PATIENT INFORMATION LEAFLET

SELFLEKS FLUKOSEL 200 mg/100 mL I.V. Bag Containing Solution for Infusion Administered intravenously
Sterile

- ***Drug substance:*** Each 100 mL PVC Bag contains 200 mg fluconazole.
- ***Excipients:*** Contains sodium chloride and water for injection.

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 pharmacist.*
- *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.*
- *Tell your doctor that you are taking this medicine when you go to the doctor or hospital during the use of this medicine.*
- *Follow exactly what is written in this instruction. Do not use **high or low** doses other than the recommended dosage.*

What is in this leaflet:

Headings are included.

1. What SELFLEKS FLUKOSEL is and what it is used for?

SELFLEKS FLUKOSEL clear, colorless solution should comply with standards of intravenous use.

It should be in clear, PVC bags.

SELFLEKS FLUKOSEL is one of a group of drugs called antifungal. The active ingredient is Fluconazole. SELFLEKS FLUKOSEL is used to treat infections caused by fungi, including yeasts. It can also be used to prevent you from getting a fungal infection. The most common cause of fungal infections is yeast called *Candida*.

This medicine can be given to you by your doctor to treat the following types of fungal infections.

- Mucosal thrush, mouth or throat infection. Normal or immunocompromised patients can be treated.

- Skin infections - athlete's foot, fungal disease, itching.

- Internal (systemic) fungal infections caused by:
    - Candida in the blood circulation, body organs (heart, lungs), peritoneum, membrane consisting of a row of squamous epithelial tissue covering the inside of the heart, eye or urinary tract
    - *Cryptococcus*, meningitis, and infections in other areas such as lungs and skin
- In patients with adequate immune system, developing systemic fungal diseases

You may also be given SELFLEKS FLUKOSEL for the following.

- Preventing a fungal infection (if your immune system is not working properly). In the prevention of fungal infections in patients who predispose to fungal infections as a result of drug therapy in cell-killing cancer or radiation therapy in cancer due to malignant disease.
- Preventing the return of an infection caused by *Cryptococcus* (in AIDS patients)

Your doctor may begin your treatment before the results of culture and other laboratory studies are known. Once results are available, treatment will be arranged by your doctor as needed.

2. What you need to know before you use SELFLEKS FLUKOSEL
DO NOT USE SELFLEKS FLUKOSEL

If:

- If you are *hypersensitive* to:
    - Any component of SELFLEKS FLUKOSEL
    - Other medicines you take to treat fungal infections.
    - Symptoms of hypersensitivity may include itching, redness of the skin, or difficulty breathing.
- If you are taking terfenadine or astemisol, an antihistamine intended to treat allergies
- If you are taking cisapride used for stomach upset
- If you have schizophrenia and are taking pimozide, an antipsychotic drug
- If you are taking quinidine-containing medication for heart rhythm disorder.

USE SELFLEKS FLUKOSEL CAREFULLY in the following cases

If:

- You have liver or kidney problems
- Your potassium, calcium or magnesium levels in your blood are abnormal
- You have serious illnesses, especially AIDS and cancer
- You are taking medicines that potentially damage or irritate more than one concurrent liver and an underlying disease develops that will kill your liver tissues (hepatic necrosis). If your liver is damaged or irritated with fluconazole, it is reversible. Your doctor will follow you in case of severe liver damage during treatment, if necessary, he may stop your medicine.
- Rash skin reactions such as toxic epidermal necrolysis and Stevens-Johnson syndrome

develop. Your doctor may discontinue your treatment if there is a fluid-filled bubble on the skin, or if there is a hypersensitivity condition that usually goes away spontaneously and causes lace-like rash on the hands, face and feet.

- You use less than 400 mg of terfenadine per day
- Very severe response of the body to allergenic substances, if sudden hypersensitivity develops
- You have any electrolyte disturbances in the blood
- You are using other medicines with fluconazole
- You are taking concomitant medicines that are not destroyed by CYP3A4, an enzyme in the liver, but known to prolong the QT interval on the ECG recording.

Prolongation of the QT interval was observed in the recording of the electrical activity of the heart (ECG) with some azole drugs, including fluconazole.

- You have heart disease, including heart rhythm problems
- There is a congenital or documented condition of the heart that can lead to serious arrhythmias and sudden death
- You have acute, subacute or chronic disease in your heart muscle, especially when there is heart failure
- Your heart beats less than 60 minutes per minute (sinus bradycardia)

Please consult your physician if these warnings apply to you, even at any time in the past.

Use of SELFLEKS FLUKOSEL with food and drink
It is not valid due to the route of administration.

Pregnancy
Consult your doctor or your pharmacist before using the drug.

Do not use SELFLEKS FLUKOSEL during pregnancy unless your doctor tells you otherwise.

If you notice that you are pregnant during your treatment, consult your doctor or pharmacist immediately.

Breast-feeding
Consult your doctor or your pharmacist before using the drug.
Do not use SELFLEKS FLUKOSEL during pregnancy.

Driving and using machines
When driving or operating machinery, it should be noted that occasional dizziness or seizure may occur.

Important information about some of the excipients contained in SELFLEKS FLUKOSEL
SELFLEKS FLUKOSEL contains sodium. This should be considered for patients on a controlled sodium diet.

