

AVFLU 150
(Fluconazole Capsules BP 150 mg)



Summary of Product Characteristics

1. Name of the medicinal product

AVFLU 150 (Fluconazole Capsules BP 150 mg)

2. Qualitative and quantitative composition

Each Hard gelatin capsules contains 150 mg Fluconazole.

Excipients of Known effects:

Each Capsule contains 81.0 mg of lactose monohydrate.

3. Pharmaceutical form

A Hard gelatin capsule size "0" having Light Blue cap and white body containing White colour powder.

4. Clinical Particulars:

4.1 Therapeutic indications

- Cryptococcosis, including cryptococcal meningitis and infections of other locations (e.g. lungs, skin), including patients with normal immune response and patients with AIDS, organ transplant recipients and patients with other immunodeficiency forms; supporting therapy to prevent cryptococcosis relapse in AIDS patients.
- Generalized candidiasis, including candidemia, disseminated candidiasis and other forms of invasive candidiasis such as peritoneal, eye, urinary and respiratory tract infections, endocarditis, including patients with malignant tumours in ICU and administered cytotoxic or immunosuppressive agents, also patients with other candidiasis risk factors.
- Mucosal candidiasis including oropharyngeal, oesophageal candidiasis, non-invasive bronchopulmonary infections, candiduria and mucocutaneous and chronic oral atrophic candidiasis (denture sore mouth) including patients with normal and weakened immune function; preventative measures against oropharyngeal candidiasis relapse in AIDS patients.
- Genital candidiasis; acute or recurrent vaginal candidiasis; preventative measures to reduce the incidence of recurrent vaginal candidiasis (3 and more episodes a year), candidal balanitis - Prophylaxis of candidal infections in patients with malignant tumours predisposed to such infections due to received cytotoxic therapy or chemotherapy
- Dermatomycosis including tinea pedis, tinea corporis, tinea cruris, tinea versicolor, tinea unguis and dermal candida infections.
- Deep endemic mycoses in patients with normal immune system, coccidioidomycosis, paracoccidioidomycosis, sporotrichosis and histoplasmosis.

4.2 Posology and method of administration

Posology:

Use in adults

For cryptococcal meningitis and cryptococcal infections at other sites, the usual dose is 400 mg on the first day followed by 200 – 400 mg once daily. Duration of

AVFLU 150
(Fluconazole Capsules BP 150 mg)



treatment for cryptococcal infections will depend on the clinical and mycological response but is usually at least 6 – 8 weeks for cryptococcal meningitis.

For the prevention of relapse of cryptococcal meningitis in patients with AIDS, Fluconazole daily dose of 200 mg is recommended.

For candidaemia, disseminated candidiasis and other invasive candidal infections the usual dose is 400 mg on the first day followed by 200 mg daily. Depending on the clinical response the dose may be increased to 400 mg daily. Duration of treatment is based upon the clinical and mycological response.

For oropharyngeal candidiasis the usual dose is 200 mg on the first day, then continue with 100 mg once daily. Treatment lasts for 2 weeks to reduce the probability of relapse.

For atrophic oral candidiasis associated with dentures the usual dose is 50 mg once daily for 14 days administered concurrently with local antiseptic measures to the denture.

For other candidal infections of mucosa (except genital candidiasis, see below), e.g. oesophagitis, non-invasive bronchopulmonary infections, candiduria, cutaneous candidiasis the usual effective dose is 50-100 mg daily, given for 14 – 30 days.

For the prevention of relapses of oropharyngeal candidiasis in AIDS patients after the patient receives a full course of primary therapy, Fluconazole can be administered in the dose of 150 mg once weekly.

For vaginal candidiasis, oral dose of 150 mg once. For the prevention of vaginal candidiasis the medicine may be taken in the dose of 150 mg once a month. Duration of treatment is determined individually; it varies from 4 to 12 months.

For candidal balanitis the usual oral dose of Fluconazole is 150 mg.

For the prevention of fungal infections in patients with malignant tumours the dose of Fluconazole should be 50 to 400 mg once daily, based on the patient's risk for developing fungal infection. For patients at high risk of systemic infection e.g. profound or long-lasting neutropenia, the recommended dose is 400 mg once daily.

For cutaneous infections, including tinea pedis, corporis, cruris, the recommended dosage is 150 mg once weekly or 50 mg once daily. Duration of treatment is normally 2 to 4 weeks but tinea pedis may require longer treatment (up to 6 weeks).

For tinea versicolour the recommended dosage is 300 mg once weekly for 2 weeks. Some patients need third dose of 300 mg a week, whereas 300-400 mg dose once may be sufficient for some patients. Alternative scheme of treatment is the dose of 50 mg once daily for 2-4 weeks.

