharyngeal candidiasis is 200 mg on the first day, followed by 100 mg once daily. Clinical evidence of oropharyngeal candidiasis generally resolves within several days, but treatment should be continued for at least 2 weeks to decrease the likelihood of relapse.

Esophageal candidiasis: The recommended dosage of fluconazole for esophageal candidiasis is 200 mg on the first day, followed by 100 mg once daily. Doses up to 400 mg/day may be used, based on medical judgment of the patient's response to therapy. Patients with esophageal candidiasis should be treated for a minimum of three weeks and for at least two weeks following resolution of symptoms.

Urinary tract infections and peritonitis: For the treatment of Candida urinary tract infections and peritonitis, daily doses of 50 to 200 mg have been used in open, noncomparative studies of small numbers of patients.

Cryptococcal meningitis: The recommended dosage for treatment of acute cryptococcal meningitis is 400 mg on the first day, followed by 200 mg once daily. A dosage of 400 mg once daily may be used, based on medical judgment of the patient's response to therapy. The recommended duration of treatment for initial therapy of cryptococcal meningitis is 10 to 12 weeks after the cerebrospinal fluid becomes culture negative. The recommended dosage of fluconazole for suppression of relapse of cryptococcal meningitis in patients with AIDS is 200 mg once daily.

Prophylaxis in patients undergoing bone marrow transplantation: The recommended fluconazole daily dosage for the prevention of candidiasis of patients undergoing bone marrow transplantation is 400 mg, once daily. Patients who are anticipated to have severe granulocytopenia (less than 500 neutrophils per cu mm) should start fluconazole prophylaxis several days before the anticipated onset of neutropenia, and continue for 7 days after the neutrophil count rises above 1000 cells per cu mm.

4.3 Contraindications

Fluconazole is contraindicated in patients who have shown hypersensitivity to fluconazole or to any of its excipients.

Caution should be used in prescribing fluconazole to patients with hypersensitivity to other azoles.

Co-administration of terfenadine is contraindicated in patients receiving fluconazole at multiple doses of 400 mg or higher based upon results of a multiple dose interaction study.

Co-administration of cisapride is contraindicated in patients receiving fluconazole

4.4 Special warnings and precautions for use

WARNING & PRECAUTIONS:

WARNINGS

(1) Hepatic injury: Fluconazole has been associated with rare cases of serious hepatic toxicity. Fluconazole should be discontinued if clinical signs and symptoms consistent with liver disease develop that may be attributable to fluconazole.

(2) Anaphylaxis: In rare cases, anaphylaxis has been reported.

(3) Dermatologic: Patients have rarely developed exfoliative skin disorders during treatment with fluconazole. The drug should be discontinued if lesions progress.

PRECAUTIONS

Some azoles, including fluconazole, have been associated with prolongation of the QT interval on the electrocardiogram. Fluconazole should be administered with caution to patients with these potentially proarrhythmic conditions.

4.5 Interaction with other medicinal products and other forms of interaction

Oral contraceptives: Fluconazole dosing resulted in small increases in the mean AUCs of levonorgestrel, ethinyl estradiol and norethindrone compared to similar placebo dosing. however, in some patients there were decreases up to 47% and 33% of ethinyl estradiol and levonorgestrel levels.

Oral hypoglycemics: Clinically significant hypoglycemia may be precipitated. Fluconazole reduces the metabolism of tolbutamide, glyburide, and glipizide and increases the plasma concentration of these agents. Blood glucose concentrations should be carefully monitored and the dose of the sulfonylurea should be adjusted as necessary.

Coumarin-type anticoagulants: Prothrombin time may be increased. Bleeding events (bruising, epistaxis, gastrointestinal bleeding, hematuria, and melena) have been reported. Careful monitoring of prothrombin time is recommended.

Phenytoin: Fluconazole increases the plasma concentrations of phenytoin.

Cyclosporine: Fluconazole may significantly increase cyclosporine levels in renal transplant patients with or without renal impairment. Careful monitoring of cyclosporine concentrations and serum creatinine is recommended

Rifampin: Rifampin enhances the metabolism of concurrently administered fluconazole. The dose of fluconazole can be increased.

