Package leaflet: Information for the user

FLUCONAZOLO Bioindustria L.I.M. 100 mg/50 ml solution for infusion
FLUCONAZOLO Bioindustria L.I.M. 200 mg/100 ml solution for infusion
FLUCONAZOLO Bioindustria L.I.M. 400 mg/200 ml solution for infusion
fluconazole
Equivalent medicine

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or nurse.
- If you get any of the side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What FLUCONAZOLO Bioindustria L.I.M. is and what it is used for
2. What you need to know before you take FLUCONAZOLO Bioindustria L.I.M.
3. How to take FLUCONAZOLO Bioindustria L.I.M.
4. Possible side effects
5. How to store FLUCONAZOLO Bioindustria L.I.M.
6. Contents of the pack and other information

1. What FLUCONAZOLO Bioindustria L.I.M. is and what it is used for

FLUCONAZOLO Bioindustria L.I.M. contains the active substance fluconazole, which belongs to a group of medicines called "antifungals," used to treat infections caused by fungi and yeasts.

FLUCONAZOLO Bioindustria L.I.M. is indicated for the treatment of infections caused by fungi (mycoses) and can be used to prevent *Candida* infections. The most common cause of fungal infections is a yeast called *Candida*.

Adults
Your doctor may prescribe this medication for the treatment of the following fungal infections:
- Infection of the tissues lining the brain (cryptococcal meningitis);
- Disease of the bronchopulmonary system (coccidioidomycosis);
- Infection caused by *Candida* and found in the blood stream, organs (e.g., heart, lungs) or urinary tract;
- Infection of the throat and oral mucosa (oropharyngeal candidiasis, esophageal candidiasis, candiduria and chronic mucocutaneous candidiasis, invasive candidiasis);
- Inflammation of the mouth from dentures and in those cases where oral hygiene and other treatments are not sufficient (chronic atrophic oral candidiasis, stomatitis from dentures).

This medicine is also indicated for:
- prevent the reappearance of an infection to the tissues lining the brain (cryptococcal meningitis) if you have already suffered from it and there is a high risk that the infection may reoccur;
- prevent the reoccurrence of mucosal candidiasis (oropharyngeal or esophageal candidiasis);
- prevent *Candida* infections if he or she has low white blood cell counts, such as if he or she has blood diseases (hematological malignancies) and is undergoing chemotherapy or receiving blood cell transplantation (Hemopoietic Stem Cells).

Children and adolescents (0 to 17 years old)
Your doctor may prescribe this medicine for the following fungal infection:
- treat *Candida* infections of the mucous membranes (oral mucosal infection, throat infection);

- infections caused by *Candida* and found in the blood stream, organs (e.g., heart, lungs) or urinary tract;
- treat infections of the tissues lining the brain (cryptococcal meningitis).

FLUCONAZOLO Bioindustria L.I.M. may also be prescribed to:
- prevent *Candida* infections (if the immune system is weak or not functioning properly);
- prevent the recurrence of cryptococcal meningitis.

2. What you need to know before you take FLUCONAZOLO Bioindustria L.I.M.

Do not take FLUCONAZOLO Bioindustria L.I.M.
- if you are allergic (hypersensitive) to fluconazole, to similar medicines (azole compounds) that you have used to treat fungal infections, or to any of the other components of this medicine (listed in section 6). Symptoms may be itching, reddening of the skin, or difficulty breathing;
- if you are taking the following medicines (see the section "Other medicines and FLUCONAZOLO Bioindustria L.I.M." and "Warnings and Precautions"):
  - certain medicines used to treat allergies such as astemizole, terfenadine;
  - cisapride, a medicine used to treat certain stomac disorders ;
  - some medicines used to treat irregularities of the heartbeat (cardiac arrhythmias), such as quinidine;
  - pimozide, used for some mental disorders;
  - erythromycin, an antibiotic used to treat some infections caused by bacteria.

