PATIENT INFORMATION LEAFLET

FLUKODEKS 2 mg/ml Solution for I.V. Infusion
Used intravenously.
Sterile, apyrogen

Active ingredient: Each ml of infusion solution contains 2 mg of fluconazole.

Excipients: Dextrose anhydrous, water for injection

Please read this PATIENT INFORMATION LEAFLET carefully before starting to use the drug; because important information is included here.

- *Keep this PATIENT INFORMATION LEAFLET. You may need to re-read it later.*
- *In case you have additional questions, please consult your doctor or pharmacist.*
- *This drug is prescribed personally for you, do not give to others.*
- *During the use of this drug, please tell your doctor that you are using this drug when you visit your doctor or a hospital.*
- *Please follow these instructions strictly. Do not use dosages* ***higher or lower*** *than the dosage recommended to you.*

The following topics are included in this PATIENT INFORMATION LEAFLET:

1. What is FLUKODEKS and what it is used for?

FLUKODEKS clear, colorless solution should comply with intravenous use standards. It is offered in 100 and 200 ml PP bags. Each 100 ml bag contains 200 mg fluconazole and each 200 ml bag contains 400 mg fluconazole. The product has 2 forms, with and without set.

FLUKODEKS is one of a group of medicines called “antifungals”. The active substance is fluconazole.

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

You might be given this medicine by your doctor to treat the following types of fungal infections:

• Mucosal moniliasis, infections in the mouths or throat. Normal patients or patients with degraded immune functions can be treated.
• Skin infections – e.g. athlete’s foot, fungal diseases, itching.
• Internal (systemic) fungal infections due to the following:
    • *Candida* found in the bloodstream, body organs (e.g. heart, lungs), peritoneum, the membrane comprising a series of squamous epithelium tissue covering the inside of the heart, eye, or the urine
    • *Cryptococcus,* e.g. meningitis and infections at other areas such as the lung and the skin
• For systemic fungal diseases developing in patients with adequate immune systems

FLUKODEKS can also be administrated to you for the following:

• To prevent you from catching a fungal infection (if your immune system is compromised). For prevention of fungal infections in patients which are susceptible to fungal infections due to using cytocide against malignant diseases, or drug treatment against cancer or ray treatment against cancer.

• Prevention of recurrence of an infection due to *Cryptococcus* (for AIDS patients)

Your doctor can begin the treatment before learning about the results of cultures or other laboratory studies. When the results are obtained your treatment will be adjusted by your doctor as necessary.

2. Before you are given FLUKODEKS
DO NOT USE FLUKODEKS under following conditions:

If,
• You have had heightened sensitivity against the following:
    • Any ingredient of FLUKODEKS
    • Other drugs you have used in order to treat fungal infections.
    The symptoms of hyper sensitivity can cover itching, redness on the skin or difficulty in breathing.

• If you are using terfenadine or astemizole for treatment of allergies
• If you are using cisapride for the treatment of an upset stomach
• If you are a schizophrenic patient and are using pimozide which is an anti-psychotic drug
• If you are using drug that contains quinidine against cardiac arrhythmia.

USE FLUKODEKS CAREFULLY under the following conditions:
If,
•You have liver or renal problems
• The potassium, calcium or magnesium levels in your blood are abnormal
• If you have a serious illness, particularly such as AIDS or cancer
• If you're concurrently using more than one drug which could potentially harm or irritate the liver and an underlying disease that would kill your liver tissues (hepatic necrosis) occurs. Any damage or irritation to your liver due to fluconazole is reversible. Your doctor will monitor you in case severe liver damage occurs during treatment, and can terminate your treatment if required.
• If skin reactions with eruptions develop, such as toxic epidermal necrolysis and Stevens-Johnson syndrome. If a disorder with fluid filled blisters develops or a hypersensitivity which usually heals by itself, creates lacelike redness on hands, face and feet develops your doctor can terminate your treatment.
• If you are using less than 400 mg/day of terfenadine
• If the body develops a severe reaction or sudden hyper sensibility against substances that cause allergy
• If you have electrolyte disturbances
• If you are using another drug with fluconazole
• If concurrently you are using another drug that is not decomposed by CY3A4 which is an enzyme in the liver, however is known to extend the QT interval in the ECG record
Some drugs in the azole group, including fluconazole, have been observed to extend the QT interval in the electrical activity record of the heart (ECG).
• If you have any cardiac diseases, including cardiac rhythm disorders
•If there's a condition from birth or documented, which could lead to severe cardiac arrhythmia or sudden death
• Particularly when there's a cardiac failure, if you have an acute, sub-acute or chronic disorder on your cardiac muscle
• If you heart rate is lower than 60 per minute (sinus bradycardia)

If these warnings apply to you, even if for a period in the past, please consult your doctor.

