Fluconazole

Composition
Candivast 150 mg: Each capsule contains 150 mg fluconazole.
Candivast 50 mg: Each capsule contains 50 mg fluconazole.

Properties
Fluconazole is a systemic antifungal agent belonging to the triazole class; it inhibits the conversion of 14-alpha methyl sterol to ergosterol, leading to alteration in fungal membrane function & leakage of essential elements. Fluconazole is active against a wide range of fungi including Candida spp., Cryptococcus neoformans, Blastomyces dermatitidis, Coccidioides immitis, Histoplasma capsulatum, Trichophyton spp., and Microsporum spp.

The pharmacokinetic properties of fluconazole are similar following administration by the intravenous or oral rout. After oral administration fluconazole is well absorbed with systemic bioavailability 90%. Absorption is not affected by concomitant food intake. Peak plasma concentrations occur between 30 & 90 minutes post dose. In adults the plasma elimination half-life is approximately 30 hours. 90% steady state levels are reached by day 4-5 with multiple once daily dosing and with a volume of distribution of 700 ml/Kg which approximates to total body water. Plasma protein binding is 12%. Fluconazole achieves good penetration into body fluids. 80% of the administered dose is recovered in the urine as unchanged drug.

Indications
Candivast is used for the treatment of:
- Vaginal candidiasis, acute or recurrent.
- Mucosal candidiasis.
- Systemic candidiasis.
- Cryptococcosis.

Dosage & administration

• Adults:
1. Vaginal candidiasis: 150 mg single oral dose. To reduce the incidence of recurrent vaginal candidiasis, another 150 mg dose should be administered 72 hours after the first dose and maintenance therapy may be recommended by giving 150 mg once monthly dose for 4-12 months.
2. Mucosal candidiasis: The usual dose is 50-100 mg once daily for 7-14 days. If necessary treatment can be continued for longer periods in patients with severely compromised function.
3. Systemic candidiasis: Initial dose 400 mg on day one followed by 200 mg once daily. Dosage can be increased to 400 mg daily and duration of treatment depends on the clinical response.
4. Cryptococcosis: Initial dose 400 mg on day one followed by 200 mg once daily. Duration of treatment depends on the clinical & mycological response, but usually not less than 6-8 weeks in cryptococcal meningitis.
5. Prevention of relapse in cryptococcal meningitis: a dose of at least 100 mg daily should be given indefinitely.
6. Immunocompromised patients: The recommended dosage for the prevention of candidiasis is 50 to 400 mg once daily based on patients risk for developing fungal infections.
7. Dermatomycosis: For dermal infections including *Tinea pedis*, *corporis*, *cruris*, *pityriasis versicolor* & *candida* infections, the usual dose is 50-100 mg once daily for 2-4 weeks of therapy. *Tinea pedis* may require treatment up to 6 weeks. Alternatively, 150 mg once weekly regimen may be given and duration of treatment depend on the type of infection.

8. Deep endemic mycosis: Candivast can be administered according to the following dosage schedule:

<table>
<thead>
<tr>
<th>Infection</th>
<th>Dosage</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coccidioidomycosis</td>
<td>200-400 mg</td>
<td>11-24 months</td>
</tr>
<tr>
<td>Para coccidioidomycosis</td>
<td>200-400 mg</td>
<td>2-17 months</td>
</tr>
<tr>
<td>Sporotrichosis</td>
<td>200-400 mg</td>
<td>1-16 months</td>
</tr>
</tbody>
</table>

**Elderly:**

Where there is no evidence of renal failure, normal dosage recommendations should be adopted. For patients with renal impairment (creatinine clearance < 50 ml/min) the dosage schedule should be adjusted as following table:

<table>
<thead>
<tr>
<th>Creatinine clearance (ml/ min)</th>
<th>Dosage interval/daily dose (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;40</td>
<td>24 hours (normal dosage regimen)</td>
</tr>
<tr>
<td>21-40</td>
<td>48 hours (or half normal daily dose)</td>
</tr>
<tr>
<td>10-20</td>
<td>72 hours (or one third normal daily dose)</td>
</tr>
</tbody>
</table>

Contraindications

Fluconazole is contraindicated in the following conditions:

- In patients with known hypersensitivity to fluconazole or to related triazole compounds.
- In patients with acute and chronic hepatopathies and hepatic failure.
- During pregnancy and lactation.

