Summary of Product Characteristic

Contents

Summary of Product Characteristic

1. Name of the Medicinal Product:

TRIFLUCON (Fluconazole Capsules 150mg

2. Quality and Quantitative Composition:

2.1 Qualitative Declaration

Each capsule contains:
Fluconazole USP 150mg
Excipients Q.S.
Approved colours used in empty capsule shell

2.2 Quantitative Declaration

Components	Amount / Unit(mg)	Reference
Fluconazole	150	USP (NF)
Lactose monohydrate	322.45	Ph Eur (BP)
Maize Starch	15	Ph Eur (BP)
Sodium Benzoate	0.85	Ph Eur (BP)
Magnesium Stearate	3.3	Ph Eur (BP)
Colloidal anhydrous silica	1.70	Ph Eur (BP)
Sodium Lauryl sulfate	1.70	Ph Eur (BP)
Purified water	q.s	Ph Eur (BP)

3. Pharmaceutical Form:

Capsule (Oral use)

4. Clinical Particulars:

4.1 Therapeutic indications

Adults
You might be given this medicine by your doctor to treat the following types of fungal infections:
- Cryptococcal meningitis – a fungal infection in the brain
- Coccidioidomycosis – a disease of the bronchopulmonary system
- Infections caused by Candida and found in the blood stream, body organs (e.g. heart, lungs) or urinary tract
- Mucosal thrush - infection affecting the lining of the mouth, throat and denture sore mouth
- Genital thrush – infection of the vagina or penis
- Skin infections - e.g. athlete's foot, ringworm, jock itch, nail infection

You might also be given Fluconazole to:
- stop cryptococcal meningitis from coming back

- stop mucosal thrush from coming back
- reduce recurrence of vaginal thrush
- stop you from getting an infection caused by Candida (if your immune system is weak and not working properly)

Children and adolescents (0 to 17 years old)
You might be given this medicine by your doctor to treat the following types of fungal infections:
- Mucosal thrush - infection affecting the lining of the mouth, throat
- Infections caused by Candida and found in the blood stream, body organs (e.g. heart, lungs) or urinary tract
- Cryptococcal meningitis – a fungal infection in the brain

4.2 Posology and method of administration

Adults:

Condition	**Dose**
To treat cryptococcal meningitis	400 mg on the first day then 200 mg to 400 mg once daily for 6 to 8 weeks or longer if needed. Sometimes doses are increased
To stop cryptococcal meningitis from coming back	200 mg once daily until you are told to stop
To treat coccidioidomycosis	200 mg to 400 mg once daily from 11 months for up to 24 months or longer
To treat internal fungal infections caused by *Candida*	800 mg on the first day then 400 mg once daily until you are told to stop
To treat mucosal infections affecting the lining of mouth, throat and denture sore mouth	200 mg to 400 mg on the first day then 100 mg to 200 mg until you are told to stop
To treat mucosal thrush – dose depends on where the infection is located	50 mg to 400 mg once daily for 7 to 30 days until you are told to stop
To stop mucosal infections affecting the lining of mouth, throat	100 mg to 200 mg once daily, or 200 mg 3 times a week, while you are at risk of getting an infection
To treat genital thrush	150 mg as a single dose
To reduce recurrence of vaginal thrush	150 mg every third day for a total of 3 doses (day 1, 4 and 7) and then once a week for 6 months while you are at risk of getting an
To treat fungal skin and nail infections	Depending on the site of the infection 50 mg once daily, 150 mg once weekly, 300 to 400 mg once weekly for 1 to 4 weeks (Athlete's
To stop you from getting an infection caused by *Candida* (if your immune system is weak and not working properly)	200 mg to 400 mg once daily while you are at risk of getting an infection

Use in adolescents from 12 to 17 years old
Follow the dose prescribed by your doctor (either adults or children posology).

Use in children to 11 years old
The maximum dose for children is 400 mg daily.

The dose will be based on the child's weight in kilograms.

