165mm

277mm

Country: **Philippines**
Date: 09-02-2021

Rx FLUCONAZOLE

DIFLU-150

150 mg Capsule
Antifungal

FORMULATION:
Each capsule contains:
Fluconazole, USP.....150 mg

PRODUCT DESCRIPTION:
Hard gelatin capsule size "2" having light yellow opaque body and light grey opaque cap imprinted with ARISTO/DIFLU-150 on cap and body in black ink color. The capsules are filled with almost white crystalline powder.

PHARMACOKINETICS:
Fluconazole is well absorbed after oral doses. Bioavailability from the oral route being 90% or more of that from the intravenous route. Mean peak plasma concentrations of 6.72 micrograms/mL have been reported in healthy subjects after a 400 mg oral dose. Peak concentrations are reached within 1 to 2 hours of oral dose. Plasma concentrations are proportional to the dose over a range of 50 to 400 mg. Multiple dosing leads to increase in peak plasma concentrations: steady-state concentrations are reached in 5 to 10 days but may be attained on day 2 a loading dose is given.

Fluconazole is widely distributed and the apparent volume of distribution is close to that of total body water. Concentrations in breast milk. joint fluid, saliva. sputum, vaginal fluids, and peritoneal fluid are similar to those achieved in plasma. Concentrations in the CSF range from 50 to 90% of plasma concentrations, even in the absence of meningeal inflammation. Protein binding is only about 12%.
About 80% of a dose is excreted unchanged in the urine and about 11% as metabolites. The elimination half-life of fluconazole is about 30 hours and is increased in patients with renal impairment. Fluconazole is removed by dialysis.

INDICATIONS:
Fluconazole is a triazole antifungal used for superficial mucosal (oropharyngeal, oesophageal, or vaginal) candidiasis and for fungal skin infections. It is also given for systemic infections including systemic candidiasis, coccidioidomycosis, and cryptococcosis, and has been tried in blastomycosis, histoplasmosis, and sporotrichosis.

DRUG INTERACTIONS:
In general, fewer interactions are considered to occur with fluconazole than with either itraconazole or ketoconazole.
Use of rifampicin with fluconazole results in reduced plasma concentrations of fluconazole. Use of hydrochlorothiazide and fluconazole has resulted in clinically insignificant increases in plasma-fluconazole concentrations.
Fluconazole may interfere with the metabolism of some other drugs, mainly through inhibition of the cytochrome P450 isoenzymes CYP3A4 and CYP2C9. This may account for the reported increases in plasma concentrations of bosentan. Cyclosporine, midazolam, nevirapine, amitryptytine, phenytoin, rifaburin, sulfonylurea hypoglycaemics and nateglinide, selective cyclo-oxygenase-2-inhibitors such as celecoxib and parecoxib, tacrolimus, triazolam, warfarin, and zidovudine, fluconazole may inhibit the formation of a toxic metabolite of sulfamethoxazole.
Increases in terfenadine concentrations following high doses of fluconazole have been associated with ECG abnormalities. A similar effect may be anticipated with astemizole. Use of fluconazole with cisapride could result in increased cisapride concentrations and associated toxicity. The use of fluconazole with astemizole, cisapride. or terfenadine should therefore be avoided because of the risk of cardiac arrhythmias. Syncope attributed to increased amitriptyline concentrations has occurred when amitriptyline was given with fluconazole.
Fluconazole may also reduce the clearance of theophylline. The concentration of contraceptive steroids has been reported to be both increased and decreased in patients receiving fluconazole and the efficacy of oral contraceptives may be affected.

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

REPORTING OF SUSPECTED ADVERSE REACTIONS:
To allow continued monitoring of the benefit/risk balance of the medicinal product, reporting of suspected adverse reaction is necessary. Healthcare professionals are encouraged to report any suspected adverse reactions directly to the importer/distributor and/or report to FDA: www.fda.gov.ph.
Patients are advised to seek immediate medical attention at the first sign/s of adverse reactions.

ADVERSE EFFECTS:
Adverse effects reported with fluconazole most commonly affect the gastrointestinal tract and include abdominal pain, diarrhea, flatulence, nausea and vomiting, and taste disturbance. Other adverse effects include headache, dizziness, leukopenia, thrombocytopenia, hyperlipidaemias, and raised liver enzyme values. Serious hepatotoxicity has been reported in patients with severe underlying disease such as AIDS or malignancy. Anaphylaxis and angioedema have been reported rarely.
Skin reactions are rare but exfoliative cutaneous reactions such as toxic epidermal necrolysis and Stevens-Johnson syndrome have occurred more commonly in patients with AIDS.

