

Package leaflet: Information for the user

Fluconazole 2mg/ml Solution for Infusion fluconazole

Read all of this leaflet carefully before you are given 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, pharmacist or nurse.
- If you get any side effects talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Fluconazole 2mg/ml Solution for Infusion is and what it is used for
2. What you need to know before you are given Fluconazole Infusion
3. How Fluconazole Infusion is given to you
4. Possible side effects
5. How to store Fluconazole Infusion
6. Contents of the pack and other information

1. What Fluconazole 2mg/ml Solution for Infusion is and what it is used for

Fluconazole 2mg/ml Solution for Infusion is for treating and preventing fungal infections.

Fluconazole 2mg/ml Solution for Infusion (called Fluconazole Infusion throughout the rest of this leaflet) belongs to a group of antifungal medicines called imidazoles. It works by stopping the growth of the fungus. It is used for the treatment/prevention of the following types of fungal infection:

Adults

- Treatment of:
 - candida fungal infections affecting the whole body
 - a fungal infection in the brain called cryptococcal meningitis
 - severe candida fungal infections affecting mucous membranes (mouth, throat, oesophagus, bronchuses and lungs) where oral treatment is not possible.
- Prevention of:
 - candida fungal infections in patients with reduced amounts of white blood cells (neutropenia) following bone marrow transplants

Children and adolescents

- Treatment of:
 - candida fungal infections affecting the whole body
 - severe candida fungal infections affecting mucous membranes (mouth, throat, oesophagus, bronchuses and lungs) where oral treatment is not possible.

2. What you need to know before you are given Fluconazole Infusion

You must not be given Fluconazole Infusion

- if you are allergic to fluconazole or other similar medicines such as ketoconazole and itraconazole or to any of the other ingredients of this medicine (listed in section 6).
- if you are taking other drugs known to affect your heart and be metabolised in the same way as fluconazole, such as cisapride, astemizole, pimozide, erythromycin and quinidine.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before you are given Fluconazole Infusion

- if you are currently, or have previously had problems with your liver
- if you have AIDS or have an infection that affects your whole body
- if you have heart disease
- if you receive warfarin or any other drug which prolongs blood coagulation
- if you have kidney disease
- if you have a yeast infection called cryptococcosis
- if you have a fungal infection after travelling outside of Europe
- if the fungal infection does not improve, as alternative antifungal therapy may be needed.
- if you develop signs of ‘adrenal insufficiency’ where 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 have ever developed a severe skin rash or skin peeling, blistering and/or mouth sores after you have been given Fluconazole Infusion.

Serious skin reactions including drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported in association with Fluconazole Infusion treatment. Fluconazole Infusion should be stopped and seek medical attention immediately if you notice any of the symptoms related to these serious skin reactions described in section 4.

Other medicines and Fluconazole Infusion

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

If Fluconazole Infusion and certain other medications are taken at the same time, the effect of treatment may be affected. This applies for example to the following:

- **Alfentanil** (synthetic opioid analgesic drug – used against pain).
- **Amitriptyline** (for depression).
- **Amphotericin B** (for fungal infections).
- **Astemizole** (antihistamine).
- **Azithromycin** (for bacterial infections).
- **Benzodiazepines** such as midazolam or triazolam (certain sleeping pills).
- **Calcium channel antagonists:** nifedipine, isradipine, nicardipine, amlodipine, felodipine (used in the control of heart rhythm and blood pressure).
- **Carbamazepine** (for epilepsy).
- **Celecoxib** (for inflammation).
- **Ciclosporin** (used in organ transplantation).
- **Cisapride** (used to treat heart burn and reduce the amount of acid in the stomach).
- **Cyclophosphamide** (used in cancer treatment).
- **Didanosine** (treatment used in AIDS).