Warnings and precautions
Talk to your doctor or nurse before you are given FLUCONAZOLO Bioindustria L.I.M.:
- if you have kidney problems (impaired kidney function);
- if you have liver problems, because serious problems, including death, may occur. If the symptoms of a liver problem such as reduced appetite (anorexia), nausea, vomiting, fatigue, and yellow discoloration of the skin and white part of the eyes (jaundice) occur, stop treatment with this medicine and inform your doctor immediately;
- if you have heart disease (structural heart disease, electrolyte abnormalities) or if you are taking other medicines that may alter the normal heartbeat (cardiac arrhythmia) (see section "Other medicines and FLUCONAZOLO Bioindustria L.I.M.");
- if you have abnormal levels of potassium, calcium or magnesium in your blood;
- if you develop severe skin reactions (itching, reddening of the skin or difficulty breathing);
- if you develop signs of "adrenal insufficiency", whereby the adrenal glands do not produce adequate amounts of certain steroid hormones such as cortisol (chronic or long lasting fatigue, muscle weakness, loss of appetite, weight loss, abdominal pain);
- if you are taking terfenadine, a medicine used to treat allergies or if you are taking halofantrine, a medicine used to treat malaria (see section "Other medicines and FLUCONAZOLO Bioindustria L.I.M.");
- if you have ever developed a severe rash or skin peeling, blistering and/or mouth sores after taking FLUCONAZOLO Bioindustria L.I.M.

Serious skin reactions including drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported in association with FLUCONAZOLO Bioindustria L.I.M. treatment. Stop taking FLUCONAZOLO Bioindustria L.I.M. and seek medical attention immediately if you notice any of the symptoms related to these serious skin reactions described in section 4.

Talk to the doctor, the nurse or the pharmacist whether the fungal infection does not improve, an alternative antifungal therapy may be needed.

If you experience skin irritation (rash) or other more serious complaints associated with blistering and lesions (exfoliative skin reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis) occur during

treatment with this medication, discontinue treatment with this medication. These problems may be more likely to occur if you have AIDS.

FLUCONAZOLO Bioindustria L.I.M. should not be used to treat infections caused by tinea capitis.

There are no data available regarding the dose to be used when treating cryptococcosis and deep endemic mycoses (paracoccidioidomycosis, lymphocutaneous sporotrichosis, and histoplasmosis).

Other medicines and FLUCONAZOLO Bioindustria L.I.M.
Tell your doctor or nurse if you are taking, have recently taken or might take any other medicines.

Tell your doctor **immediately** if you are taking:
- cisapride, a medicine used for stomach upsets;
- terfenadine, a medicine used to treat allergies, as alterations in heartbeat may occur. Avoid taking terfenadine and FLUCONAZOLO Bioindustria L.I.M. at the same time if your prescribed dose of FLUCONAZOLO Bioindustria L.I.M. is 400 mg or more per day. If you have to take a dose of FLUCONAZOLO Bioindustria L.I.M. less than 400 mg and terfenadine, your doctor should monitor your condition while you are being treated with the two medicines;
- astemizole, used to treat allergies;
- quinidine, a medicine used to treat irregularities of the heartbeat (cardiac arrhythmias);
- erythromycin, antibiotic used to treat some infections caused by bacteria;
- pimozide, a medicine used for some mental disorders;

As they should not be taken with FLUCONAZOLO Bioindustria L.I.M. (see section: "Do not use FLUCONAZOLO Bioindustria L.I.M.").