Condition	**Daily dose**
Mucosal thrush and throat infections caused by *Candida* – dose and duration depends on the severity of the infection and on where the infection is located	3 mg per kg of body weight (6 mg per kg of body weight might be given on the first day)
Cryptococcal meningitis or internal fungal infections caused by *Candida*	6 mg to 12 mg per kg of body weight once daily
To stop cryptococcal meningitis from coming back	6mg per kg of body weight once daily
To stop children from getting an infection caused by *Candida* (if their immune system is not working properly)	3 mg to 12 mg per kg of body weight once daily

Use in children 0 to 4 weeks of age
Use in children of 3 to 4 weeks of age:
The same dose as above but given once every 2 days. The maximum dose is 12 mg per kg of body weight every 48 hours.

Use in children less than 2 weeks old:
The same dose as above but given once every 3 days. The maximum dose is 12 mg per kg of body weight every 72 hours.

4.3 Contraindications
• Hypersensitivity to the active substance, to related azole substances, or to any of the excipients listed.
• Co-administration of terfenadine is contra-indicated in patients receiving fluconazole at multiple doses of 400 mg per day or higher based upon results of a multiple dose interaction study.
• Co-administration of other medicinal products known to prolong the QT interval and which are metabolised via the cytochrome P450 (CYP) 3A4 such as cisapride, astemizole, pimozide quinidine and erythromycin are contra-indicated in patients receiving fluconazole

4.4 Special warning and precautions for use

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, Triflucon should not be used for tinea capitis.

Summary of Product Characteristic

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
Triflucon 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. Adrenal insufficiency relating to concomitant treatment with prednisone 'The effect of fluconazole on other medicinal products'.

Hepatobiliary system
Triflucon should be administered with caution to patients with liver dysfunction.

Triflucon 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 hepato-toxicity, 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.

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 Triflucon . 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 hypokalaemia and advanced cardiac failure are at an increased risk for the occurrence of life threatening ventricular arrhythmias and torsades de pointes

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.

<u>Hypersensitivity</u>
In rare cases anaphylaxis has been reported.

<u>Cytochrome P450</u>
Fluconazole is a moderate CYP2C9 and CYP3A4 inhibitor. Fluconazole is also a strong inhibitor of CYP2C19. Fluconazole 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.

4.5 Interaction

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Tell your doctor immediately if you are taking astemizole, terfenadine (an antihistamine for treating allergies) or cisapride (used for stomach upsets) or pimozide (used for treating mental illness) or quinidine, amiodarone (used for treating heart arrhythmia) or erythromycin (an antibiotic for treating infections) as these should not be taken with Fluconazole.
There are some medicines that may interact with Fluconazole.

Make sure your doctor knows if you are taking any of the following medicines:
- rifampicin or rifabutin (antibiotics for infections)
- hydrochlorothiazide (used to treat fluid retention and high blood pressure)
- alfentanil, fentanyl (used as anaesthetic)
- amitriptyline, nortriptyline (used as anti-depressant)
- amphotericin B, voriconazole (anti-fungal)
- medicines that thin the blood to prevent blood clots (warfarin or similar medicines)
- benzodiazepines (midazolam, triazolam or similar medicines) used to help you sleep or for anxiety
- carbamazepine, phenytoin (used for treating fits)
- nifedipine, isradipine, amlodipine, verapamil, felodipine and losartan (for hypertension- high blood pressure)
- olaparib (used for treating ovarian cancer)
- ciclosporin, everolimus, sirolimus or tacrolimus (to prevent transplant rejection)
- cyclosphosphamide, vinca alkaloids (vincristine, vinblastine or similar medicines) used for treating cancer
- halofantrine (used for treating malaria)
- statins (atorvastatin, simvastatin and fluvastatin or similar medicines) used for reducing high cholesterol levels
- methadone (used for pain)
- celecoxib, flurbiprofen, naproxen, ibuprofen, lornoxicam, meloxicam, diclofenac (NSAID)
- oral contraceptives
- prednisone (steroid)
- zidovudine, also known as AZT; saquinavir (used in HIV-infected patients)
- medicines for diabetes such as chlorpropamide, glibenclamide, glipizide or tolbutamide
- theophylline (used to control asthma)
- tofacitinib (used for treating rheumatoid arthritis)
- vitamin A (nutritional supplement)
- ivacaftor (used for treating cystic fibrosis)
- amiodarone (used for treating uneven heartbeats ‘arrhythmias’
- hydrochlorothiazide (a diuretic)

- irutinib (used for treating blood cancer)

4.6 Pregnancy and lactation

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

You should not take Fluconazole if you are pregnant, think you may be pregnant, are trying to become pregnant or breast-feeding unless your doctor has told you so. Fluconazole taken during the first trimester of pregnancy may increase the risk of miscarriage. Fluconazole taken at low doses during the first trimester may slightly increase the risk of a baby being born with birth defects affecting the bones and/or muscles.