- **Erythromycin** (for bacterial infections).
- **Everolimus** (used after organ transplants and in the treatment of cancer).
- **Fentanyl** (a strong painkiller).
- **Halofantrin** (for malaria).
- **HMG-CoA-reductase-inhibitors:** atorvastatin, simvastatin, fluvastatin (agents that reduce blood lipids).
- **Hydrochlorothiazide** (a diuretic).
- **Losartan** (for high blood pressure).
- **Methadone** (opioid analgesic drug – used against pain).
- **Non-Steroidal Anti-inflammatory Drugs (NSAIDs)** (used to treat pain and inflammation).
- **Oral Contraceptives**
- **Phenytoin** (for epilepsy).
- **Pimozide** (for mental disorders).
- **Prednisone** (used in inflammation and organ transplants).
- **Quinidine** (for heart disorders).
- **Rifabutin and Rifampicin** (for tuberculosis and other infections).
- **Saquinavir** (used to treat HIV infections).
- **Sulphonylureas** such as chlorpropamide, glibenclamide, glipizide and tolbutamide (used for diabetes).
- **Tacrolimus and sirolimus** (used in organ transplantation).
- **Terfenadine** (used to treat hay fever and allergies).
- **Theophylline** (for respiratory problems).
- **Trimetrexate** (used in pneumonia).
- **Vinca Alkaloids** (used in cancer treatment).
- **Vitamin A**
- **Voriconazole** (for serious fungal infections).
- **Warfarin and other coumarin type medicines** (certain blood-thinning agents).
- **Xanthine bases, other antiepileptic drugs and isoniazid.**
- **Zidovudine** (treatment used in AIDS).
- **Ketoconazole** (used to treat infections caused by a fungus or yeast)
- **Amiodarone** (used for treating uneven heartbeats ‘arrhythmias’)

Fluconazole Infusion with food, drink and alcohol

- Fluconazole Infusion can be used 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 contraception during treatment which should continue for one week after the last dose.

You should not be given Fluconazole infusion if you are pregnant, think you may be pregnant, are trying to become pregnant or breast-feeding, 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.

Pregnancy

- Women of child-bearing potential should use reliable contraception during long-term treatment with Fluconazole Infusion.
- 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 the 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

Breast-feeding

- Fluconazole enters breast milk so women are advised not to breast-feed their babies while on Fluconazole Infusion.

Fertility

- There is no data regarding the effects of Fluconazole on the human fertility.

Driving and using machines

- Occasionally dizziness or fits can occur in people taking fluconazole so care should be taken when driving or operating machinery (see section 4 of this leaflet for more information on possible side effects).

Fluconazole Infusion contains Sodium chloride

- Fluconazole Infusion contains sodium chloride (salt). The infusion contains 3.5mg of sodium per ml of infusion (a total of 88mg sodium in a 25ml bottle, 177mg sodium in a 50ml bottle, 354mg sodium in a 100ml bottle and 709mg sodium in a 200ml bottle). If you are on a low sodium (salt) diet tell your doctor, pharmacist or nurse before they give you Fluconazole Infusion.

3. How Fluconazole Infusion is given to you

A doctor or nurse will administer the infusion via a drip (slow injection into a vein).

Treatment will normally continue until the infection has gone.

Adults

- Candida infections affecting the whole body:
 - The recommended dose is 800mg on the first day, then 400mg once daily until you are told to stop.
- Cryptococcal meningitis:
 - The recommended dose is 400mg on the first day, then 200-400mg once daily.
 - The maximum daily dose is 400mg daily.
 - Depending on how you respond, your treatment can last for 6 – 8 weeks.
 - In life-threatening infections the daily dose can be increased to 800mg.
- Prevention of cryptococcal meningitis:
 - The recommended dose is 200mg once daily, until you are told to stop by your doctor.
- Coccidioidomycosis:
 - The recommended dose is 200-400mg on the first day, then 200-400mg once daily.

- Depending on how you respond, your treatment can last for 11-24 months.
- Candida infections affecting mucous membranes:
 - For oropharyngeal candidiasis the recommended dose is 200-400mg on the first day then 100-200mg once daily for 7-21 days.
 - For oesophageal candidiasis the recommended dose is 200-400mg on the first day, then 100-200mg once daily for 14-30 days.
 - For Candiduria the recommended dose is 200-400mg for 7-21 days.
 - For chronic atrophic candidiasis the recommended dose is 50mg once daily for 14 days.
 - For chronic mucocutaneous candidiasis the recommended dose is 50-100mg once daily for up to 28 days.
- Prevention of oropharyngeal candidiasis and oesophageal candidiasis for patients at risk of getting an infection:
 - The recommended dose is 100-200mg once daily, or 200mg 3 times per week until you are told to stop.
- Prevention of candida infections in patients following bone marrow transplants:
 - The recommended dose is 400mg per day.