Use of FLUKODEKS with food and drink
There are none.

Pregnancy

Consult your doctor or pharmacist before using this drug.

FLUKODEKS must not be used during pregnancy unless it is told by your doctor.

In case you become aware that you are pregnant during treatment, immediately consult your doctor or pharmacist.

Lactation

Do not use FLUKODEKS during pregnancy.

Consult your doctor or pharmacist before using this drug.

Driving and using machines

It should be taken into consideration that during vehicle or machine use, occasional dizziness or seizures could happen.

Important information about some ingredients of FLUKODEKS

FLUKODEKS contains dextrose. If you have dextrose intolerance, consider this.

Taking other medicines

Immediately inform your doctor as they shouldn't be used together with FLUKODEKS.

• If you are using terfenadine or astemizole for treatment of allergies
• If you are using cisapride for the treatment of an upset stomach
• If you are a schizophrenic patient and are using pimozide which is an anti-psychotic drug
• If you are using drugs that contain quinidine against cardiac arrhythmia.

It is not recommended that erythromycin, which is an antibiotic, be used together.

Inform your doctor if you're using any of the following drugs. Some of the drugs which could interact with FLUKODEKS are the following. Use with these medical products requires precautions and dosage adjustment:

- Alfentanyl, fentanyl used in anesthesia
- Amitriptyline and nortriptyline used in treatment of depression
- Amphotericin B used for severe fungal diseases
- Blood thinning warfarin to prevent blood clots (or similar drugs)
- Azithromycin which is an antibiotic
- Benzodiazepines such as midazolam, triazolam that helps sleeping or against anxiety or angst

- Calcium channel blockers such as nifedipine, isradipine, amlodipine and felodipine which lower blood pressure and are also used in certain heart diseases
- Celecoxib which is used in the treatment of arthrolith
- Cyclophosphamide used in cancer treatment
- Halofantrine used in the treatment malaria
- With HMG-Co A reductase inhibitors used for lipid disorders, which are metabolized with CYP3A4 such as atorvastatin and simvastatin or metabolized with CYP2C9 such as fluvastatine
- Losartan which is a drug which lowers blood pressure
- Methadone which is used in the treatment of heroin addiction
- Drugs effective against pain, fever and inflammation such as naproxen, lornoxicam, meloxicam, diclofenac
- Oral contraceptives which are birth control drugs
- Endogenous steroids
- Prednisone which is used for acute organ rejection and anti-inflammation
- Saquinavir which is used in the treatment of AIDS disease
- Vinca alkaloids which are used in the treatment of various cancer types
- Vitamin A
- Diabetic drugs such as chlorpropamide, glibenclamide, glipizide or tolbutamide
- Water tablets such as hydrochlorotiazid, used for fluid retention and treatment of high blood pressure
- Phyenytoin, carbamazepine which are used to keep epilepsy under control
- Rifampisin or rifabutin which are antibiotics effective against infections
- Cyclosporin or tacrolimus to prevent transfer rejection
- Theophylline used to control asthma
- Zidovudine, which is also known as AZT, used in patients infected with Human Immune Deficiency Virus (HIV)
- Halofantrine

If you are currently using any prescribed drug or OTC, or if you have used them recently, please inform your doctor or pharmacist about these.

3. How FLUKODEKS will be given?

Instructions for use and dose/ frequency of administration:

The daily dosage of fluconazole should depend on the type and severity of the fungal infection. For infections that require treatment with repeated doses, the treatment should continue until the clinical parameters or laboratory tests reveal that the fungal infection is over. And insufficient treatment duration causes the fungal infection to reappear. In order to prevent reappearance in patients with AIDS and cryptococsic meningitis or a type of fungal disease in the mouth and pharynx which is called oropharyngeal candidiasis frequent maintenance treatments are required.