Fluconazole contains lactose
This medicine contains a small amount of lactose (milk sugar). If you have been told by your doctor that you have an intolerance to some sugars, please contact your doctor before taking this medicine

4.8 Undesirable effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Stop taking fluconazole and seek medical attention immediately if you notice any of the following symptoms:

- Widespread rash, high body temperature and enlarged lymph nodes (DRESS syndrome or drug hypersensitivity syndrome).

A few people develop allergic reactions although serious allergic reactions are rare. If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. If you get any of the following symptoms, tell your doctor immediately.

- sudden wheezing, difficulty in breathing or tightness in the chest
- swelling of eyelids, face or lips
- itching all over the body reddening of the skin or itchy red spots
- skin rash
- severe skin reactions such as a rash that causes blistering (this can affect the mouth and tongue).

Fluconazole may affect your liver. The signs of liver problems include:
- tiredness
- loss of appetite
- vomiting
- yellowing of your skin or the whites of your eyes (jaundice)

Fluconazole may affect your adrenal glands and the levels of steroid hormones produced. The signs of adrenal problems include:
- tiredness
- muscle weakness
- loss of appetite
- weight loss

- abdominal pain

If any of these happen, stop taking Fluconazole and tell your doctor immediately.

Other side effects:

Additionally, if any of the following side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

Common side effects which may affect up to 1 in 10 people are:
- headache
- stomach discomfort, diarrhoea, feeling sick, vomiting
- increases in blood tests of liver function
- rash

Uncommon side effects which may affect up to 1 in 100 people are:
- reduction in red blood cells which can make skin pale and cause weakness or breathlessness
- decreased appetite
- inability to sleep, feeling drowsy
- fit, dizziness, sensation of spinning, tingling, pricking or numbness, changes in sense of taste
- constipation, difficult digestion, wind, dry mouth
- muscle pain
- liver damage and yellowing of the skin and eyes (jaundice)
- wheals, blistering (hives), itching, increased sweating
- tiredness, general feeling of being unwell, fever

Rare side effects which may affect up to 1 in 1,000 people are:
- lower than normal white blood cells that help defend against infections and blood cells that help to stop bleeding
- red or purple discoloration of the skin which may be caused by low platelet count, other blood cell changes
- blood chemistry changes (high blood levels of cholesterol, fats)
- low blood potassium
- shaking
- abnormal electrocardiogram (ECG), change in heart rate or rhythm
- liver failure
- allergic reactions (sometimes severe), including widespread blistering rash and skin peeling, severe skin reactions, swelling of the lips or face
- hair loss.

4.9 Overdose and treatment

There have been reports of overdose with fluconazole, 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 hemodialysis session decreases plasma levels by approximately 50%.

5. Pharmacological Properties:

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: Antimycotics for systemic use, triazole derivatives, ATC code: J02AC01.
Mechanism of action

Fluconazole is a triazole antifungal agent. Its primary mode of action is the inhibition of fungal cytochrome P-450-mediated 14-alpha-lanosterol demethylation, an essential step in fungal ergosterol biosynthesis. The accumulation of 14-alpha-methyl sterols correlates with the subsequent loss of ergosterol in the fungal cell membrane and may be responsible for the antifungal activity of flucon-azole. Fluconazole has been shown to be more selective for fungal cytochrome P-450 enzymes than for various mammalian cytochrome P-450 enzyme systems.

Fluconazole 50 mg daily given up to 28 days has been shown not to effect testosterone plasma Concentrations in males or steroid concentration in females of child-bearing age. Fluconazole 200 mg to 400 mg daily has no clinically significant effect on endogenous steroid levels or on ACTH stimulated response in healthy male volunteers. Interaction studies with antipyrine indicate that single or multiple doses of fluconazole 50 mg do not affect its metabolism.

Susceptibility in vitro
In vitro, fluconazole displays antifungal activity against clinically common Candida species (including C. albicans, C. parapsilosis, C. tropicalis). C. glabrata shows reduced susceptibility to fluconazole while C. krusei and C. auris are resistant to fluconazole. The MICs and epidemiological cut-off value (ECOFF) of fluconazole for C. guilliermondii are higher than for C. albicans.

