The format of this leaflet was determined by the Ministry of health and its content was checked and approved by it in December 2012

Prescribing Information

FLUCONAZOL

1. NAME OF THE MEDICAL PRODUCT

FLUCONAZOL Solution for Infusion 2 mg/ml

2. QUALITY AND QUANTITATIVE COMPOSITION

Solution for Infusion at 100 mg/50ml:
Fluconazole ..... 100.0 mg
Excipient q.s. ..... 50 ml

Solution for Infusion at 200 mg/100ml:
Fluconazole ..... 200.0 mg
Excipient q.s. ..... 100 ml

Solution for Infusion at 400 mg/200ml:
Fluconazole ..... 400.0 mg
Excipient q.s. ..... 200 ml

3. PHARMACEUTICAL FORM

Solution for Infusion.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

FLUCONAZOL is indicated in the treatment of:
Systemic candidiasis
Mucosal candidiasis
Cryptococcosis

4.2 Posology and Method of Administration

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit.

FLUCONAZOL Solution for Infusion 2 mg/ml is intended for intravenous Infusion only.

FLUCONAZOL Solution for Infusion 2 mg/ml may be administered by intravenous Infusion at a rate of approximately 5-10 ml/min, the route being dependent on the clinical state of the patient. The intravenous *Infusion* of FLUCONAZOL Solution for Infusion 2 mg/ml should be administered at a maximum rate of approximately 200 mg/hour, given as a continuous infusion.

On transferring from the intravenous to the oral route or vice versa, there is no need to change the daily dose.

FLUCONAZOL Solution for Infusion 2 mg/ml is formulated in 0.9% sodium chloride solution, each 200 mg (100ml bottle) containing 15 mmol each of Na^+ and Cl^-. Because FLUCONAZOL Solution for Infusion 2 mg/ml is available as a dilute saline solution, in patients requiring sodium or fluid restriction, consideration should be given to the rate of fluid administration.

The daily dose of FLUCONAZOL Solution for Infusion 2 mg/ml should be based on the nature and severity of the fungal infection.

Therapy for those types of infections requiring multiple dose treatment should be continued until clinical parameters or laboratory tests indicate that active fungal infection has subsided. An inadequate period of treatment may lead to recurrence of active infection. Patients with AIDS and cryptococcal meningitis usually require maintenance therapy to prevent relapse.

Adults

Cryptococcal meningitis and cryptococcal infections at other sites: The usual dose is 400mg on the first day followed by 200mg-400mg once daily. Duration of 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, after the patient receives a full course of primary therapy, FLUCONAZOL Solution for Infusion 2 mg/ml may be administered indefinitely at a daily dose of 200mg.

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

Mucosal Candidiasis:

- Oropharyngeal candidiasis: The usual dose is 50mg once daily for 7-14 days. Treatment can be continued for longer periods in patients with severely compromised immune function. For atrophic oral candidiasis associated with dentures, the usual dose is 50mg once daily for 14 days administered concurrently with local antiseptic measures to the denture.
- Other candidal infections of mucosa (except vaginal candidiasis, e.g. esophagitis, non-invasive bronchopulmonary infections, candiduria, mucocutaneous candidiasis etc.: The usual effective dose is 50mg-100mg daily, given for 14-30 days.

Children

A maximum dosage of 400 mg 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. FLUCONAZOL Solution for Infusion 2 mg/ml is administered as a single daily dose.

Children over four weeks of age

The recommended dose of FLUCONAZOL Solution for Infusion 2 mg/ml for mucosal candidiasis 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 the treatment of systemic candidiasis and cryptococcal infection, the recommended dosage is 6-12 mg/kg daily, depending on the severity of the disease.

Despite extensive data supporting the use of fluconazole in children, there are limited data available on the use of fluconazole for genital candidiasis in children below 16 years. Use at present is not recommended unless antifungal treatment is imperative and no suitable alternative agent exists.

Children four weeks of age and younger

Neonates excrete fluconazole slowly. In the first two weeks of life, the same mg/kg dosing used in older children should be adopted but administered every 72 hours. During weeks 2-4 of life, the same dose should be given every 48 hours.