Theophylline: Fluconazole increases the serum concentrations of theophylline.

Terfenadine: The occurrence of serious cardiac dysrhythmias secondary to prolongation of the QT interval. The combined use of fluconazole at doses of 400 mg or greater with terfenadine is contraindicated. The coadministration of fluconazole at doses lower than 400 mg/day with terfenadine should be carefully monitored.

Cisapride: There have been reports of cardiac events, including torsade de pointes. The combined use of fluconazole with cisapride is contraindicated.

Astemizole: May be associated with elevations in serum levels of these drugs.

Rifabutin: There have been reports of uveitis.

Tacrolimus: There have been reports of nephrotoxicity. Patients should be carefully monitored.
Short-acting Benzodiazepines: Fluconazole resulted in substantial increases in midazolam concentrations and psychomotor effects. Consideration should be given to decreasing the benzodiazepine dosage, and the patients should be appropriately monitored

4.6 Fertility, pregnancy and lactation

PREGNANCY

Nursing Mothers
Fluconazole is secreted in human milk at concentrations similar to plasma. Therefore, the use of fluconazole in nursing mothers is not recommended.

4.7 Effects on ability to drive and use machines

Non e stated

4.8 Undesirable effects

In Patients Receiving a Single Dose for Vaginal Candidiasis: Headache (13%), nausea (7%), and abdominal pain (6%), diarrhea (3%), dyspepsia (1%), dizziness (1%), and taste perversion (1%). Rarely, angioedema and anaphylactic reaction have been reported in marketing experience.

Hepatobiliary: Rare cases of serious hepatic reactions including mild transient elevations in transaminases to clinical hepatitis, cholestasis and fulminant hepatic failure, including fatalities. In each of these cases, liver function returned to baseline on discontinuation of fluconazole.

4.9 Overdose

In the event of overdose, symptomatic treatment (with supportive measures and gastric lavage if clinically indicated) should be instituted. Fluconazole is largely excreted in urine. A three-hour hemodialysis session decreases plasma levels by approximately 50%.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Mechanism of Action

Fluconazole is a highly selective inhibitor of fungal cytochrome P-450 dependent enzyme lanosterol 14-a-demethylase. This enzyme functions to convert lanosterol to ergosterol. The subsequent toss of normal sterols correlates with the accumulation of 14-alpha-methyl sterols in fungi and may be responsible for the fungistatic activity of fluconazole. Mammalian cell demethylation is much less sensitive to fluconazole inhibition.

5.2 Pharmacokinetic properties

Pharmacokinetics and Metabolism

In normal volunteers, the bioavailability of orally administered fluconazole is over 90% compared with intravenous administration. Peak plasma concentrations (C_{max}) in fasted normal volunteers occur between 1 and 2 hours with a terminal plasma elimination half-life of approximately 30 hours (range: 20 to 50 hours) after oral administration.

In fasted normal volunteers, administration of a single oral 400 mg dose of fluconazole leads to a mean C_{max} of 6.72 mcg/mL (range: 4.12 to 8.08 mcg/mL) and after single oral doses of 50 to 400 mg, fluconazole plasma concentrations and AUC (area under the plasma concentration-time curve) are dose proportional.

Plasma protein binding is low (11 to 12%). Following either single or multiple-oral doses for up to 14 days, fluconazole penetrates into all body fluids studied. Fluconazole is cleared primarily by renal excretion. The dose of fluconazole may need to be reduced in patients with impaired renal function.

5.3 Preclinical safety data

None stated

6. Pharmaceutical particulars

6.1 List of excipients

Lactose monohydrate

Maize starch

Talc

Magnesium Stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store in a cool & dry place below 30^0C .Protect from light.

KEEP OUT OF REACH OF CHILDREN

6.5 Nature and contents of container

1 x 10 tablets

6.6 Special precautions for disposal and other handling

No special requirements.

7. Applicant / manufacturer :

Flourish Pharma

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Ind Estate, Somnath road,

Dabhel,Daman-396 215.