Elderly

- If your kidneys are working normally you will be given the recommended adult dose.

Adolescents (from 12 to 17 years old)

- The recommended dose is between 3 and 12mg/kg of body weight per day.
- Your doctor will decide what dose is right for you.

Children (4 weeks of age to 11 years old)

- Treatment of cryptococcal meningitis:
 - The recommended dose is 6 – 12mg/kg per day.
- Prevention of cryptococcal meningitis in children who are at risk of getting an infection:
 - The recommended dose is 3-12 mg/kg per day.
- Treatment of mucosal candidiasis:
 - The recommended dose is 3mg/kg per day. 6mg/kg may be given on day 1.

Children (under 4 weeks of age)

- In the first two weeks of life babies can be given the same dose as children but the dose must be given every 72 hours.
- In weeks three and four of life babies can be given the same dose as children but the dose must be given every 48 hours.

Patients with kidney problems

- Your doctor will adjust the dose based on your kidney function.

If you are given more Fluconazole Infusion than you should

- It is unlikely that you will be given too much infusion. However, in the unlikely event that this does occur you will be monitored carefully by medical staff.
- In most patients overdosing may result in gastrointestinal complaints and skin reactions like itching and rash.
- If you are worried you have been given too much or have any questions about the dose talk to your doctor or nurse.

If you think you have missed a dose of Fluconazole Infusion

- It is unlikely that you will miss a dose as your doctor or nurse will monitor when to give you each dose.
- If you think you have missed a dose speak to your doctor or nurse.

If you have any further questions on the use of this product, ask your doctor, nurse or pharmacist.

4. Possible side effects

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

Serious side effects

If you notice any of the following symptoms, you should inform the doctor or nurse immediately and the infusion should be stopped:

Uncommon: may affect up to 1 in 100 people

- Fits (convulsions)
- Yellowing of the skin and eyes (jaundice) and liver abnormalities

Rare: may affect up to 1 in 1,000 people

- Anaphylaxis (allergic reaction): Swollen face, lips, tongue or throat, difficulty swallowing, hives and difficulties breathing
- Severe skin reaction which causes the outer layer of skin to detach (Toxic epidermal necrolysis)
- Severe rashes that may involve blistering and peeling of the skin (Stevens-Johnson syndrome).
 - Lesions or ulcers in the throat, mouth and skin due to changes in white blood cells
 - Liver problems and toxicity, including liver failure and hepatitis

Not known: frequency cannot be estimated from the available data

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

Other side effects

Common: may affect up to 1 in 10 people

- Headache
- Rash
- Feeling sick (nausea)
- Being sick (vomiting)
- Stomach ache or pain
- Diarrhoea
- Increase in the blood of substances produced by the liver called liver enzymes

Uncommon: may affect up to 1 in 100 people

- Decreases in certain blood cells (Red blood cells, white blood cells and platelets)
- Changes in taste, dry mouth
- Constipation
- Dizziness
- Indigestion
- Wind (flatulence)
- Itching or rash, wheals, swelling or blistering (hives)
- Increased sweating
- Loss of appetite or increased appetite
- Changes to some body chemicals and liver and kidney enzymes
- Abnormal sleep
- Paraesthesia, vertigo
- Pain in muscles
- Feeling weak and tired
- Fever
- Decreased appetite
- Fixed Drug eruption (Type of allergic reaction with patches of redness, swelling of skin and blisters to a medicine usually recurring in same site)

Rare: may affect up to 1 in 1,000 people

- Increased levels of fats in the blood (cholesterol and triglycerides)
- Decreased levels of potassium leading to weakness and an irregular or fast heart beat
- Tremor
- Hair loss (alopecia)
- Itching, reddening or scaling of the skin
- Patches of red, blistering skin

Very rare: may affect up to 1 in 10,000 people

- Severe rash, blistering or scaling decay of the skin

Not known: frequency cannot be estimated from the available data

- Fluconazole Infusion 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.