A maximum dosage of 12 mg/ kg every 72 hours should not be exceeded in children in the first two weeks of life. For children between three and four weeks of life, 12 mg/kg every 48 hours should not be exceeded.

For children with impaired renal function, the daily dose should be reduced in accordance with the guidelines given for adults.

Elderly

The normal adult 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 described below.

Patients with renal impairment (Adults)

Fluconazole is excreted predominantly in the urine as unchanged drug. No adjustments in single dose therapy are required for those with renal impairment. In patients with impaired renal function 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 on the following table:

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

Patients receiving regular dialysis

One dose after every dialysis session; on non-dialysis days, patients should receive a reduced dose according to their creatinine clearance.

Hepatic impairment

Limited data are available in patients with hepatic impairment, therefore fluconazole should be administered with caution to patients with liver dysfunction (see sections 4.4 and 4.8).

4.3 Contraindications

FLUCONAZOL Solution for Infusion 2 mg/ml should not be used in patients with known hypersensitivity to fluconazole or to related azole compounds or any of the excipients (For excipients, see section 6.1).

There is no information regarding cross-hypersensitivity between fluconazole and other azole antifungal agents. Caution should be used in prescribing fluconazole to patients with hypersensitivity to other azoles. Coadministration of terfenadine is contraindicated in patients receiving fluconazole at multiple doses of 400 mg or higher based upon results of a multiple dose interaction study. Coadministration of other drugs known to prolong the QT interval and which are metabolized via the enzyme CYP3A4 such as cisapride, astemizole, pimozide, quinidine and erythromycin are contraindicated in patients receiving fluconazole (See sections 4.4 and 4.5).

4.4 Special warnings and precautions for use

In some patients, particularly those with serious underlying diseases such as AIDS and cancer, abnormalities in haematological, hepatic, renal and other biochemical function test results have been observed during treatment with fluconazole. However, the clinical significance and relationship to treatment is uncertain.

Very rarely, patients who died with severe underlying disease and who had received multiple doses of fluconazole, had post-mortem findings which included hepatic necrosis. These patients were receiving multiple concomitant medications, some known to be potentially hepatotoxic and/or had underlying diseases which could have caused the hepatic necrosis.

In cases of hepatotoxicity, no obvious relationship to the total daily dose of fluconazole, the duration of therapy or the sex or age of the patient has been observed. The abnormalities have usually been reversible on discontinuation of fluconazole therapy.

As a casual relationship with fluconazole cannot be excluded, patients who developed abnormal liver function tests during fluconazole therapy should be monitored for the development of more serious hepatic injury. FLUCONAZOL Solution for Infusion 2 mg/ml should be discontinued, if clinical signs or symptoms consist with liver disease develop during treatment.

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 drugs.

If a rash develops in a patient treated for a superficial infection, which is considered attributable to fluconazole, further therapy with this agent should be discontinued. If patients with invasive/systemic fungal infections develop rashes, they should be monitored closely and FLUCONAZOL Solution for Infusion 2 mg/ml discontinued if bullous lesions or erythema multiforme develop.

FLUCONAZOL Solution for Infusion 2 mg/ml is formulated in a 0.9% sodium chloride solution, with each 100 mg (50 ml vial) containing 7.7 mmol of NaCl, each 200mg (100 ml vial) containing 15.4 mmol of NaCl and each 400 mg (200 ml vial) containing 30.8 mmol NaCl. This should be considered in patients on a sodium or fluid restricted diet.

In rare cases, as with other azoles, anaphylaxis has been reported.

Use in Pregnancy:

There are no adequate and well-controlled studies of fluconazole in pregnant women.

Available human data do not suggest an increased risk of congenital anomalies following a single maternal dose of 150 mg. A few published case reports describe a rare pattern of distinct congenital anomalies in infants exposed in-utero to high dose maternal fluconazole (400-800 mg/day) during most or all of the first trimester. These reported anomalies are similar to those seen in animal studies. If this medicine is used during pregnancy, or if the patient becomes pregnant while taking the medicine, the patient should be informed of the potential hazard to the fetus (See Section 4.6, 'Pregnancy and lactation').