For tinea unguim the recommended dose is 150 mg once weekly. Treatment should be continued until a healthy nail plate grows completely. For new nails and toenails to grow it usually takes 3-6 months and 6-12 months respectively. Though the speed can vary over a wide range in different people, also it depends on the age. After successful treatment of long lasting chronic infections nail deformation may sometimes be observed.

AVFLU 150
(Fluconazole Capsules BP 150 mg)



For deep endemic mycosis dose of 200-400 mg daily may be required. Duration of treatment should be decided individually.

Children

As with similar infections in adults, the duration of treatment is based on the clinical and mycological response.

For mucosal candidiasis: The recommended dose of Fluconazole for the age 7 years and over is 3 mg/kg daily. A loading dose of 6 mg/kg may be used on the first day to achieve steady state levels more rapidly.

For generalised candidiasis and cryptococcal infection: The recommended dosage is 6 – 12 mg/kg daily, depending on the severity of the disease.

For prevention of fungal infections in patients with malignant tumours considered at risk in association with neutropenia following cytotoxic chemotherapy or radiotherapy: The dose should be 3 – 12 mg/kg daily, depending on the extent and duration of the induced neutropenia.

Elderly

The normal dose should be used if there are no signs of renal impairment. In patients with renal impairment (creatinine clearance less than 50 ml/min) the dosage schedule should be adjusted as described below. Use in renal impairment No adjustments in single dose therapy are required. In patients with impaired renal function who will receive multiple doses of fluconazole, the loading dose of 50-400 mg is recommended, followed by a daily dose (according to indication) based on the following table:

Creatinine clearance (ml/min)	Percent of recommended doses
>50	100%
≤50 (no dialysis)	50%
Patients receiving regular dialysis	100% after each dialysis

Method of administration

For oral use.

4.3 Contraindications

- Hypersensitivity to fluconazole or to any other ingredient within the formulation or to azole compounds with similar to fluconazole structure
- Co-administration with terfenadine at multiple fluconazole doses of 400mg per day or higher
- Co-administration with cisapride
- Pregnancy and lactation
- Children below 7 years

With caution Worsening of liver function due to administration of fluconazole; rash due to fluconazole administered to patients with superficial fungal infections and invasive/systemic fungal infections; coadministration of terfenadine with fluconazole in doses less 400mg per day; potential

proarrhythmia conditions with multiple risk factors (organic heart disease, electrolyte disturbance and therapy leading to such disorders).

4.4 Special warnings and precautions for use

Fluconazole has been associated with rare cases of hepatic toxicity including fatalities, primarily in patients with serious underlying medical conditions. 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. Upon identification of clinical signs of hepatic injury which may be associated with fluconazole administration, Fluconazole should be discontinued. In rare cases Fluconazole can inflict anaphylaxis.

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 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.

Fluconazole may be associated with prolongation of the QT interval on the electrocardiogram. There have been very rare cases of QT prolongation and torsades de pointes in patients taking Fluconazole. These reports included seriously ill patients with multiple confounding risk factors, such as organic heart diseases, electrolyte disbalance and concomitant treatment that may have been contributory. Fluconazole should be administered with caution to patients with these potentially proarrhythmic conditions. Patients with liver, heart, and kidney conditions prior to use of Fluconazole should consult a physician. Prior to initiation of vaginal candidiasis treatment with 150 mg Fluconazole, patients should be warned, that symptoms usually improve within 24 h, but for their complete elimination several days are sometimes required. If symptoms persist for several days, consult a physician.

4.5 Interaction with other medicinal products and other forms of interaction

Bleeding events (bruising, epistaxis, gastrointestinal bleeding, hematuria, and melena) can occur with the increase in prothrombin time (for 12%) as the result of receiving fluconazole with warfarin concomitantly. In patients receiving coumarin-type anticoagulants the prothrombin time should be carefully monitored.

Concomitant administration of fluconazole with azithromycin has not shown pronounced pharmacokinetic interaction between two medicinal preparations. Benzodiazepines (Short Acting): Following oral administration of midazolam, fluconazole resulted in substantial increases in midazolam concentrations and psychomotor effects. This effect on midazolam appears to be more pronounced following oral administration of fluconazole than with fluconazole administered intravenously. If concomitant benzodiazepine therapy is necessary in patients

AVFLU 150
(Fluconazole Capsules BP 150 mg)



being treated with fluconazole, patients should be monitored with consideration to decrease the benzodiazepine dosage.

200 mg daily of fluconazole leads to the increase of cyclosporine concentration in patients with transplanted kidney. Although multiple doses of fluconazole 100 mg daily have not demonstrated changes in cyclosporine concentration in marrow recipients. It is recommended to monitor cyclosporine concentration in blood when it is co-administered with fluconazole.

Coadministration of multiple-dose hydrochlorothiazide with fluconazole increases plasma concentrations of fluconazole by 40%. An effect of this magnitude should not necessitate a change in the fluconazole dose regimen in subjects receiving concomitant diuretics.