Additional side effects more common in children

- Irritability
- Anaemia (low blood iron levels causing tiredness and fatigue)

Fluconazole Infusion may cause a reduction in the number of white blood cells and your resistance to infection may be decreased. If you experience an infection with symptoms such as fever and serious deterioration of your general condition, or fever with local infection symptoms such as sore throat/pharynx/mouth or urinary problems you should see your doctor immediately. A blood test will be taken to check possible reduction of white blood cells (agranulocytosis). It is important to inform your doctor about your medicine.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellow-card or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Fluconazole Infusion

You will not be asked to store the medicine. It will be brought to you ready to be administered, which should be done straight away.

Do not use this medicine after the expiry date stated on the carton or bottle. The expiry date refers to the last day of that month.

Do not refrigerate or freeze.

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

6. Contents of the pack and other information

What Fluconazole Infusion contains

- The active substance is fluconazole. Each ml of infusion contains 2mg fluconazole. Each 25ml bottle of Fluconazole Infusion contains 50mg of fluconazole. Each 50ml bottle of Fluconazole Infusion contains 100mg of fluconazole. Each 100ml bottle of Fluconazole Infusion contains 200mg of fluconazole. Each 200ml bottle of Fluconazole Infusion contains 400mg of fluconazole.
- The other ingredients are: sodium chloride, water for injections, hydrochloric acid for pH adjustment and sodium hydroxide for pH adjustment.

What Fluconazole Infusion looks like and contents of the pack

Fluconazole Infusion is a clear sterile and colourless solution for infusion. The infusion is supplied in a glass bottle closed with a rubber stopper and a flip-off aluminium cap.

Fluconazole Infusion is available in a bottle containing 25ml, 50ml, 100ml or 200ml of solution for infusion. Not all pack sizes may be marketed.

Marketing Authorisation Holder

Focus Pharmaceuticals Limited
Dashwood House, 69 Old Broad Street, London, EC2M 1QS, United Kingdom.

Manufacturer

Pharmathen S.A., 6 Dervenakion str, 15344 Pallini, Attiki, Greece

For any information about this medicinal product, please contact the Marketing Authorisation Holder, details provided above.

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

1. Administration

For intravenous use as infusion.

Fluconazole is dissolved in an isotonic saline solution, with an electrolyte content of 150mmol Na⁺ and 150mmol Cl⁻ per 1000ml, and may be administered directly as an infusion. The product can be infused at a maximum rate of 10ml/minute. In children the rate of intravenous infusion should not exceed 5ml/minute. For premature infants the infusion time should be no less than 15 minutes. In patients requiring sodium or fluid restriction, the rate of administration should be taken into consideration as Fluconazole Infusion consists of a salt solution. In such cases the infusion should be given over a longer period.

2. Handling Instructions

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

The product should be inspected visually for particles and discolouration prior to administration. Only clear and colourless solutions should be used.

Fluconazole 2mg/ml Solution for Infusion is compatible with the following infusion fluids:

- a. Glucose 20%
 - b. Ringer's solution
 - c. Hartmann's solution
 - d. Potassium chloride in glucose
 - e. Sodium carbonate 4.2%
 - f. 0.9% sodium chloride (isotonic saline)
- Compatibility has been shown for short duration (10 minutes).

Dilution of Fluconazole 2mg/ml Solution for Infusion is not required prior to administration. If necessary, Fluconazole and the solutions mentioned above should be administered through separate infusion containers. The two reservoirs should be connected using a "Y" connection. The two solutions are then mixed in a single line and the administration is performed. The above method is recommended in order to avoid effects such as the "layering effect" if the two solutions were mixed in one infusion container for the total period of the administration.

3. Storage information

Do not use after the expiry date stated on the carton or bottle. The expiry date refers to the last day of that month.

Do not refrigerate or freeze.

After first opening

From the microbiological point of view, unless the method of opening precludes the risk of microbial contamination, the product should be used immediately.

If not used immediately, in-use storage times and conditions are the responsibility of the user.