4.5 Interaction with other medicinal products and other forms of interaction

The following drug interactions relate to the use of multiple-dose fluconazole; their relevance to single-dose has not yet been established.

Anticoagulants: In an interaction study, fluconazole increased the prothrombin time (12%) after warfarin administration in healthy males. In post-marketing experience, as with other azole antifungals, bleeding events (bruising, epistaxis, gastrointestinal bleeding, hematuria and melaena) have been reported in association with increases in prothrombin time, in patients receiving fluconazole concurrently with warfarin. Prothrombin time in patients receiving coumarin-type anticoagulants should be carefully monitored.

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 being treated with fluconazole, consideration should be given to decreasing the benzodiazepine dosage and the patients should be appropriately monitored.

Endogenous steroids: Fluconazole 50 mg daily does not affect endogenous steroid levels in females: 200 - 400 mg daily has no clinically significant effect on endogenous steroid levels or on ACTH stimulated response in healthy male volunteers.

Sulphonylureas: Fluconazole has been shown to prolong the serum half-life of concomitantly administered oral sulphonylureas (chlorpropamide, glibenclamide, glipizide and tolbutamide) in healthy volunteers. Fluconazole and oral sulphonylureas may be given jointly to diabetic patients, although the possibility of hypoglycaemic episode must be considered. Blood glucose levels must therefore be monitored and the dose of sulphonylurea adjusted accordingly.

Hydrochlorothiazide: In a pharmacokinetic interaction study, the co-administration of multiple doses of hydrochlorothiazide in healthy volunteers receiving fluconazole, increased the plasma concentrations of fluconazole by 40%. An effect of this magnitude should not require any change in the dosage regimen of fluconazole in patients simultaneously receiving diuretics, although this should be taken into consideration by the prescriber.

Phenytoin: the concomitant administration of fluconazole and phenytoin may increase levels of phenytoin to a clinically significant degree. If both drugs need to be given concomitantly, levels of phenytoin must be monitored and the dose of phenytoin adjusted to maintain therapeutic levels.

Oral contraceptives: Two pharmacokinetic studies were conducted with combined oral contraceptives and multiple fluconazole doses. In the study using 50 mg fluconazole, there were no relevant effects on hormone level. However, using 200 mg fluconazole daily, the area under the curve (AUC) for ethinyloestradiol and levonorgestrel, increased by 40% and 24% respectively. Thus, multiple dose use of fluconazole at these levels is unlikely to affect the efficacy of combined oral contraceptives.

Rifampicin: The concomitant administration of fluconazole and rifampicin gave rise to a 25% reduction in the AUC and a 20% shorter half-life of fluconazole. Thus, an increase in the dose of fluconazole should be considered for patients receiving concomitant rifampicin.

Cyclosporin: A pharmacokinetic study conducted on kidney transplant patients, showed that a daily dose of 200 mg fluconazole slowly increased the concentrations of cyclosporin. However, another multiple-dose study using 100 mg fluconazole daily, showed that levels of cyclosporin were not affected in patients following bone marrow transplants. Thus, the monitoring of the plasma concentration of cyclosporin is recommended in patients taking fluconazole.

Theophylline: In a placebo-controlled interaction study, the administration of 200 mg fluconazole daily for 14 days, led to a reduction of 18% in the mean plasma clearance figure of theophylline. Therefore, patients receiving high doses of theophylline or patients with high risk of theophylline toxicity, should be carefully monitored for signs of theophylline toxicity when receiving fluconazole. Treatment should be appropriately modified if signs of toxicity develop.

Terfenadine: Due to the occurrence of serious dysrrhythmias (secondary to prolongation of the QTc interval), in patients receiving other azole antifungals in conjugation with terfenadine, interaction studies have been performed. In one study, a 200 mg daily dose of fluconazole failed to demonstrate a prolongation in QTc interval. In another study, a 400 mg and 800 mg daily dose of fluconazole demonstrated that fluconazole, taken in multiple doses of 400 mg per day or greater, significantly increased plasma levels of terfenadine when taken concomitantly. There have been spontaneously reported cases of palpitations, tachycardia, dizziness and chest pain in patients taking concomitant fluconazole and terfenadine, where the relationship of the reported adverse events to drug therapy or underlying medical conditions was not clear. Because of the potential seriousness of such an interaction, it is recommended that terfenadine should not be taken in combination with fluconazole. (See section 4.3, 'contraindications'.)

