# 1.3.1

# Summary of Product Characteristics (SmPC)

## 1. Name of the medicinal Product

### 1.1 Name of the medicinal Product

Fluconazole Capsules USP 200 mg

### 1.2 Strength

Each hard gelatin capsules contains:

| | |
|---|---|
| Fluconazole USP | 200 mg |
| Excipients | Q.S. |

## 2. Qualitative and Quantitative Composition

### 2.1 Qualitative Declaration

Fluconazole USP

### 2.2 Quantitative Declaration

| Sr. No. | Ingredients | Specifications | Label Claim (mg/Capsule) | Rational |
|---|---|---|---|---|
| 1 | Fluconazole | USP | 200.00 | Antifungal |
| 2 | Lactose (Lactose Monohydrate) | BP | 30.00 | Disintegrant |
| 3 | Polyoxyl 35- Castor Oil | USP-NF | 6.00 | Binder |
| 4 | Sodium Lauryl Sulphate | BP | 4.00 | Diluent |
| 5 | Sodium Chloride | BP | 15.00 | Lubricant |
| 6 | Crospovidone (Polyplasdone) | USP-NF | 20.00 | |
| 6 | Colloidal Anhydrous Silica (Aerosil) | BP | 5.00 | Diluent |
| 7 | Black/orange Size “2” Hard Gelatin empty Capsule | IH | -- | -- |

## 3. Pharmaceutical Form

Hard Gelatin Capsules.

Black/orange coloured, size "2" capsule containing white to off-white coloured powder.

## 4. Clinical Particulars

## 4.1 Therapeutic Indications

**Mucosal candidiasis:** Oropharyngeal and oesophageal candidiasis.

**Systemic candidiasis:** Candidaemia, disseminated candidiasis, peritonitis, candida\ infections of the endocardium, and the pulmonary and urinary tracts, candida\ infections in patients with malignancy, in intensive care units, or those receiving cytotoxic or immunosuppressive therapy may be treated.

**Cryptococcosis:** Cryptococcal meningitis and infections of other sites (e.g. pulmonary, cutaneous), normal hosts and patients with AIDS, organ transplants or other causes of immunosuppression may be treated. It can be used as maintenance therapy to prevent the relapse of cryptococcal disease in patients with AIDS.

**Prophylaxis:** It is also indicated to decrease the incidence of candidiasis in patients undergoing bone marrow transplantation who receive cytotoxic chemotherapy and/or radiation therapy.

## 4.2 Posology and Method of Administration

**Adults:** Orophmyngeal Candidiasis: 100-200 mg once daily for at least 2 weeks.

**Esophageal Candidiasis:** 200-400 mg once daily for2-3 weeks.

**Systemic candidiasis:** 400 mg daily, duration of treatment is based upon the clinical response.

**Urinary tract infections and peritonitis:** 50-200 mg daily.

**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 of400 mg once daily may be used based on medical judgement of the patient's response to therapy. The recommended duration of treatment for initial therapy of cryptococcal meningitis is I 0-- 12 weeks after the CSF becomes culture-negative. The recommended dosage of fluconazole l. V. for suppression of a re lapse of cryptococcal meningitis in patients with AIDS is 200 mg once daily.

**Prophylaxis in patients undergoing bone marrow transplantation**: 400 mg once daily for 7 days.

**Prevention of fungal infections in immunocompromised patients:** For patients considered at risk as a consequence of neutropenia following cytotoxic chemotherapy or radiotherapy, the dose should be 50-400 mg once daily, based on the patient's risk for developing fungal infection.

**Elderly:** The normal adult dose should be used if there is no evidence of renal impairment.

**Children:** Orophmyngeal Candidiasis: 6 mg/kg on the first day, followed by 3 mg/kg once daily. Treatment should be administered for at least 2 weeks.

**Esophageal Candidiasis:** Initial dose 6 mg/kg, maintenance dose should be 3-12 mg/kg once daily for 21 days and at least 2 weeks following resolution of symptoms.

**Systemic candidiasis:** 6- 12 mg/kg daily, depending on the severity of the disease.

**Cryptococcal infections:** 12 mg/kg on the first day, followed by 6 mg/kg once daily. The recommended du ration of treatment for initial therapy of cryptococcal meningitis is 10 - 12 weeks after the CSF becomes culture-negative. For suppression of re lapse of cryptococcal meningitis in children with AIDS, the recommended dose of fluconazole I. V. infusion is 6 mg/kg once daily.

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

## 4.3 Contraindications

Fluconazole 200 mg capsule should not be used in patients with known hypersensitivity to fluconazole or to related azoic compounds or any other ingredient in the formulation.

Co-administration of terfenadine, erythromycin, astemizole, pimozide, quinidine or cisapride is contra-indicated in patients receiving fluconazole.

## 4.4 Special Warnings and Special Precautions for Use

**Arrhythmias:** Fluconazole should be administered with caution to patients with these potentially proarryhthmic conditions.

**Dermatologic reactions:** Rash (including diffuse rash accompanied by eosinophilia) and pruritus have been reported.

**Pregnancy:** Use in pregnancy should be avoided except in patients with severe or potentially life-threatening fungal infections in whom fluconazole may be used if the anticipated benefit outweighs the possible risk to the fetus.

**Lactation:** Fluconazole is found in human breast milk at concentrations similar to plasma, hence its use in nursing mothers is not recommended.