There are some medicines that may interact with FLUCONAZOLO Bioindustria L.I.M.
Tell your doctor if you are taking any of the following medicines as an adjustment or monitoring of the dose may be necessary to ensure that the drugs continue to have the desired effect:
- halofantrine, a medicine used to treat malaria;
- rifampicin, rifabutin, azithromycin, used to treat certain infections caused by bacteria;
- abrocitinib (used for the atopic dermatitis treatment, also known as atopic eczema)
- alfentanil and fentanyl, medicines used as anesthetics;
- amitriptyline, nortriptyline, medicines used to treat depression (antidepressants);
- amphotericin B, voriconazole used to treat some infections caused by fungi (antifungals);
- medicines used to make the blood more fluid and prevent blood clots (warfarin or similar medicines);
- certain medicines used to treat anxiety or as tranquilizers, such as midazolam and triazolam or similar medicines (benzodiazepines);
- medicines used to treat seizures (carbamazepine, phenytoin);
- certain medicines used to treat high blood pressure (hypertension) (calcium antagonists, such as nifedipine, isradipine, amlodipine, verapamil and felodipine and losartan);
- olaparib (used to treat ovarian cancer);
- some medicines used to treat certain cancers (cyclophosphamide, vinca alkaloids (vincristine, vinblastine or similar medicines));
- cyclosporine, everolimus, sirolimus and tacrolimus, medicines used after organ transplants to prevent organ rejection;
- methadone, a medicine used to treat pain;
- medicines used to treat inflammation (celecoxib, flurbiprofen, naproxen, ibuprofen, lornoxicam, meloxicam, diclofenac (Non-Steroidal Anti-Inflammatory Drugs (NSAIDs));
- medicines used to treat inflammation, asthma and allergies (prednisone (steroid));
- saquinavir, zidovudine also known as AZT, used to treat AIDS;
- medicines used to treat diabetes (chlorpropamide, glibenclamide, glipizide, and tolbutamide);
- theophylline, used to control asthma;
- tofacitinib, used to treat rheumatoid arthritis;
- tovalptan, used to treat hyponatremia (low blood sodium levels) or to slow the decline in kidney fuction;
- vitamin A medicines (nutritional supplement);

- ivacaftor (used for the treatment of cystic fibrosis);
- amiodarone (used to treat "arrhythmias," irregular heartbeats);
- hydrochlorothiazide (a diuretic);
- ibrutinib (used for treating blood tumor);
- lurasidone (used to treat schizophrenia);
- medicines used to prevent pregnancy (oral contraceptives);
- statins (atorvastatin, simvastatin, fluvastatin and similar medicines) used to reduce high cholesterol levels.

FLUCONAZOLO Bioindustria L.I.M. with food and drink
You can take the medicine with or without food.

Pregnancy, breast-feeding and fertility
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.

If you are planning to become pregnant, it is recommended to wait a week after a single dose of fluconazole before becoming pregnant.

For longer courses of treatment with fluconazole, talk to your doctor on the need for appropriate concentration during treatment which should continue for one week after the last dose.

You should not take fluconazole if you are pregnant, think you may pregnant, are trying to become pregnant, unless your doctor has told you so. If you become pregnant while taking this medicine or within 1 week of the most recent dose, contact your doctor.

Fluconazole taken during the first or second trimester of pregnancy may increase the risk of miscarriage. Fluconazole taken during the first trimester may increase the risk of a baby being born with birth defects affecting the heart, bones and/or muscles.

There have been reports of babies born with birth defects affecting the skull, ears, and bones of thigh and elbow in women treated for three months or more with high doses (400-800 mg daily) of fluconazole for coccidioidomycosis. The link between fluconazole and these cases is not clear.

You can continue breast-feeding after taking a single dose of FLUCONAZOLO Bioindustria L.I.M. 150 mg. You should not breast-feed if you are taking repeated doses of FLUCONAZOLO Bioindustria L.I.M.

Driving and using machines
When driving vehicles or using machines it should be taken into account that occasionally dizziness or fits may occur.

FLUCONAZOLO Bioindustria L.I.M. contains sodium
This medicine contains 3.54 mg sodium (0.154 mmol) per ml.
FLUCONAZOLO Bioindustria L.I.M. contains 177 mg of sodium (main component of cooking/table salt) per 50 ml. This is equivalent to 8.8 % of the recommended maximum daily dietary intake of sodium for an adult.
To be considered in people with reduced kidney function or those on a low-sodium diet.