SPECIAL PRECAUTIONS:
Tinea capitis: Fluconazole has been studied for treatment of tinea capitis in children. It was shown not to be superior to griseofulvin and the overall success rate was less than 20%. Therefore, Fluconazole capsule should not be used for tinea capitis.
Cryptococcosis: The evidence for efficacy of fluconazole in the treatment of cryptococcosis of other sites (e.g. pulmonary and cutaneous cryptococcosis) is limited, which prevents dosing recommendations.
Deep endemic mycoses: The evidence for efficacy of fluconazole in the treatment of other forms of endemic mycoses such as paracoccidioidomycosis, lymphocutaneous sporotrichosis and histoplasmosis is limited, which prevents specific dosing recommendations.
Renal system: Fluconazole capsule should be administered with caution to patients with renal dysfunction.
Adrenal insufficiency: Ketoconazole is known to cause adrenal insufficiency, and this could also although rarely seen be applicable to fluconazole.
Hepatobiliary system: Fluconazole capsule should be administered with caution to patients with liver dysfunction.
Fluconazole capsule has been associated with rare cases of serious hepatic toxicity including fatalities, primarily in patients with serious underlying medical conditions. In cases of fluconazole associated hepatotoxicity, no obvious relationship to total daily dose, duration of therapy, sex or age of patient has been observed. Fluconazole hepatotoxicity has usually been reversible on discontinuation of therapy.
Patients who develop abnormal liver function tests during fluconazole therapy must be monitored closely for the development of more serious hepatic injury.
The patient should be informed of suggestive symptoms of serious hepatic effect (important asthenia, anorexia, persistent nausea, vomiting and jaundice). Treatment of fluconazole should be immediately discontinued and the patient should consult a physician.

Cardiovascular system: Some azoles, including fluconazole, have been associated with prolongation of the QT interval on the electrocardiogram. Fluconazole causes QT prolongation via the inhibition of Rectifier Potassium Channel current (Ikr). The QT prolongation caused by other medicinal products (such as amiodarone) may be amplified via the inhibition of cytochrome P450 (CYP) 3A4. During post-marketing surveillance, there have been very rare cases of QT prolongation and torsades de pointes in patients taking Fluconazole capsule. These reports included seriously ill patients with multiple confounding risk factors, such as structural heart disease, electrolyte abnormalities and concomitant treatment that may have been contributory. Patients with hypokalemia and advanced cardiac failure are at an increased risk for the occurrence of life threatening ventricular arrhythmias and torsades de pointes.
Fluconazole capsule should be administered with caution to patients with these potentially proarrhythmic conditions. Coadministration of other medicinal products known to prolong the QT interval and which are metabolised via the cytochrome P450 (CYP) 3A4 are contraindicated.
Halofantrine: Halofantrine has been shown to prolong QTc interval at the recommended therapeutic dose and is a substrate of CYP3A4. The concomitant use of fluconazole and halofantrine is therefore not recommended.
Dermatological reactions: Patients have rarely developed exfoliative cutaneous reactions, such as Stevens-Johnson syndrome and toxic epidermal necrolysis, during treatment with fluconazole. AIDS patients are more prone to the development of severe cutaneous reactions to many medicinal products. If a rash, which is considered attributable to fluconazole, develops in a patient treated for a superficial fungal infection, further therapy with this medicinal product should be discontinued. If patients with invasive/systemic fungal infections develop rashes, they should be monitored closely and fluconazole discontinued if bullous lesions or erythema multiforme develop.
Hypersensitivity: In rare cases anaphylaxis has been reported.
Cytochrome P450: Fluconazole is a moderate CYP2C9 and CYP3A4 inhibitor. Fluconazole is also an inhibitor of CYP2C19. Fluconazole capsule treated patients who are concomitantly treated with medicinal products with a narrow therapeutic window metabolised through CYP2C9, CYP2C19 and CYP3A4, should be monitored.
Terfenadine: The coadministration of fluconazole at doses lower than 400 mg per day with terfenadine should be carefully monitored.