Warnings

- Patients who develop abnormal liver function tests should be monitored for the development of more serious hepatic injury. Fluconazole should be discontinued if signs or symptoms consistent with liver disease develop that may be attributable to fluconazole.
- Fluconazole has been associated with rare cases of serious hepatic toxicity primarily in patients with serious underlying medical conditions. Fluconazole hepatotoxicity has usually been reversible on discontinuation of therapy.
- Patients have rarely developed exfoliative cutaneous reactions such as Steven-Johnson Syndrome and toxic epidermal necrolysis during treatment with fluconazole. Acquired Immune Deficiency Syndrome patients are more prone to the development of severe cutaneous reactions to many drugs. If a rash develops which is considered attributable to fluconazole, therapy with fluconazole should be discontinued.

**Children:**

- Thrush & dermal mycosis: The usual daily dose is 1 mg/kg/day for 7-14 days for thrush and for 14-28 days for dermal mycosis.
- Oropharyngeal candidiasis: The usual daily dose including immunocompromised children is 2-3 mg/kg/day for 7-14 days.
- Candida, localized and systemic infections and for cryptococcosis: The recommended dosage is 6 mg/kg/day up to 12 mg/kg/day according to the severity of the pathology.
- For the prevention of fungal infections in immunocompromised patients, particularly in patients receiving chemo-and/or radiotherapy causing neutropenia: The recommended dosage is 3-12 mg/kg/day, according to the extension and duration of the induced neutropenia.
- In children below 4 weeks of age: In this group of patients, fluconazole is excreted more slowly; therefore, in the first 4 weeks of life the drug should be administered at the same dosages (mg/kg) used in older children, but according to a different time schedule as the following table:

<table>
<thead>
<tr>
<th>Weeks of life</th>
<th>Frequency of administration (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-2</td>
<td>Every 72 hrs</td>
</tr>
<tr>
<td>3-4</td>
<td>Every 48 hrs</td>
</tr>
<tr>
<td>&gt;4</td>
<td>Every 24 hrs</td>
</tr>
</tbody>
</table>
Precautions
- In diabetic patients: The concurrent use of fluconazole with sulphonylurea hypoglycemic agents may increase the plasma concentration of such agents, hypoglycemia has been noted and the dose of oral hypoglycemic agents is to be reduced.
- Use in patients with renal impairment: Fluconazole is mainly excreted in the urine as unchanged drug. No adjustments in the single dose therapy (vaginal candidiasis) are necessary. However, in multiple dose treatment of patients with renal impairment, an initial loading dose of 50 mg to 400 mg should be given. After the loading dose, the daily dose (according to indication) should be based on the previous table depending to the degree of renal impairment.
- For children with renal impairment, the daily dose should be reduced in accordance with the guidelines given for adults depending to the degree of renal impairment.

Side effects
Fluconazole is generally well tolerated, and the most common side effects are associated with symptoms related to the gastrointestinal tract such as nausea, vomiting, abdominal pain, diarrhea and flatulence. Less commonly observed side effects include skin rash, headache, asthenia, dizziness, and hepatic abnormalities are also possible. In some patients particularly in those with serious underlying diseases such as Acquired Immune Deficiency Syndrome and cancer, changes in renal and hematological function test results and hepatic abnormalities have been observed during treatment with fluconazole and comparative agents. However, the clinical significance and relationship to treatment is uncertain. In rare cases, as with other azoles, anaphylaxis has been reported.

Drug Interactions
- Concomitant use of rifampicin with fluconazole, results in reduced fluconazole serum levels.
- Concomitant use of warfarin with fluconazole, results in increased prothrombin time.
- Concomitant use of sulphonylureas with fluconazole, results in increased serum levels of concomitantly administered sulphonylureas.

Overdose
Supportive measures and symptomatic treatment with gastric lavage (if necessary) may be adequate. Haemodialysis decreases fluconazole plasma levels by 50%.

Presentation available
Candivast is available as 150 mg capsule in one capsule pack.
Candivast is available as 50 mg capsule in 7 capsules pack.