The following dosages can be used unless the doctor recommends otherwise:

Mucosal moniliasis – dose depends on the area that is infected	50 mg per day for a period of 7-14 or 14-30 days. The dosage can sometimes be increased to 100 mg. If you're an AIDS patient, a single dose of 150 mg/week can be administered after complete primary cure, in order to prevent recurrence. For atrophic fungal disease connected with the usage of prosthesis the routine fluconazole dose is, 50 mg per day for 14 days, together with local antiseptic measures applied on the prosthesis.
Fungal skin infections	50 mg per day for a period of 2-4 weeks (For athletic foot it can be increased to 6 weeks)
Systemic fungal infections	400 mg on the first day and after that 200-400mg per day for a period of 6-8 weeks or longer if necessary. If you're an AIDS patient, you can use 200 mg/day for indefinitely after complete primary cure, in order to prevent recurrence.
To prevent catching a fungal infection	50-40 mg per day when you have a risk of catching an infection. If you have a high risk of systemic infection the dose is 400 mg / day. Fluconazole application should begin a few days before the onset for patients with a predicted decreased number of fragmented cell count (neutropenia) and should be continued for 7 more days after the neutrophil count increases above 1000/ mm3.
Prevent recurrence of an infection due to Cryptococcus (a type of fungal infection)	100-200 mg/day indefinitely
For systemic fungal diseases occurring in patients with adequate immune systems	Between 11-24 months for Coccidioidomycosis Between 2-17 months for Paracoccidioidomycosis, Between 1- 16 months for sporotrichosis and Between 3-17 months for histoplasmosis, The appropriate duration should be selected for each patient

Route of administration and method:
It is administrated intravenously.

This drug will be administered to you by your doctor or your nurse through slow injection (infusion) into your vein over 30 minutes.

FLUKODEKS is provided as a solution. It shouldn't be diluted more. This drug should not be mixed with another drug before infusion.

Different age groups
Pediatric use:

4 weeks- 15 years	mucosal infections	3 mg/kg once a day. 6 mg/ kg on the first day.
	Systemic fungal Infections	6-12 mg/kg once a day
	Prevention of fungal infections	When there's a risk of catching an infection 3-12 mg/kg once a day
3-4 weeks	The same dosage as mentioned above, but administered once per two days. Maximum dose for once per two days 12 mg/kg.	
Less than 2 weeks	The same dosage as mentioned above, but administered once per three days. Maximum dose for once per three days 12 mg/kg.	

The maximum dose of 400 mg / day should not be exceeded in children.

Use in the elderly:
Normal adult dose will be administrated if you don't suffer from any renal problems.

Conditions of special use:
Renal Failure
No dose adjustment is required in a treatment that requires a single dose. Your doctor can change your dose depending on your renal infection.

Liver failure:
There are none.

If you have an impression that the effect of FLUKODEKS is very strong or weak, please tell your doctor or pharmacist.

If you use more FLUKODEKS than you should:

Consult a doctor or a pharmacist if you have used FLUKODEKS in an amount more than you should.

If you forget to use FLUKODEKS:
Since this drug is administered to you under close medical monitoring it is not very probable to skip a dose. Even then, if you think a dose is skipped inform your doctor or pharmacist.

If FLUKODEKS treatment stopped, effects may occur:
Do not stop taking FLUKODEKS unless your doctor tells you to. Your doctor will determine the best method in cases where you need to stop taking FLUKODEKS. If you have any questions regarding the use of FLUKODEKS please consult your doctor.

4. Possible side effects
Like all drugs, FLUKODEKS can cause adverse effects in individuals who are sensitive to the contents.

Even though severe allergic reactions are encountered rarely, some people will develop allergic reactions. If you encounter any of the following symptoms immediately inform your doctor:

- Sudden wheezing, difficulty in breathing or compression in chest
- Swelling in eyelids, face or lips
- Itching on the entire body, redness on the skin or itchy red spots
- Skin eruption
- Severe skin reactions such as eruptions that cause blisters (can affect the mouth and tongue).
- If you're an AIDS patient, you have a higher chance to develop severe skin reactions to drugs, including FLUKODEKS.

