

Package leaflet: Information for the user

Fluconazole 2 mg / mL Solution for infusion

Fluconazole

Read all of this leaflet carefully before this medicine is given to you 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.
 - This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any of the side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

The name of your medicine is Fluconazole 2 mg / mL Solution for infusion

In the rest of this leaflet Fluconazole 2 mg / mL Solution for infusion is called Fluconazole.

What is in this leaflet:

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

1. What Fluconazole is and what it is used for

Fluconazole is one of a group of medicines called "antifungals". The active substance is fluconazole.

Fluconazole is used to treat infections caused by fungi and may also be used to stop you from getting candida infection. The most common cause of fungal infections is a yeast called *Candida*.

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

You might also be given Fluconazole to:

- stop cryptococcal meningitis from coming back
- stop mucosal thrush from coming back
- 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

You might also be given Fluconazole to:

- stop you from getting an infection caused by *Candida* (if your immune system is weak and not working properly)
- stop cryptococcal meningitis from coming back

2. What you need to know before Fluconazole is given to you

You must not be given Fluconazole

- If you are allergic (hypersensitive) to fluconazole, to other medicines you have taken to treat fungal infections or to any of the other ingredients of Fluconazole. The symptoms may include itching, reddening of the skin or difficulty in breathing
- If you are taking astemizole, terfenadine (antihistamine medicines for allergies)
- If you are taking cisapride (used for stomach upsets)
- If you are taking pimozide (used for treating mental illness)
- If you are taking quinidine (used for treating heart arrhythmia)
- If you are taking erythromycin (an antibiotic for treating infections)

Warning and precautions

Talk to your doctor or nurse before you are given Fluconazole

- if you have ever developed a severe skin rash or skin peeling, blistering and/or mouth sores after using Fluconazole
Serious skin reactions including drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported in association with Fluconazole treatment. Stop using Fluconazole and seek medical attention immediately if you notice any of the symptoms related to these serious skin reactions described in section 4 .
- if you have liver or kidney problems
- if you suffer from heart disease, including heart rhythm problems
- 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 in breathing)
- 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
- the fungal infection does not improve, as alternative antifungal therapy may be needed.

Other medicines and Fluconazole

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 (used for treating heart arrhythmia) or erythromycin (an antibiotic for treating infections) as these should not be taken with Fluconazole (see section: "You must not be given 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)
- 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)
- cyclophosphamide, 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 (Non-Steroidal Anti-Inflammatory Drugs (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)
- ibrutinib (used for treating blood cancer)

Pregnancy, breast-feeding and fertility

- You should not be given 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 given during the first trimester of pregnancy may increase the risk of miscarriage.
- Fluconazole given 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.
- If you are breast-feeding, you must tell your doctor as the fluconazole will be in the breast-milk and may affect your baby.

Your doctor will not usually give you this medicine if you are breast-feeding. You can continue breast-feeding after being given a single dose of 150 mg Fluconazole. You should not breast-feed if you are being given a repeated dose of Fluconazole.

Driving and using machines

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

Fluconazole contains sodium (salt)

Fluconazole contains salt 3.54 mg sodium chloride per mL.

This medicine contains 708 mg sodium (main component of cooking/table salt) in each 200 mL bottle. This is equivalent to 35.4 % of the recommended maximum daily dietary intake of sodium for an adult.

Talk to your doctor or pharmacist if you need 400 mg or more bottles / bags daily for a prolonged period, especially if you have been advised to follow a low salt (sodium) diet.

3. How Fluconazole is given

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

The recommended doses of this medicine for different infections are below. Check with your doctor or nurse if you are not sure why you are being given Fluconazole.

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 <i>Candida</i>	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 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 <i>Candida</i> (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

Adolescents from 12 to 17 years old

Follow the dose prescribed by your doctor (either adults or children posology)

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 <i>Candida</i> – 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 <i>Candida</i>	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 <i>Candida</i> (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.

Elderly

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

Patients with kidney problems

Your doctor may change your dose, depending on your kidney function.

If you have been given more Fluconazole than you should

If you are concerned that you may have been given too much Fluconazole, tell your doctor or nurse immediately. The symptoms of a possible overdose may include hearing, seeing, feeling and thinking things that are not real (hallucination and paranoid behaviour).