**Renal impairment:** Use with caution in patients with renal impairment.

**Hepatic impairment:** Serious (and rarely fatal) hepatic toxicity (e .g., hepatitis, cholestasis, fulminant failure) has been observed with azoic therapy. Use with caution in patients with pre-existing hepatic impairment.

## 4.5 Interaction with other medicinal products and other forms of interaction

Fluconazole is interacts with anticoagulants (warfarin), rifampicin, hydrochlorothiazide, oral sulphonylureas (chlorpropamide, glibenclamide, glipizide and tolbutamide), cyclosporin, theophylline, terfenadine, cisapride, zidovudine, rifabutin, tacrolimus, astemizole.

## 4.6 Fertility, Pregnancy and Lactation

**Pregnancy:** Use in pregnancy should be avoided except in patients with severe or potentially life-threatening fungal infections in whom fluconazole may be used if the anticipated benefit outweighs the possible risk to the fetus.

**Lactation:** Fluconazole is found in human breast milk at concentrations similar to plasma, hence its use in nursing mothers is not recommended.

## 4.7 Effects on ability To Drive and use Machines

No studies on the effects on the ability to drive and use machines have been performed.

## 4.8 Undesirable Effects

**Cardiovascular**: Angioedema, pallor, QT prolongation, torsade de pointes.

**Central nervous System:** Headache, dizziness, seizure

**Dermatologic:** Rash, alopecia, toxic epidermal necrolysis, Stevens-Johnson syndrome

**Endocrine & metabolic:** Hypercholesterolemia, hypertriglyceridemia, hypokalemia

**Gastrointestinal**: Nausea, abdominal pain, vomiting, diarrhea, dyspepsia, taste perversion.

**Hematologic**: Agranulocytosis, leukopenia, neutropenia, thrombocytopenia

**Hepatic**: Alkaline phosphatase increased, ALT increased, AST increased, cholestasis, hepatic failure, hepatitis, jaundice

**Respiratory**: Dyspnea

**Miscellaneous**: Anaphylactic reactions

## 4.9 Overdose

**Symptoms**: Symptoms may include changes in behavior; hallucinations.

**Treatment**: In the event of over dosage, supportive measures and symptomatic treatment, with 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 hemodialysis session decreases plasma levels by approximately 50%.

## 5. Pharmacological Properties

### 5.1 Pharmacodynamics Properties

Anti-fungal

Fluconazole, a member of the triazole class of antifungal agents, is a potent and selective inhibitor of fungal enzymes necessary for the synthesis of ergosterol. Fluconazole interferes with fungal cytochrome P450 activity (lanosterol 14-a-demethylase), it decrease ergosterol synthesis (principal sterol in fungal cell membrane) and inhibiting cell membrane formation.

### 5.2 Pharmacokinetic Properties

**Absorption:** The pharmacokinetic properties of fluconazole are similar following administration by the intravenous or oral route. 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.

**Distribution**: Fluconazole achieves good penetration in all body fluids. High skin concentrations of fluconazole, above serum concentrations, are achieved in the stratum comeum, epidennis-dermis and eccrine sweat. Fluconazole accumulates in the stratum comeum. Plasma protein binding is low (11-12%).

**Elimination:** 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 creatine clearance. There is no evidence of circulating metabolites.

### 5.3 Preclinical Safety Data

Not Applicable

## 6 Pharmaceutical Particulars

### 6.1 List of Excipients

Lactose (Lactose monohydrate) BP

Polyoxyl 35-Castor oil USP-NF

Sodium Lauryl Sulphate BP

Sodium Chloride BP

Crosspovidone (Polypasdone) USP-NF

Colloidal Anhydrous Silica (Aerosil) BP

Black/orange Size "2" hard gelatin empty capsule IH

**6.2 Incompatibilities**

None.

**6.3 Shelf Life**

36 months

**6.4 Special Precautions for Storage**

Store below $30^0$C. Protect from light.

**6.5 Nature and Contents of Container**

Black/orange coloured, size "2" hard gelatin capsule containing white to off-white coloured powder. 10 capsules are packed in blister pack. 1 Blister packed in printed carton along with packaging insert.

**6.6 Special precaution for disposal and other handling**

Any unused product or waste material should be disposed of in accordance with local requirements.

**7. Registrant (Marketing Authorization Holder And Manufacturing Site Addresses)**

**7.1 Name and Address of Marketing Authorization Holder**

**GENERICS AND SPECIALITIES LTD.**

31, AWONIYI ELEMO STREET,

OFF LATEEF SALAMI STREET.

AJAO ESTATE, LAGOS,

NIGERIA.

E-mail: info@zolonhealthcare.com

**7.2 Name and Address of manufacturing site(s)**

Lincoln Parenteral Limited

11, Trimul Estate, Khatraj, Taluka: Kalol,

District: Gandhinagar Gujarat, India.

Telephone no.: +91-02764-665000

Fax: +91-02764-281809

Email: info@lincolnpharma.com

Website: www.lincolnpharma.com

**7.3 Marketing Authorization Number**

To be included after obtaining first registration.

**7.4 Date of First <Registration> / Renewal of The <Registration>**

It will be applicable after registration of this product.

**8. Date of Revision of the Text**

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**9. Dosimetry (If Applicable)**

Not Applicable

**10. Instructions for preparation of radiopharmaceuticals (if Applicable)**

Not Applicable