Fluconazole also exhibits activity in vitro against Cryptococcus neoformans and Cryptococcus. gattii as well as the endemic moulds Blastomyces dermatiditis, Coccidioides immitis, Histoplasma capsulatum and Paracoccidioides brasiliensis.

Pharmacokinetic/pharmacodynamic relationship
In animal studies, there is a correlation between MIC values and efficacy against experimental mycoses due to *Candida* spp. In clinical studies, there is an almost 1:1 linear relationship between the AUC and the dose of fluconazole. There is also a direct though imperfect relationship between the AUC or dose and a successful clinical response of oral candidosis and to a lesser extent candidaemia to treatment. Similarly cure is less likely for infections caused by strains with a higher fluconazole MIC.

Mechanisms of resistance
Candida spp have developed a number of resistance mechanisms to azole antifungal agents. Fungal strains which have developed one or more of these resistance mechanisms are known to exhibit high minimum inhibitory concentrations (MICs) to fluconazole which impacts adversely efficacy *in vivo* and clinically.

In usually susceptible species of Candida, the most commonly encountered mechanism of resistance development involves the target enzymes of the azoles, which are responsible for the biosynthesis of

ergosterol. Resistance may be caused by mutation, increased production of an enzyme, drug efflux mechanisms, or the development of compensatory pathways.

There have been reports of superinfection with *Candida* species other than *C. albicans*, which often have inherently not susceptible to fluconazole (e.g. *Candida krusei*) reduced susceptibility (*C. glabrata*) or resistance to fluconazole (e.g. *C. krusei*, *C. auris*). Such infections may require alternative antifungal therapy. The resistance mechanisms have not been completely elucidated in some intrinsically resistant (*C. krusei*) or emerging (*C. auris*) species of *Candida.*

5.2 Pharmacokinetic Properties

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

Absorption

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. Plasma concentrations are proportional to dose. Ninety percent 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.

Distribution

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 levels of fluconazole in saliva and sputum are similar to plasma levels. In patients with fungal meningitis, fluconazole levels in the CSF are approximately 80% the corresponding plasma levels.

High skin concentration of fluconazole, above serum concentrations, are achieved in the stratum corneum, epidermis-dermis and eccrine sweat. Fluconazole accumulates in the stratum corneum. At a dose of 50 mg once daily, the concentration of fluconazole after 12 days was 73 μg/g and 7 days after cessation of treatment the concentration was still 5.8 μg/g. At the 150 mg once-a-week dose, the concentration of fluconazole in stratum corneum on day 7 was 23.4 μg/g and 7 days after the second dose was still 7.1 μg/g.

Concentration of fluconazole in nails after 4 months of 150 mg once-a-week dosing was 4.05 μg/g in healthy and 1.8 μg/g in diseased nails; and, fluconazole was still measurable in nail samples 6 months after the end of therapy.

Biotransformation

Fluconazole is metabolised only to a minor extent. Of a radioactive dose, only 11% is excreted in a changed form in the urine. Fluconazole is a moderate inhibitor of the isozymes CYP2C9 and CYP3A4. Fluconazole is also a strong inhibitor of the isozyme CYP2C19.

Elimination

Plasma elimination half-life for fluconazole is approximately 30 hours. 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.

The long plasma elimination half-life provides the basis for single dose therapy for vaginal candidiasis, once daily and once weekly dosing for other indications.

Pharmacokinetics in renal impairment

In patients with severe renal insufficiency, (GFR< 20 ml/min) half life increased from 30 to 98 hours. Consequently, reduction of the dose is needed. Fluconazole is removed by haemodialysis and to a lesser extent by peritoneal dialysis. After three hours of haemodialysis session, around 50% of fluconazole is eliminated from blood.

Pharmacokinetics during lactation

A pharmacokinetic study in ten lactating women, who had temporarily or permanently stopped breast-feeding their infants, evaluated fluconazole concentrations in plasma and breast milk for 48 hours following a single 150 mg dose of fluconazole. Fluconazole was detected in breast milk at an average concentration of approximately 98% of those in maternal plasma. The mean peak breast milk concentration was 2.61 mg/L at 5.2 hours post-dose. The estimated daily infant dose of fluconazole from breast milk (assuming mean milk consumption of 150 ml/kg/day) based on the mean peak milk concentration is 0.39 mg/kg/day, which is approximately 40% of the recommended neonatal dose (<2 weeks of age) or 13% of the recommended infant dose for mucosal candidiasis.