3. How to take FLUCONAZOLO Bioindustria L.I.M.

This medicine will be given by your doctor or nurse as a slow injection (infusion) into your vein.
FLUCONAZOLO Bioindustria L.I.M. is supplied as a solution. It will not be further diluted. There are more informations for healthcare professionals in a section at the end of the leaflet.

The recommended dose and the duration of the treatment depend on the severity and type of infection, as listed below. Check with your doctor or nurse if you are not sure why you are begin FLUCONAZOLO Bioindustria L.I.M.

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 up to 800 mg
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 if needed. Sometimes doses are increased up to 800 mg
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 infection 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 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 treat mucosal infections affecting the lining of mouth, throat from coming back	100 mg to 200 mg once daily, or 200 mg 3 times a week, while you are at risk of getting an infection
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
The dose will be determined by the doctor.
Always take the dose prescribed by your doctor (or the dosage for adults or children).

Use in children up to 11 years old
The dose will be determined by the doctor based on the child's body weight in kilograms.
The maximum recommended dose is 400 mg per day.

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 once daily (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	6 mg 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 dosage as for children up to 11 years of age but given once every 2 days. The maximum dose is 12 mg per kg body weight every 48 hours.

Use in children less than 2 weeks of age:

- The same dosage as for children up to 11 years of age but administered once every 3 days. The maximum dose is 12 mg per kg body weight every 72 hours.

Use in elderly
The usual adult dose should be given unless you have kidney problems.

Use in patients with kidney problems
Your doctor may change your dose, depending on your kidney function.

If you take more FLUCONAZOLO Bioindustria L.I.M. than you should
If you are concerned that you may have been given a higher dose of FLUCONAZOLE Bioindustria L.I.M. than you should have, inform your doctor or other health care professional immediately.
Following accidental administration of overdoses of this medicine, symptoms may include hearing, seeing, perceiving, and thinking things that are not real (hallucinations and altered behaviour (paranoia)).

If you forget to take FLUCONAZOLO Bioindustria L.I.M.
This medicine will be administered to you under close medical supervision, so it is unlikely that a dose will be forgotten. However, if you think a dose has not been given to you, contact your doctor or nurse.

If you have any doubts about the use of this medicine, see your doctor, nurse or pharmacist immediately.

4. Possible side effects

Like all medicines, this medicine may cause side effects, although not everybody gets them.

Stop taking FLUCONAZOLO Bioindustria L.I.M. and see your doctor 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 severe allergic reactions are rare. If you get any side effects, including those not listed in this leaflet, see your doctor. If you get any of the following symptoms, **tell your doctor immediately**:
- sudden wheezing, difficulty breathing or tightness in the chest;
- swelling of the 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 cause blistering (may affect the mouth and tongue).

FLUCONAZOLO Bioindustria L.I.M. may affect the liver. Symptoms of liver problems include:
- tiredness;
- loss of appetite;
- vomiting;
- yellowing of the skin and white part of the eyes (jaundice).

If you get any of these symptoms, stop taking FLUCONAZOLO Bioindustria L.I.M. and **inform your doctor immediately**.

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

Common (may affect up to 1 in 10 people):
- headache;
- stomach discomfort (abdominal pain), diarrhea, nausea, vomiting;

- increases in liver function values in blood tests;
- skin irritation (rashes).

Uncommon (may affect up to 1 in 100 people):
- reduction in red blood cell count (anemia), which may cause pallor, weakness or breathlessness;
- decreased appetite;
- insomnia, drowsiness;
- convulsions; dizziness, sensation of spinning, tingling, pricking or numbness; altered taste;
- constipation, digestive problems (dyspepsia), flatulence, dry mouth;
- muscle pain (myalgia);
- liver damage (cholestasis, increased bilirubin) and yellowing of the skin and eyes (jaundice);
- swelling, blistering, skin irritation (rash, hives, itching), increased sweating;
- tiredness, general feeling of being unwell, decreased strength in muscles (asthenia), fever.