DOSAGE AND ADMINISTRATION:
For superficial mucosal candidiasis (other than genital candidiasis), the usual dose of fluconazole in the UK is 50 mg daily by mouth. Although 100 mg daily may be given necessary. Treatment usually continues for 7 to 14 days in oropharyngeal candidiasis (except in severely immune-compromised patients) for 14 days in atrophic oral candidiasis associated with dentures, and for 14 to 30 days in other mucosal candidal infections including oesophagitis. Higher dose are recommended in the USA where an initial dose of fluconazole 200 mg is followed by 100 mg daily and where the minimum treatment period is 14 days for oropharyngeal infection, or a minimum of 21 days and at least 14 days after resolution of symptoms for oesophageal infections, doses of up to 400 mg daily may be used for oesophageal candidiasis If necessary.
Fluconazole 150 mg as a single oral dose may be used for genital candidias If necessary.
Fluconazole 150 mg as a single oral dose may be used for genital candidiasis (vaginal candidiasis or candidal balanitis).
Dermatophytosis, pityriasis versicolor, and candida infections of the skin may be treated with fluconazole 50 mg daily by mouth for up to 6 weeks.
Systemic candidiasis, cryptococcal meningitis, and other cryptococcal infections may be treated with fluconazole orally or by intravenous infusion: the initial dose is 400 mg followed by 200 to 400 mg daily. Duration of therapy is based on clinical and mycological response, but is usually at least 6 to 8 weeks in cryptococcal meningitis, in the USA, treatment for 10 to 12 weeks after the CSF cultures become negative is recommended. Fluconazole may also be used in daily doses of 100 to 200 mg orally or intravenously to prevent relapse after a primary course of antifungal treatment for acute cryptococcal meningitis in patients with AIDS.
In immunocompromised patients at risk of fungal infections, fluconazole may be given prophylactically in a dose of 50 to 400 mg daily orally or by intravenous infusion, although long term prophylaxis has been associated with the emergence of resistant organisms.
Doses for children over 4 weeks of age are 3 mg/kg daily for superficial infections (a loading dose of 6 mg/kg may be used on the first day if necessary), and 6 to 12 mg/kg daily for systemic infections. For prophylaxis in immunocompromised children a dose of 3 to 12 mg/kg daily may be given. For infants under 2 weeks of age, all these doses should be given once every 72 hours: for those aged between 2 and 4 weeks, the doses should be given every 48 hours. A maximum dose of 400 mg daily should not be exceeded in children, or 12 mg/kg at appropriate intervals in infants.
Dosage may need to be reduced in patients with renal impairment or as prescribed by the physician.

PREGNANCY AND LACTATION:
PREGNANCY:
An observational study has suggested an increased risk of spontaneous abortion in women treated with fluconazole during the first trimester. There have been reports of multiple congenital abnormalities (including brachycephalia, ears dysplasia, giant anterior fontanelle, femoral bowing and radio-humeral synostosis) in infants whose mothers were treated for at least three or more months with high doses (400-800 mg daily) of fluconazole for coccidioidomycosis. The relationship between fluconazole use and these events is unclear.
Fluconazole in standard doses and short-term treatments should not be used in pregnancy unless clearly necessary. Fluconazole in high dose and/or in prolonged regimens should not be used during pregnancy except for potentially life-threatening infections.
BREAST-FEEDING:
Fluconazole passes into breast milk to reach concentrations similar to those in plasma (see section 5.2). Breast-feeding may be maintained after a single dose of 150 mg fluconazole . Breast-feeding is not recommended after repeated use or after high dose fluconazole. The developmental and health benefits of breast-feeding should be considered along with the mother's clinical need for Fluconazole capsules and any potential adverse effects on the breast-fed child from Fluconazole capsules or from the underlying maternal condition.

OVERDOSE AND TREATMENT:
There have been reports of overdose with Fluconazole capsule and hallucination and paranoid behaviour have been concomitantly reported.
In the event of overdose, symptomatic treatment (with supportive measures and gastric lavage if necessary) may be adequate.
Fluconazole is largely excreted in the urine; forced volume diuresis would probably increase the elimination rate. A three-hour haemodialysis session decreases plasma levels by approximately 50%.

CAUTION:
Foods, Drugs, Devices and Cosmetics Act Prohibits dispensing without prescription.

STORAGE CONDITION:
Store at temperature not exceeding 30°C.

AVAILABILITY:
Alu-alu blister pack 6's (Box of 12's)

FDA Registration No. : DR-XY41571
Date of first Authorization : 11 November 2021
Date of Revision of package insert : 28 January 2022

20002134/03

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Imported and Distributed by:
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