Pharmacokinetics in children

Pharmacokinetic data were assessed for 113 paediatric patients from 5 studies; 2 single dose studies, 2 multiple dose studies and a study in premature neonates. Data from one study were not interpretable due to changes in formulation pathway through the study. Additional data were available from a compassionate use study.

After administration of 2 – 8 mg/kg fluconazole to children between the ages of 9 months to 15 years, an AUC of about 38 µg.h/ml was found per 1 mg/kg dose units. The average fluconazole plasma elimination half-life varied between 15 and 18 hours and the distribution volume was approximately 880 ml/kg after multiple doses. A higher fluconazole plasma elimination half-life of approximately 24 hours was found after a single dose. This is comparable with the fluconazole plasma elimination half-life after a single administration of 3 mg/kg i.v. to children of 11 days-11 months old. The distribution volume in this age group was about 950 ml/kg.

Experience with fluconazole in neonates is limited to pharmacokinetic studies in premature newborns. The mean age at first dose was 24 hours (range 9-36 hours) and mean birth weight was 0.9 Kg (range 0.75-1.10 Kg) for 12 pre-term neonates of average gestation around 28 weeks. Seven patients completed the protocol; a maximum of five 6 mg/kg intravenous infusions of fluconazole were administered every 72 hours. The mean half-life (hours) was 74 (range 44-185) on day 1 which decreased with time to a mean of 53 (range 30-131) on day 7 and 47 (range 27-68) on day 13. The area under the curve (microgram.h/ml) was 271 (range 173-385) on day 1 and increased with a mean of 490 (range 292-734) on day 7 and decreased with a mean of 360 (range 167-566) on day 13. The volume of

distribution (ml/kg) was 1183 (range 1070-1470) on day 1 and increased with time to a mean of 1184 (range 510-2130) on day 7 and 1328 (range 1040-1680) on day 13.

Pharmacokinetics in elderly
A pharmacokinetic study was conducted in 22 subjects, 65 years of age or older receiving a single 50 mg oral dose of fluconazole. Ten of these patients were concomitantly receiving diuretics. The Cmax was 1.54 μg/ml and occurred at 1.3 hours post-dose. The mean AUC was 76.4 ± 20.3 μg·h/ml, and the mean terminal half-life was 46.2 hours. These pharmacokinetic parameter values are higher than analogous values reported for normal young male volunteers. Coadministration of diuretics did not significantly alter AUC or Cmax. In addition, creatinine clearance (74 ml/min), the percent of medicinal product recovered unchanged in urine (0-24 h, 22%) and the fluconazole renal clearance estimates (0.124 ml/min/kg) for the elderly were generally lower than those of younger volunteers. Thus, the alteration of fluconazole disposition in the elderly appears to be related to reduced renal function characteristics of this group.

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 2-7 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 embryo lethality 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

Summary of Product Characteristic

6. Pharmaceutical Particulars:

6.1 List of excipients
Lactose monohydrate, Maize Starch, Sodium Benzoate, Magnesium Stearate, Colloidal anhydrous silica, Sodium Lauryl sulphate, Purified water

6.2 Incompatibilities
None known

6.3 Shelf life
36 months

6.4Special precautions for storage
Store in a cool dry place. Protect from light.
Keep out of reach of children.

6.5 Nature and contents of container
1 blister of 10 capsules packed in carton with insert.

7. Marketing Authorization Holder:

Name: Novopharm Formulations (P) Ltd.
Address: 105.Rajmandir , 62- Alkapuri Society,
R.C Dutt Road, Vadodara – 390007,
Gujarat, India.

8. Marketing Authorization Number (s):
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9. Product license / registration Number (s)
----

10. Manufacturer Name:
Name:Novopharm Formulations (P) Ltd.
C/O Baroque Pharmaceuticals Pvt. Ltd.
Address: No. 192/2 &3 At.Sokhada-388620, Ta. Khambhat,
Dist- Anand Gujarat, India.

11. Date of first authorization/renewal of the authorization:
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12. Date of revision of the text:
Aug 2023