Rare (may affect up to 1 in 1,000 people):
- lower than normal levels of white blood cell levels that help defend against infection (agranulocytosis, leukopenia, neutropenia);
- decreased levels of blood platelets (thrombocytopenia), which make blood clotting possible;
- altered skin coloring (red or purplish), which may be caused by a reduction in platelets; other alterations in blood cells;
- altered chemical composition of the blood; increased levels of cholesterol and fat in the blood (hypercholesterolemia, hypertriglyceridemia);
- decreased blood potassium levels (hypokalemia);
- chills;
- altered electrocardiogram (ECG), changes in heartbeat (Torsades de Pointes, QT prolongation);
- liver problems (liver failure, hepatocellular necrosis), liver inflammation (hepatitis), liver cell damage (hepatocellular damage);
- allergic reactions (sometimes severe) of the skin, including eruptions with diffuse blistering and peeling of the skin, severe skin reactions (toxic epidermal necrolysis, Stevens Johnson syndrome, acute generalized exanthematous pustulosis, exfoliative dermatitis), swelling of the lips and face;
- hair loss (alopecia).

Frequency not known but may occur (frequency cannot be estimated from the available data):
- hypersensitivity reaction with skin rash, fever, swollen glands, increase in a type of white blood cell (eosinophilia), and inflammation of internal organs (liver, lungs, heart, kidneys, and large intestine) (drug reaction or rash with eosinophilia and systemic symptoms (DRESS)).

Reporting of side effects
If you get any side effects, including those not listed in this leaflet, contact your doctor or pharmacist. You may also report side effects directly through the national reporting system at:
https://www.aifa.gov.it/en/content/segnalazioni-reazioni-avverse
Reporting side effects can help provide more information about the safety of this medicine.

5. How to store FLUCONAZOLO Bioindustria L.I.M.

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the package after "EXP."
The expiry date refers to the last day of that month.

Do not freeze.

This medicine should be used only once (single-use). Once opened, the product should be used immediately. Any unused infusion should be discarded.

Do not use this medicine if you notice visible particles or if the solution is unclear or discolored.

Do not throw any medicine into sewage water or household waste. Ask your pharmacist how to dispose of medicines you no longer use. This will help protect the environment.

6. Contents of the pack and other information

What FLUCONAZOLO Bioindustria L.I.M. 100 mg/50 ml, 200 mg/100 ml and 400 mg/200 ml solution for infusion contains
- The active ingredient is fluconazole. Each ml contains 2 mg of fluconazole.
- The other components are: sodium chloride (see section 2, "FLUCONAZOLO Bioindustria L.I.M. contains sodium"), water for injections.

What FLUCONAZOLO Bioindustria L.I.M. looks like and contents of the pack
FLUCONAZOLO Bioindustria L.I.M. is a clear, colorless solution with no visible particles.
It is available in packs of 25 and 50 vials of 50 ml, 25 vials of 100 ml and 25 vials of 200 ml.

Marketing Authorization Holder and Manufacturer
Bioindustria Laboratorio Italiano Medicinali S.p.A.
(Bioindustria L.I.M. S.p.A.)
Via De Ambrosiis 2, 15067 Novi Ligure (AL) - Italy

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The following information is intended only for medical or healthcare professionals:

POSOLOGY
The dose should be based on the nature and severity of the fungal infection. Treatment of infections requiring multiple dosing 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.