If you forget to take Fluconazole

As you will be given this medicine under close medical supervision, it is unlikely that a dose would be missed. However tell your doctor or pharmacist if you think that a dose has been forgotten.

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

4. Possible side effects

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

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).
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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).

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)

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 (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 (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 (may affect up to 1 to 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)
- shaking
- low blood potassium
- 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
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Frequency not known, but may occur (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, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via

For UK: Yellow Card Scheme, Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

For IE: HPRA Pharmacovigilance, Website: www.hpra.ie.

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Fluconazole

Your doctor, nurse or pharmacist will usually store your medicine for you.

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 carton and the label of the plastic container after EXP.

The expiry date refers to the last day of that month. Do not use if the solution is cloudy, discoloured or contains particles.

Store below 25°C. Do not freeze or refrigerate.

Keep the bag and the bottle in the outer carton to protect from light.

For single use only. Use immediately after first opening the bottle.

Chemical and physical in-use stability after dilution has been demonstrated for 24 hours at 25°C. From a microbiological point of view, the product 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.

Your medicine may be mixed with certain other medicines that may also be given by infusion. Please ask your doctor, nurse or pharmacist if you want any more information about this.

Medicines should not be disposed of via wastewater or Household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Contents of the pack and other information

What Fluconazole contains

- The active substance is fluconazole.
1 mL of solution contains 2 mg of fluconazole
Each 50 mL (millilitre) bag will contain 100 mg (milligram) of fluconazole.
Each 100 mL (millilitre) bag / bottle will contain 200 mg (milligram) of fluconazole.
Each 200 mL (millilitre) bottle will contain 400 mg (milligram) of fluconazole.

- The other ingredients are sodium chloride (see Section 2), hydrochloric acid and water for injections.

What Fluconazole looks like and contents of the pack

Fluconazole 2 mg / mL Solution for infusion is a clear and colourless aqueous solution for infusion.

It is a ready to use plastic bag with rubber closures, and aluminium caps.

It is a ready to use plastic bottle with either rubber gasket, plastic caps and a pull ring or with plastic caps and twin ports.

Pack sizes: 50 mL bags (100 mg fluconazole) in packs of 10 bags
100 mL bags (200 mg fluconazole) in packs of 10 bags
100 mL bottles (200 mg fluconazole) in packs of 10 or 20 bottles
200 mL bottles (400 mg fluconazole) in packs of 10 or 20 bottles

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder: Noridem Enterprises Limited, Evagorou & Makariou, Mitsi Building 3, Office 115, 1065 Nicosia, Cyprus.

Manufacturer: DEMO S.A. PHARMACEUTICAL INDUSTRY, 21st km National Road Athens-Lamia, 14568 Krioneri, Attiki, Greece, **T:** +30210 8161802, **F:** +30210 8161587

This medicinal product is authorised in the Member States of the EEA under the following names:

UK: Fluconazole 2 mg / mL Solution for infusion
IE: Fluconazole 2 mg / mL Solution for infusion
AT: Fluconazol Noridem 2 mg/ml Infusionslösung
EL: FLUCONAZOLE/NORIDEM, Διάλυμα για έγχυση 2 mg/mL

This leaflet was last revised in: **04/2021**

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

Intravenous infusion should be administered at a rate not exceeding 10 ml/minute. Fluconazole is formulated in sodium chloride 9 mg/ml (0.9%) solution for infusion, each 200 mg (100 ml bottle) containing 15 mmol each of Na⁺ and Cl⁻. Because Fluconazole 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.

Fluconazole intravenous infusion is compatible with the following administration fluids:

<i>Diluent</i>	<i>Resulting concentration of fluconazole</i>
Sodium chloride injection 0.9%	1.0 mg / mL
Dextrose injection 20%	1.0 mg / mL
Lactated Ringer's injection	1.0 mg / mL
Ringer's injection	1.0 mg / mL
Potassium chloride 0,3%-Dextrose 5% injection	1.0 mg / mL
Sodium Bicarbonate 4.2% injection	1.0 mg / mL

Fluconazole 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.