The adverse effects are listed as shown in the following categories.

Very common	: Can be observed in at least 1 of 10 patients.
Common	: Can be observed in less than 1 of 10 patients but more than 1 in 100 patients.
Uncommon	: Can be observed in less than 1 of 100 patients but more than 1 in 1000 patients.
Rare	: Can be observed in less than 1 of 1000 patients.
Very rare	: Can be observed in less than 1 of 10.000 patients.
Unknown	: Cannot be estimated with the available data.

Common:
- Headache
- Stomachache

- Nausea
- Vomiting
- Upset stomach
- Diarrhea
- Gas
- Eruption
- High alkaline phosphatase levels
- Increased aspartate aminotransferase
- Increased blood alkaline phosphatase

Uncommon:

- Insomnia
- Sleepiness
- Seizures
- Drowsiness
- Numbness
- Distorted sense of taste
- Dizziness due to balance disorder (vertigo)
- Indigestion, dyspepsia
- Gas and dryness of the mouth
- Slowing down or stopping of bile juice
- Hepatitis
- Increased bilirubin
- Itching
- Urticaria
- Increased sweating
- Muscle pains
- Tiredness
- Unwellness
- Weakness
- Fever

Rare:

- Decreased white blood cell count
- Decreased leucocyte count
- Decrease in the number of fragmented cells in blood
- Decrease in the number of thrombocyte-blood platelet
- Body's severe response to allergic substances, sudden hypersensitivity (including swelling in face and throat, edema on face, itching, urticarial due to allergy)
- High cholesterol
- High triglyceride

- Blood potassium level increasing above normal level
- Trembling
- QT extension
- Life threatening irregular cardiac rhythm (torsade de pointes)
- Liver-related toxicity, also rarely leading to death
- Liver failure
- Liver inflammation
- Hepatitis
- Death of or damage to the tissues belonging to the liver cells or affecting liver cells
- A serious condition which is associated with fluid filled blisters on the skin (toxic epidermal necrolysis)
- Blood settling on skin and around eye, inflammation associated with swelling and redness (Stevens-Johnson syndrome)
- Acute generalized exanthematous pustulosis expholiative skin diseases
- Edema on face
- Hair loss

Pediatric patients

The adverse event incidence and models recorded during pediatric clinical studies and the laboratory abnormalities are comparable to those observed in adults.

In case you encounter any adverse effects not mentioned in this PATIENT INFORMATION LEAFLET, please inform your doctor or pharmacists.

5. How to store FLUKODEKS

Keep FLUKODEKS out of the reach and sight of children and store in the original container.

Store at room temperature below 25 °C.

Use in accordance with the expiration date.

Do not use FLUKODEKS after the expiration date which is stated on the package.

Marketing Authorisation Holder and Manufacturer:

POLİFARMA İLAÇ SANAYİ VE TİC. A.Ş.

Vakıflar OSB Mahallesi,

Sanayi Caddesi, No:22/1

Ergene/TEKİRDAĞ

Tel: (0282) 675 14 04 Fax: (0282) 675 14 05

This leaflet was approved in 31.08.2015

THE FOLLOWING INFORMATION IS INTENDED FOR HEALTHCARE PROFESSIONALS.

Fluconazole is administered both orally and also in the form of intravenous infusion at a rate not exceeding 10 ml per minute. The method administration depends on the clinical condition of the patient. When changing from intravenous method to oral method or vice versa, there's no need to change the daily dosage. FLUKODEKS injectable form is formulated in 5% dextrose solution and every 100 ml contains 5 g dextrose. This should be considered for patients with known diabetes mellitus or those with subclinical diabetes (blood glucose higher than normal but not sufficiently high to diagnose diabetes) and those who are sensitive to sugar for any reason. FLUKODEKS intravenous infusion is compatible with the following application fluids.

a) %20 Dextrose
b) Ringer solution
c) Hartmann solution
d) Potassium chloride in dextrose
e) % 4.2 sodium bicarbonate
f) Physiological saline

FLUKODEKS can be administered through an existing IV set, in one of the solutions mentioned above. Although no specific incompatibilities have been observed, it is not recommended to be mixed with any other drug prior to infusion.