Adults

Indications		**Posology**	**Duration of treatment**
Cryptococcosis	- Treatment of cryptococcal meningitis.	Loading dose: 400 mg on Day 1 Subsequent dose: 200 mg to 400 mg once daily	Usually at least 6 to 8 weeks. In life threatening infections the daily dose can be increased to 800 mg.
	- Maintenance therapy to prevent relapse of cryptococcal meningitis in patients with high risk of recurrence.	200 mg once daily	Indefinitely at a daily dose of 200 mg.
Coccidioidomycosis		200 mg to 400 mg once daily.	11 months up to 24 months or longer depending on the patient. 800 mg daily may be considered for some infections and especially for meningeal disease.

Invasive candidiasis		Loading dose: 800 mg on Day 1 Subsequent dose: 400 mg once daily	In general, the recommended duration of therapy for candidemia is for 2 weeks after first negative blood culture result and resolution of signs and symptoms attributable to candidemia.
Treatment of mucosal candidiasis	- Oropharyngeal candidiasis	Loading dose: 200 mg to 400 mg on Day 1 Subsequent dose: 100 mg to 200 mg once daily	7 to 21 days (until oropharyngeal candidiasis is in remission). Longer periods may be used in patients with severely compromised immune function.
	- Oesophageal candidiasis	Loading dose: 200 mg to 400 mg on Day 1 Subsequent dose: 100 mg to 200 mg once daily	14 to 30 days (until oesophageal candidiasis is in remission). Longer periods may be used in patients with severely compromised immune function.
	- Candiduria	200 mg to 400 mg once daily	7 to 21 days. Longer periods may be used in patients with severely compromised immune function.
	- Chronic atrophic candidiasis	50 mg once daily	14 days
	- Chronic mucocutaneous candidiasis	50 mg to 100 mg once daily	Up to 28 days. Longer periods depending on both the severity of infection or underlying immune compromisation and infection.
Prevention of relapse of mucosal candidiasis in patients infected with HIV who are at high risk of experiencing relapse	- Oropharyngeal candidiasis	100 mg to 200 mg once daily or 200 mg 3 times per week.	An indefinite period for patients with chronic immune suppression.

	- Oesophageal candidiasis	100 mg to 200 mg once daily or 200 mg 3 times per week	An indefinite period for patients with chronic immune suppression.
Genital candidiasis	-Acute vaginal candidiasis - *Candida* Balanitis	150 mg	Single dose
	- Treatment and prophylaxis of relapses of vaginal candidiasis (4 or more episodes a year)	150 mg every third day for a total of 3 doses (days 1, 4, and 7) followed by a maintenance dose of 150 mg once a week.	Duration of treatment: maintenance dose: 6 months.
Prophylaxis of candidal infections in patients with prolonged neutropenia		200 mg to 400 mg once daily	Treatment should start several days before the anticipated onset of neutropenia and continue for 7 days after recovery from neutropenia after the neutrophil count rises above 1000 cells per mm^3.

Special populations
Elderly
Dosage should be adjusted based on the renal function (see "Renal impairment").
Renal impairment
FLUCONAZOLO Bioindustria L.I.M. is predominantly excreted in the urine as unchanged active substance. No adjustments in single dose therapy are necessary. In patients (including paediatric population) with impaired renal function who will receive multiple doses of fluconazole, an initial dose of 50 mg to 400 mg, should be given, based on the recommended daily dose for the indication. After this initial loading dose, the daily dose (according to indication) should be based on the following table:

Creatinine clearance (ml/min)	**Percent of recommended dose**
> 50	100%
≤ 50 (no haemodialysis)	50%
Haemodialysis	100% after each haemodialysis

Patients on haemodialysis should receive 100% of the recommended dose after each haemodialysis; 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.
Paediatric population
A maximum dose of 400 mg daily should not be exceeded in paediatric population.
As with similar infections in adults, the duration of treatment is based on the clinical and mycological response.
FLUCONAZOLO Bioindustria L.I.M. is administered as a single daily dose.

For paediatric patients with impaired renal function, see dosing in section "Renal impairment". The pharmacokinetics of fluconazole has not been studied in paediatric population with renal insufficiency (for "Term newborn infants" who often exhibit primarily renal immaturity please see below).

