4.75”

7.15”

# Konacane

( F l u c o n a z o l e )

**Capsule / Dry Powder Suspension**

# کوناکین

کیپسول/ ڈرائی پاؤڈر سسپنشن

(فلوکونازول)

**COMPOSITION:**

**Konacane Capsule 150mg**

Each capsule contains:

Fluconazole .....150 mg

**(BP Specifications)**

**Konacane Suspension 50mg/5ml**

Each 5ml after reconstitution contains:

Fluconazole .....50 mg

**(USP Specifications)**

**DESCRIPTION:**

Konacane *(Fluconazole)* is *the first , a new subclass of synthetic triazole antifungal agents.* Fluconazole is a white crystalline solid which is slightly soluble in water and saline.

**INDICATIONS:**

Konacane is indicated for the treatment and prophylaxis of fungal infections where other antifungal have failed or are not tolerated, Candidiasis caused by susceptible strains of candida, Tinea corporis, Tinea cruris or Tinea pedis,Onychomycosis,Cryptococcal meningitis.

Konacane can be used first line for the following indications.

Coccidioidomycosis, Cryptococcosis, Histoplasmosis, Prophylaxis of candidiasis in immunocompromised people and Auto-brewery syndrome.

**MODE OF ACTION:**

Fluconazole inhibits the fungal cytochrome P450 enzyme 14α-demethylase. Mammalian demethylase activity is much less sensitive to fluconazole than fungal demethylase. This inhibition prevents the conversion of lanosterol to ergosterol, an essential component of the fungal cytoplasmic membrane, and subsequent accumulation of 14α-methyl sterols. Fluconazole is primarily fungistatic; however, it may be fungicidal against certain organisms in a dose-dependent manner, specifically Cryptococcus.

**DOSAGE AND ADMINISTRATION:**

**Adults**

| Indications | | Posology | Duration of Treatment |
|---|---|---|---|
| **Candidal vaginitis or balantis** | | 150mg | single oral dose |
| **Mucosal Candidiasis** | Oropharyngeal candidiasis | 50mg once daily* | 7-14 days. Treatment should not normally exceed 14 days except in severely immunocompromised patients. |
| | Atopic oral condidiasis associated with dentures | 50mg once daily* | 14 days administered concomitantly with local antiseptic measures to the dentures. |
| | Other candidal infections for mucosa e.g. oesophagitis, non-invasive broncopulmonary infections, candiduria, mucocutaneous candidiasis etc. | 50mg daily* | 14-30 days |
| **Dermatomy-cosis** | • tinea pedis<br>• tinea corporis<br>• tinea crusis<br>• tinea versicolor<br>• dermal candida infections | 50mg once daily | Normally 2 to 4 weeks** |
| • **Candidaemia**<br>• **Disseminated candidiasis** | | Loading dose: 400mg on | Based upon the clinical response. |
| • **Other invasive candidal infections** | | Day 1 Subsequent dose: 200mg daily (depending on clinical response, may be increased to 400mg daily) | |
| **Cryptococco-sis** | Treatment of cryptococcal meningitis and cryptococcal infections at other sites | Loading dose: 400mg on Day 1 Subsequent dose: 200mg - 400mg once daily | Dependant on the clinical and mycological response. Usually 6-8 weeks for cryptococcal meningitis. |
| | Prevention of relapse of cryptococcal meningitis in patients with AIDS | 100mg – 200mg daily | Indefinitely at a daily dose of 100-200 mg. |
| **Prevention of fungal infections** | Immunocompromised patients considered at risk as a consequence of neutropenia following cytotoxic chemotherapy or radiotherapy | 50 to 400mg once daily, based on the patient's risk for developing fungal infection. For patients at high risk of systemic infection e.g. patients who are anticipated to have profound or prolonged neutropenia such as during bone marrow transplantation, the recommended dose is 400mg once daily. | Administration should start several days before the anticipated onset of neutropenia and continue for 7 days after the neutrophil count rises above 1000 cells per $mm^3$ |

* In unusually difficult cases of mucosal candial infections, the dose may be increased to 100mg daily.

** tinea pedis may require treatment for up to 6 weeks. Duration of treatment should not exceed 6 weeks.

4.75”

**Use in the elderly**

The normal dose should be used if there is no evidence of renal impairment. In patients with renal impairment (creatinine clearance less than 50 ml/min) the dosage schedule should be adjusted as below.

**Use in patients with impaired renal function**

Fluconazole is excreted primarily in the urine as unchanged drug. No adjustments in single dose therapy are required. In patients (including pediatric population) with impaired renal functions who will receive multiple doses of fluconazole, the normal recommended dose (according to indication) should be given on day 1, followed by a daily dose based in the following table:

| Creatinine clearance (ml/min) | Percentage of dose recommended |
|---|---|
| > 50 | 100% |
| ≤ 50 (no dialysis) | 50% |
| Regular dialysis | 100% after each dialysis |

**Paediatric Population**

A maximum dosage of 400mg daily should not be exceeded in children.

As with similar infections in adults, the duration of treatment is based on the clinical and mycological response. Fluconazole is administered as a single daily dose each day.

To facilitate accurate measurement of doses less than 10mg, fluconazole should only be administered to children in hospital using the 50mg/5ml suspension orally or the intravenous injection, depending on the clinical condition of the child. A suitable measuring device should be used for administration of the suspension. Once reconstituted, the suspension should not be further diluted.