There were no relevant effects on hormone level in co-administration of combined oral contraceptives with 50 mg fluconazole.

Concomitant administration of fluconazole and phenytoin can be followed by clinically significant increase in phenytoin concentration. If co-administration of two drugs is necessary, phenytoin concentration levels should be monitored in order to correct its dose and achieve therapeutic concentration in serum.

Concomitant administration of fluconazole and rifabutin increases serum concentrations of the latter. There have been reports of uveitis when fluconazole and rifabutin were co-administered. Patients to whom fluconazole and rifabutin are co-administered should be under thorough control.

In patients receiving concomitant rifampicin, an increase of the fluconazole dose should be considered.

Fluconazole has been shown to prolong the half-life of concomitantly administered oral sulfonylureas (e.g., chlorpropamide, glibenclamide, glipizide, tolbutamide). Diabetic patients may be prescribed concomitant administration of fluconazole and oral sulfonylureas, but the risk of hypoglycaemia development should be considered.

Fluconazole may increase the serum concentrations of orally administered tacrolimus. There have been reported cases of nephrotoxicity. Patients to whom fluconazole and tacrolimus are coadministered should be under thorough control. Coadministration of azole antifungals and terfenadine may cause serious arrhythmia due to the 6 increase of QT interval. At a 200 mg daily dose of fluconazole there was no prolongation in QT interval. Another study at a 400 mg daily dose of fluconazole demonstrated significant increases in plasma levels of terfenadine. The combined use of fluconazole at doses of 400 mg or greater daily with terfenadine is contraindicated. The coadministration of fluconazole at doses lower than 400 mg per day with terfenadine should be carefully monitored. Concomitant administration of fluconazole and theophylline leads to the increase in serum levels of the latter.

Patients who are receiving high dose theophylline should be observed as for theophylline concentration and if required the therapy should be modified accordingly.

Concomitant administration of fluconazole and zidovudine has demonstrated increase of zidovudine concentration probably due to the decrease of metabolism of the latter. Patients receiving this combination should be monitored for the

AVFLU 150
(Fluconazole Capsules BP 150 mg)



development of zidovudine-related adverse reactions. Concomitant administration of fluconazole with astemizole or any other drugs metabolised via the cytochrome P450 may increase the serum concentration of such drugs.

Patients should be carefully monitored

Single or multiple doses of fluconazole 50 mg do not affect antipyrine metabolism when coadministered.

Listed interactions have been determined at multiple doses of fluconazole. Any interaction of medicinal preparations with fluconazole administered in single dose are not known.

4.6 Fertility, pregnancy and lactation

Contraindicated

4.7 Effects on ability to drive and use machines

No studies have been performed on the effects of fluconazole on the ability to drive or use machines. Patients should be warned about the potential for dizziness or seizures while taking fluconazole and should be advised to drive or operate machines carefully if any of these symptoms occur

4.8 Undesirable effects

Fluconazole is usually well tolerated.

Common ($\geq 1/100$ to $\leq 1/10$);

- Headache,
- Nausea, vomiting, abdominal pain, diarrhoea,
- Increase of blood alkaline phosphatase, serum aminotransferase level (ALT and AST), - Rash,

Uncommon ($\geq 1/1,000$ to $\leq 1/100$)

- Somnolence, insomnia
- Seizures, paraesthesia, dizziness, taste perversion
- Vertigo - Dyspepsia, flatulence, dry mouth.
- Cholestasis, jaundice, bilirubin increased
- Pruritus, urticaria, increased sweating.
- Myalgia
- Agranulocytosis, leukopenia, thrombocytopenia, neutropenia
- Anaphylaxis, anaphylactic shock.
- Hypercholesterolaemia, hypertriglyceridaemia, hypokalemia
- Tremor
- Tachycardia, Ventricular tachycardia/fibrillation, QT prolongation
- Hepatotoxicity, including rare death cases, hepatic failure, hepatocellular necrosis, hepatitis, hepatocellular damage.
- Toxic epidermal necrolysis, Stevens-Johnson syndrome, acute generalised exanthematouspustulosis, dermatitis exfoliative, face oedema, alopecia.

In AIDS and cancer patients when treated with Fluconazole or similar drugs, there were observed changes in blood values, liver and kidney function, however

AVFLU 150
(Fluconazole Capsules BP 150 mg)



no clinical relevance or association of such changes with treatment have been established.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via EFDA yellow Card Scheme, online at <https://primaryreporting.who-umc.org/ET> or toll free call 8482 to Ethiopian food and drug authority (EFDA).

- **Reporting of suspected adverse reactions**

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4.9 Overdose

Symptoms: - aggravation of side effects.