Cisapride: There have been reports of cardiac events including torsades de pointes, in patients to whom fluconazole and cisapride were co-administered. In most of these cases, the patients appear to have been predisposed to arrhythmias or had serious underlying illnesses and the relationship of the reported events to a possible fluconazole-cisapride drug interaction is unclear. There have been

no formal drug interaction studies with fluconazole and cisapride. Because of the potential seriousness of such an interaction, it is recommended that cisapride is not taken in combination with fluconazole. (See section 4.3, 'Contraindications'.)

Zidovudine: Two pharmacokinetic studies have shown increases in levels of zidovudine, caused very probably by the fall in the conversion of zidovudine to its main metabolite. One study determined the levels of zidovudine in AIDS or ARC patients, before and after the daily administration of 200 mg fluconazole for 15 days. A significant increase was observed in the zidovudine AUC (20%). A second randomized two-period, two-treatment crossover study, examined the levels of zidovudine in patients infected with HIV. On two occasions, with an interval of 21 days, patients received 200 mg zidovudine every 8 hours, either with or without 400 mg of fluconazole daily, for 7 days. The AUC of zidovudine increased significantly (74%) during joint administration with fluconazole. Therefore, patients receiving this combination should be monitored for the appearance of adverse reactions related to zidovudine.

Rifabutin: There have been reports that an interaction exists when fluconazole is administered concomitantly with rifabutin, leading to increased serum levels of rifabutin. There have also been reports of uveitis in patients to whom fluconazole and rifabutin were co-administered. Patients receiving rifabutin and fluconazole concomitantly should be carefully monitored.

Tacrolimus: there have been reports that an interaction exists when fluconazole is administered concomitantly with tacrolimus, leading to increased serum levels of tacrolimus. There have also been reports of nephrotoxicity in patients to whom fluconazole and tacrolimus were co-administered. Patients receiving tacrolimus and fluconazole concomitantly should be carefully monitored.

The use of fluconazole in patients concurrently taking astemizole or other drugs metabolized by the cytochrome P450 system, may be associated with elevations in serum levels of these drugs. In the absence of definitive information, caution should be used when co administering fluconazole. Patients should be carefully monitored.

While no interaction studies have been conducted with other drugs, the possible appearance of other pharmacological interactions is not ruled out.

4.6 Pregnancy and lactation

Pregnancy: Teratogenic Effects

Pregnancy Category D
A few published case reports describe a rare pattern of distinct congenital anomalies in infants exposed in-utero to high dose maternal fluconazole (400-800 mg/day) during most or all of the first trimester. These reported anomalies are similar to those seen in animal studies. If this medicine is used during pregnancy, or if the patient becomes pregnant while taking the medicine, the patient should be informed of the potential hazard to the fetus. (See Section 4.4, 'Special warnings and precautions for use')

Human Data
Several published epidemiologic studies do not suggest an increased risk of congenital anomalies associated with low dose exposure to fluconazole in pregnancy (most subjects received a single oral dose of 150 mg). A few published case reports describe a distinctive and rare pattern of birth defects among infants whose mothers received high-dose (400-800 mg/day) fluconazole during most or all of the first trimester of pregnancy. The features seen in these infants include: brachycephaly, abnormal facies, abnormal calvarial development, cleft palate, femoral bowing, thin ribs and long bones, arthrogryposis, and congenital heart disease. These effects are similar to those seen in animal studies.

Animal Data
Fluconazole was administered orally to pregnant rabbits during organogenesis in two studies at doses of 5, 10, and 20 mg/kg and at 5, 25, and 75 mg/kg, respectively. Maternal weight gain was impaired at all dose levels (approximately 0.25 to 4 times the 400 mg clinical dose based on BSA), and abortions occurred at 75 mg/kg (approximately 4 times the 400 mg clinical dose based on BSA); no adverse fetal effects were observed.