***Infants, toddlers, children and adolescents (from 28 days to 17 years)***

| Indication | Posology | Recommendations |
|---|---|---|
| Mucosal candidiasis | 3 mg/kg daily | A leading dose of 6mg/kg may be used on the first day to achieve steady state levels more rapidly. |
| Systemic candidiasis, Cryptococcal infections | 6-12 mg/kg daily | Dosage dependant on the severity of the disease |
| Prevention of fungal infections in immunocompromised patients considered at risk as a consequence of neutropenia following cytotoxic chemotherapy or radiotherapy | 3-12 mg/kg daily | Dosage dependant on the extent and duration of the induced neutopenia (see adult dosing). |

***Term newborn infants (0 to 27 days):***

Neonates excrete fluconazole slowly.

| Age group | Posology | Recommendations |
|---|---|---|
| Term newborn infants (0 to 14 days) | The same mg/kg dosing as in older children should be used but administered every 72 hours | A maximum dosage of 12 mg/kg every 72 hours should not be exceeded |
| Term newborn infants (from 15 to 27 days) | The same mg/kg dosing as in older children should be used but administered every 48 hours | A maximum dosage of 12mg/kg every 48 hours should not be exceeded |

**PHARMACOKINETICS**

The pharmacokinetic properties of fluconazole are similar following administration by the intravenous or oral route. After oral administration fluconazole is well absorbed, and plasma levels (and systemic bioavailability) are over 90% of the levels achieved after intravenous administration. 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 with a plasma elimination half-life of approximately 30 hours. Plasma concentrations are proportional to dose,90% steady state-levels are reached by day 4-5 with multiple once daily dosing.Administration of a loading dose (on day 1) of twice the usual daily dose enables plasma levels to approximate to 90% steady state-levels by day 2. The apparent volume of distribution approximates to total body water. Plasma protein binding is low (11-12%).Fluconazole achieves good penetration in all body fluids studied. The major route of excretion is renal with approximately 80% of the administered dose appearing in the urine as unchanged drug. Fluconazole clearance is proportional to creatinine clearance. There is no evidence of circulating metabolites.The long plasma elimination half life provides the basis for single dose therapy for genital candidiasis.

**DRUG INTERACTION:**

**Antacid:** Administration of antacid to 14 normal male volunteers immediately prior to a single dose of fluconazole 100 mg had no effect on the absorption or elimination of fluconazole.

**Rifampin:** Administration of a single oral 200 mg dose of fluconazole after 15 days of rifampin administered as 600 mg daily in eight healthy male volunteers resulted in a significant decrease in fluconazole AUC and a significant increase in apparent oral clearance of fluconazole. There was a mean ± SD reduction in fluconazole AUC of 23% ± 9% (range: –13 to –42%). Apparent oral clearance of fluconazole increased 32% ± 17% (range: 16 to 72%). Fluconazole half-life decreased from 33.4 ± 4.4 hours to 26.8 ± 3.9 hours.

**PRECAUTIONS:**

**General:**

Some azoles, including fluconazole, have been associated with prolongation of the QT interval on the electrocardiogram. During post marketing surveillance, there have been rare cases of QT prolongation and torsade de pointes in patients taking fluconazole. Most of these reports involved seriously ill patients with multiple confounding risk factors, such as structural heart disease, electrolyte abnormalities and concomitant medications that may have been contributory.

Fluconazole should be administered with caution to patients with these potentially proarrhythmic conditions.

**Teratogenic effects and pregnancy:**

There are no adequate and well controlled studies in pregnant women. There have been reports of multiple congenital abnormalities in infants whose mothers were being treated for 3 or more months with high dose (400-800 mg/day) fluconazole therapy for coccidioidomycosis (an unindicated use). The relationship between fluconazole use and these events is unclear. Konacane should be used in pregnancy only if the potential benefit justifies the possible risk to the fetus.

**Nursing mothers:**

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

**CONTRAINDICATIONS:**

Konacane (Fluconazole) is contraindicated in patients who have shown hypersensitivity to fluconazole or to any of its excipients. There is no information regarding cross-hypersensitivity between fluconazole and other azole antifungal agents. Caution should be used in prescribing Konacane to patients with hypersensitivity to other azoles. Coadministration of terfenadine is contraindicated in patients receiving Konacane (Fluconazole) at multiple doses of 400 mg or higher based upon results of a multiple dose interaction study. Coadministration of cisapride is contraindicated in patients receiving Konacane (Fluconazole).

**STORAGE & INSTRUCTIONS:**

Store between 15-25°C. Protect from heat, sunlight & moisture. Keep away from the reach of children. Reconstituted suspension should be stored between 5-25°C. Shake well before use.

**To be sold on the prescription of a registered medical practitioner only.**

**HOW SUPPLIED:**

**Konacane Capsule 150mg**

1's capsule.

**Konacane Suspension 50mg/5ml**

35ml in glass bottle.

خوراک وطریقہ استعمال:

ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ہدایات:

دوا کو ۱۵۔۲۵ ڈگری سینٹی گریڈ درجہ حرارت کے درمیان رکھیں۔

دھوپ، گرمی اور نمی سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔

تیار کردہ سسپنشن کو ۵۔۲۵ ڈگری سینٹی گریڈ درجہ حرارت کے درمیان رکھیں۔ استعمال سے پہلے اچھی طرح ہلائیں۔

صرف رجسٹرڈ ڈاکٹر کے نسخے کے مطابق فروخت کریں۔

Manufactured by:

PHARMASOL

**PRIVATE LIMITED**

Plot # 549, Sundar Industrial Estate, Lahore, Pakistan.