Treatment: - symptomatic (with supportive measures and gastric lavage if necessary)

Fluconazole is largely excreted in the urine; forced volume diuresis would probably increase the elimination rate.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antifungal agents for systemic use. Triazole derivatives.

ATC CODE: J02AC01

Mechanism of action

Fluconazole is a triazole antifungal agent. It is a selective inhibitor of sterol synthesis in fungal cells, and it is active against infections caused by:

- *Candida* spp., including generalized candidiasis
 - *Cryptococcus neoformans*, including intracranial infections
 - *Microsporum* spp.
 - *Trychoptyton* spp.
 - *Blastomyces dermatitides*
 - *Coccidioides immitis*
 - *Histoplasma capsulatum*
- Fluconazole is highly specific for fungal cytochrome P-450 dependent enzymes.

5.2 Pharmacokinetic properties

After oral administration fluconazole is well absorbed, and total bioavailability is 90%. Oral absorption is not affected by concomitant food intake. Peak plasma concentrations in the fasting state occur between 0.5 and 1.5 hours post-dose, and plasma elimination half-life for fluconazole is approximately 30 hours.

AVFLU 150
(Fluconazole Capsules BP 150 mg)



Plasma concentrations are proportional to dose. 90% steady state levels are reached by day 4-5 after the beginning of treatment (with multiple once daily dosing). Plasma protein binding is low (11-12%). Fluconazole achieves good penetration in all body fluids. The major route of excretion is renal, with approximately 80% of the administered dose appearing in the urine as unchanged medicinal product. Fluconazole clearance is proportional to creatinine clearance. There is no evidence of circulating metabolites.

5.3 Preclinical safety data

Effects in non-clinical studies were observed only at exposures considered sufficiently in excess of the human exposure indicating little relevance to clinical use.

Carcinogenesis

Fluconazole showed no evidence of carcinogenic potential in mice and rats treated orally for 24 months at doses of 2.5, 5, or 10 mg/kg/day (approximately 27 times the recommended human dose). Male rats treated with 5 and 10 mg/kg/day had an increased incidence of hepatocellular adenomas.

Mutagenesis
Fluconazole, with or without metabolic activation, was negative in tests for mutagenicity in 4 strains of *Salmonella typhimurium*, and in the mouse lymphoma L5178Y system. Cytogenetic studies in vivo (murine bone marrow cells, following oral administration of fluconazole) and in vitro (human lymphocytes exposed to fluconazole at 1000 µg/ml) showed no evidence of chromosomal mutations.

Reproductive toxicity Fluconazole did not affect the fertility of male or female rats treated orally with daily doses of 5, 10, or 20 mg/kg or with parenteral doses of 5, 25, or 75 mg/kg.

There were no foetal effects at 5 or 10 mg/kg; increases in foetal anatomical variants (supernumerary ribs, renal pelvis dilation) and delays in ossification were observed at 25 and 50 mg/kg and higher doses. At doses ranging from 80 mg/kg to 320 mg/kg embryoletality in rats was increased and foetal abnormalities included wavy ribs, cleft palate, and abnormal cranio-facial ossification.

The onset of parturition was slightly delayed at 20 mg/kg orally and dystocia and prolongation of parturition were observed in a few dams at 20 mg/kg and 40 mg/kg intravenously. The disturbances in parturition were reflected by a slight increase in the number of still-born pups and decrease of neonatal survival at these dose levels. These effects on parturition are consistent with the species specific oestrogen-lowering property produced by high doses of fluconazole. Such a hormone change has not been observed in women treated with fluconazole

6. Pharmaceutical particulars

6.1 List of excipients

Sr. No.	Excipients
1.	Lactose Monohydrate

AVFLU 150
(Fluconazole Capsules BP 150 mg)



2.	Sodium Starch Glycolate
3.	Talc
4.	Magnesium stearate
5.	Colloidal silicon dioxide
6.	EHG Capsule size "0" cap Light Blue and body White

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store below 30°C. Protect from light and moisture.

6.5 Nature and contents of container

1 Capsule packed in one ALU-PVC blister, manufacturing date and expiry dates print in an inner carton along with insert.

6.6 Special precautions for disposal and other handling

No special requirements

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURER

Marketing Authorisation Holder:

Aveo Pharmaceuticals Pvt. Ltd.
Plot No. C/13, Tarapur Industries area, MIDC,
Boisar, Palghar-401 506, Maharashtra, India.

MANUFACTURER

ZAIN PHARMA LTD.
Plot No: 209/13741, Colchester Park,
Go-Down No.1, 2, 3, Off Mombasa Road,
Behind Nice and Lovely House,
P.O. Box: 100167-00101, Nairobi, Kenya

8. Marketing Authorization Number: CTD12684

9. Date of First <Registration> / Renewal of The <Registration>

01.06.2026

10. Date of Revision of the Text: 20/04/2026