Infants, toddlers and children (from 28 days to 11 years old):

Indication	Posology	Recommendations
- Mucosal candidiasis	Initial dose: 6 mg/kg Subsequent dose: 3 mg/kg once daily	Initial dose may be used on the first day to achieve *steady state* levels more rapidly
- Invasive candidiasis - Cryptococcal meningitis	Dose: 6 to 12 mg/kg once daily	Depending on the severity of the disease
- Maintenance therapy to prevent relapse of cryptococcal meningitis in children with high risk of recurrence	Dose: 6 mg/kg once daily	Depending on the severity of the disease
- Prophylaxis of *Candida* in immunocompromised patients	Dose: 3 to 12 mg/kg once daily	Depending on the extent and duration of the induced neutropenia (see Adults posology)

Adolescents (from 12 to 17 years old):

Depending on the weight and pubertal development, the prescriber would need to assess which posology (adults or children) is the most appropriate. Clinical data indicate that children have a higher fluconazole clearance than observed for adults. A dose of 100, 200 and 400 mg in adults corresponds to a 3, 6 and 12 mg/kg dose in children to obtain a comparable systemic exposure.

Term newborn infants (0 to 27 days):

Neonates excrete fluconazole slowly. There are few pharmacokinetic data to support this posology in term newborn infants.

Age group	Posology	Recommendations
Term newborn infants (0 to 14 days)	The same mg/kg dose as for infants, toddlers and children should be given every 72 hours	A maximum dose of 12 mg/kg every 72 hours should not be exceeded
Term newborn infants (from 15 to 27 days)	The same mg/kg dose as for infants, toddlers and children should be given every 48 hours	A maximum dose of 12 mg/kg every 48 hours should not be exceeded

METHOD OF ADMINISTRATION

FLUCONAZOLO Bioindustria L.I.M. may be administered either orally or by intravenous infusion, the route being dependent on the clinical state of the patient. On transferring from the intravenous to the oral route, or *vice versa*, there is no need to change the daily dose. The physician should prescribe the most appropriate pharmaceutical form and strength according to age, weight and dose. The capsule formulation is not adapted for use in infants and small children. Oral liquid formulations of fluconazole are available that are more suitable in this population. Intravenous infusion should be administrated at a rate not exceeding 10 ml/minute.

FLUCONAZOLO Bioindustria L.I.M. is formulated in sodium chloride 9 mg/ml (0.9%) solution for infusion, each 200 mg (100 ml vial) containing 15 mmol each of $Na^+$and Cl^-. Since the product is available as a dilute sodium chloride solution, in patients requiring sodium or fluid restriction, consideration should be given to the rate of fluid administration.

OVERDOSE
There have been reports of overdose with FLUCONAZOLO Bioindustria L.I.M. and 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 haemodialysis session decreases plasma levels by approximately 50%.

SHELF-LIFE
3 years. This medicinal product is for single use only. Once opened, unused product should be discarded.

SPECIAL PRECAUTIONS FOR STORAGE
Do not freeze. From a microbiological point of view, the dilutions should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8 ° C, unless dilution has taken place in controlled and validated aseptic conditions.

SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING
Fluconazole solution for infusion is compatible with the following administration fluids:
Dextrose 5% and 20%, Ringer's solution, Hartmann's solution, Potassium chloride in dextrose, Sodium bicarbonate 4.2% and 5%, Aminofusine 3.5%, Sodium chloride 9 mg/ml (0.9%) solution, Dialaflex (intraperitoneal dialysis Soln 6.36%).
Fluconazole solution for infusion may be infused through an existing line with one of the above listed fluids. Although no specific incompatibilities have been noted, mixing with any other medicinal products prior to infusion is not recommended. The solution for infusion is for single use only.
The dilution is to be made under aseptic conditions. The solution is to be inspected visually for particulate matter and discoloration prior to administration. The solution should only be used if the solution is clear and free from particles.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.