In several studies in which pregnant rats received fluconazole orally during organogenesis, maternal weight gain was impaired and placental weights were increased at 25 mg/kg. There were no fetal effects at 5 or 10 mg/kg; increases in fetal 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 to 320 mg/kg (approximately 2 to 8 times the 400 mg clinical dose based on BSA), embryolethality in rats was increased and fetal abnormalities included wavy ribs, cleft palate, and abnormal cranio-facial ossification. These effects are consistent with the inhibition of estrogen synthesis in rats and may be a result of known effects of lowered estrogen on pregnancy, organogenesis, and parturition.

Nursing Mothers
Fluconazole is secreted in human milk at concentrations similar to maternal plasma concentrations. Caution should be exercised when fluconazole is administered to a nursing woman.

4.7 Effects on ability to drive and use machines
Experience with fluconazole indicates that therapy is unlikely to affect a patient's ability to drive or use machinery.

4.8 Undesirable effects
Fluconazole is generally well tolerated.

The most common side effects observed during clinical trials and associated with fluconazole are:

Central and peripheral nervous system
Headache

Gastrointestinal
Abdominal pain, diarrhoea, flatulence, nausea.

In some patients, particularly those with serious underlying diseases such as AIDS and cancer, changes in renal and haematological function test results and hepatic abnormalities have been observed during treatment with fluconazole and comparative agents but the clinical significance and relationship to treatment is uncertain, (see section 4.4 'Special warnings and special precautions for use').

Liver/biliary
Hepatic toxicity - including rare cases of fatality, elevated alkaline phosphatase, elevated bilirubin, elevated SGOT, elevated SGPT.

Dermatological
Rash.

In addition, the following adverse events have occurred during post-marketing:

Haematopoietic and lymphatic
Leukopenia (including neutropenia and agranulocytosis), thrombocytopenia.

Immunological
Anaphylaxis (including angioedema, face oedema, pruritus).

Metabolic/nutritional
Hypercholesterolaemia, hypertriglyceridaemia, hypokalaemia.

Central and peripheral nervous system
Dizziness, seizures.

Gastrointestinal
Dyspepsia, vomiting.

Liver/biliary
Hepatic failure, hepatitis, hepatocellular necrosis, jaundice.

Dermatological
Alopecia, exfoliative skin disorders, including Stevens-Johnson syndrome and toxic epidermal necrolysis.

Other senses
Taste perversion.

4.9 Overdose
There has been a reported case of overdose with fluconazole. A 42 year-old patient infected with human immunodeficiency virus, developed hallucinations and exhibited paranoid behaviour after reportedly ingesting 8200 mg fluconazole, unverified by his physician. The patient was admitted to a hospital and his condition resolved within 48 hours.

In the event of overdose, supportive measures and symptomatic treatment, with gastric lavage if necessary, may be adequate.

As fluconazole is largely excreted in the urine, forced volume diuresis would probably increase the elimination rate. A three-hour haemodialysis session decreases plasma levels by approximately 50%.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
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 shows little pharmacological activity in a wide range of animal studies. Some prolongation of pentobarbitone sleeping times in mice (p.o.), increased mean arterial and left ventricular blood pressure and increased heart rate in anaesthetised cats (i.v.) occurred. Inhibition of rat ovarian aromatase was observed at high concentrations.

Fluconazole is highly specific for fungal cytochrome P-450 dependent enzymes.

Fluconazole 50 mg daily, when given for up to 28 days, has been shown not to affect testosterone plasma concentrations in males or steroid concentrations in females of child-bearing age. Fluconazole 200 - 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.

There have been reports of cases of superinfection with Candida species other than C. albicans, which are often inherently not susceptible to fluconazole (e.g. Candida krusei). Such cases may require alternative antifungal therapy.

5.2 Pharmacokinetic properties
Plasma concentrations are proportional to the dose. 90% steady state levels are reached after 4 or 5 days with multiple once daily doses. The administration of a higher dose on the first day, double that of the normal daily dose, raises plasma levels to 90% of the equilibrium status levels by the second day.

The apparent volume of distribution is close to that of total body water. Fluconazole achieves good penetration in all body fluids studies. 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% of the corresponding plasma levels. High skin concentrations of fluconazole, above serum concentrations, are achieved on the stratum corneum, epidermis-dermis and eccrine sweat. Fluconazole accumulates in the stratum corneum. Binding to plasma proteins is low (11-12%).

Clearance is mostly renal, with approximately 80% of the unmodified dose appearing in the urine. The clearance of fluconazole is proportional to creatinine clearance. There is no evidence of circulating metabolites.

Fluconazole's long plasma elimination half-life, makes it possible to administer a single dose in the treatment of genital candidiasis and a daily dose in the treatment of other indications.

5.3 Preclinical safety data
Carcinogenesis: Fluconazole showed no evidence of carcinogenic potential in rats and mice treated orally for 24 months, with doses of 2.5, 5 or 10 mg/kg/day. 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 mutagenicity tests conducted in 4 strains of S. typhimurium and mouse lymphoma L5178Y system. In vivo cytogenetic studies (in mouse bone marrow cells, following the oral administration of fluconazole) and in vitro studies (in human lymphocytes exposed to 1,000 micrograms/ml fluconazole), showed no evidence of chromosomal mutations.

Impairment of fertility: Fluconazole did not alter the fertility of male or female rats treated parenterally with doses of 5, 25, or 75 mg/kg, although onset of parturition was slightly delayed with oral doses of 20 mg/kg. In a perinatal study on the intravenous route in rats, at doses of 5, 20 and 40 mg/kg, dystocia and prolongation of parturition was observed in some females treated with doses of 20 mg/kg and 40 mg/kg but not at the dose of 5 mg/kg. The alterations in parturition were reflected in a slight increase in the number of stillborn pups and decrease of neonatal survival at these dose levels. The effects on parturition in rats are consistent with the species specific oestrogen-lowering property produced by high doses of fluconazole. This hormonal change had not been observed in woman treated with fluconazole.

Reproductive toxicity: Increases in foetal anatomical variants (e.g., 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 - 320 mg/kg embryolethality in rats was increased and foetal abnormalities included wavy ribs, cleft palate and abnormal cranio-facial ossification.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients
Solution for Infusion at 100 mg/50 ml: sodium chloride 0.9% (450 mg), hydrochloric acid and water for injections (q.s. 50 ml).
Solution for Infusion at 200 mg/100 ml: sodium chloride 0.9% (900 mg), hydrochloric acid and water for injections (q.s. 100 ml).
Solution for Infusion at 400 mg/200 ml: sodium chloride 0.9% (1800 mg), hydrochloric acid and water for injections (q.s. 200 ml).

6.2 Incompatibilities
The administration of FLUCONAZOL Solution for Infusion 2 mg/ml with other drugs is not recommended.

6.3 Shelf-life
The shelf-life of FLUCONAZOL Solution for Infusion 2 mg/ml is 3 years.

6.4 Special precautions for storage
FLUCONAZOL Solution for Infusion 2 mg/ml should be stored at room temperature (below 25^0C).

Do not freeze.

6.5 Nature and contents of container
FLUCONAZOL Solution for Infusion 2 mg/ml is supplied in glass ampoule-vials.

Packs with 1 or 10 ampoule-vial with 50 ml of solution for Infusion dosed at 2 mg/ml in fluconazole (hospital use).

Packs with 1 or 10 ampoule-vial with 100 ml of solution for Infusion dosed at 2 mg/ml in fluconazole (hospital use).

Packs with 1 or 10 ampoule-vial with 200 ml of solution for Infusion dosed at 2 mg/ml in fluconazole (hospital use).

7. MANUFACTURER
B.Braun Medical S.A., Spain

7.1 REGISTRATION HOLDER
BioAvenir Ltd., Kibutz Glil Yam 46905

Designação:
Fluconazol BioAvenir

Código: PL Fluconazol PB0813-01

Laetus: n/a

Formato: 260x420 mm

Cor(es): Preto

Gramagem (gr/m²): 50

Elaborado a: 10 out 2013 **Por:** Marco Medeiros