Use with other medicines

Since they should not be taken with SELFLEKS FLUKOSEL, inform your doctor immediately.

- If you are taking the antihistamine terfenadine or astemizole to treat allergies
- If you are taking cisapride used for stomach upset
- If you are a schizophrenic patient and are taking the antipsychotic medication pimozide
- If you are taking medication containing quinidine for heart rhythm disturbance.

The combined use of SELFLEKS FLUKOSEL and erythromycin, an antibiotic, is not recommended.

Tell your doctor if you are taking any of the following medicines. Some drugs that may interact with SELFLEKS FLUKOSEL are as follows, their use with these medicinal products requires precaution and dose adjustment:

- Alfentanil, fentanyl used in anesthesia
- Amitriptyline and nortriptyline used to treat depression
- Amphotericin B used for severe fungal diseases
- Warfarin (or similar drugs) that thin the blood to prevent blood clots
- Azithromycin, an antibiotic
- Benzodiazepines, such as midazolam, triazolam, that help you sleep or to counter anxiety
- Calcium channel blockers such as nifedipine, isradipine, amlodipine and felodipine, which are used in blood pressure lowering and some heart diseases.
- Celecoxib used in the treatment of joint arthritis
- Cyclophosphamide used in cancer treatment
- Halofantrine used to treat malaria
- HMG-Co A reductase inhibitors used for lipid disorders that are metabolized by CYP3A4, such as atorvastatin and simvastatin, or by CYP2C9, such as fluvastatin.
- Losartan, a blood pressure lowering drug
- Methadone used in the treatment of heroin addiction
- Pain, fever and inflammation effective drugs such as naproxen, lornoxicam, meloxicam, diclofenac
- Oral contraceptives, birth control drugs
- Endogenous steroids
- Prednisone used for acute organ rejection and antiinflammation
- Saquinavir used in the treatment of AIDS disease
- Vinca alkaloids used in the treatment of various cancers

- Vitamin A
- Diabetes medications such as chlorpropamide, glibenclamide, glipizide or tolbutamide
- Diuretic tablets such as hydrochlorothiazide used to treat fluid retention and high blood pressure
- Phenytoin, carbamazepine used to control epilepsy
- Rifampicin or rifabutin, which are antibiotics for infections
- Cyclosporine or tacrolimus to prevent transplant rejection
- Theophylline used to control asthma
- Zidovudine, also known as AZT, used in patients with AIDS
- Halofantrine

If you are currently using or taking any prescription or over-the-counter medication, please inform your doctor or pharmacist.

3. How to use SELFLEKS FLUKOSEL

Instructions for appropriate use and dose / administration frequency:

The daily dose of fluconazole should depend on the type and severity of the fungal infection. For types of infections that require treatment with repeated doses, treatment should be continued until clinical parameters or laboratory tests indicate that the active fungal infection has passed. An insufficient duration of treatment causes a recurrence of active infection. To prevent relapse; Maintenance treatment is often required in patients with AIDS and a type of fungal disease of the mouth and pharynx called cryptococcal meningitis or recurrent oropharyngeal candidiasis.

Unless recommended otherwise by the doctor, the following doses can be applied:

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 200-400 mg 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	50-400 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

	administration 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/ mm^3.
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 and method of administration:
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.

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

Various age groups:

Use in children:

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.	
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.

Special conditions of use:

Renal failure:

No dose adjustment is required in a treatment that requires a single dose. In multiple dose treatments, your doctor will regulate the dose to be given, including children.

Hepatic failure:

No data available.

Please talk to your physician or pharmacist if you feel that the effect of SELFLEKS FLUKOSEL is too strong or too weak.

If you have used more SELFLEKS FLUKOSEL than you should

If you have used more SELFLEKS FLUKOSEL than you should, talk a physician or pharmacist.

If you forget to use SELFLEKS FLUKOSEL

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.

Effects which may occur when treatment with SELFLEKS FLUKOSEL is discontinued

Do not stop taking SELFLEKS FLUKOSEL unless your doctor tells you. In cases where you need to stop taking SELFLEKS FLUKOSEL, your doctor will determine the best method for you. If you have any questions about the use of SELFLEKS FLUKOSEL, consult your doctor.

4. What are the possible side effects?

As with all medicines, there may be side effects in people who are sensitive to the ingredients of SELFLEKS FLUKOSEL.
The frequency of adverse events is reported using the following categories.

Very common	: can be seen at least 1 of 10 patients.
Common	: can be seen less than one in 10 patients, but more than one in 100 patients.
Uncommon	: can be seen less than one in 100 patients, but more than one in 1,000 patients.
Rare	: can be seen less than one in 1.000 patients, but can be seen more than 10,000 patients in one.
Very rare	: can be seen less than one in 10,000 patients.
Unknown	: cannot be estimated from available data.

Common:

- Headache
- Abdominal pain
- Nausea
- Vomiting
- Discomfort in the stomach
- Diarrhea
- Gas

- Rash
- High alkaline phosphatase (ALP) levels
- Increase in aspartate aminotransferase (AST)
- Increase in 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:

- Rare serious allergic reactions, including:
- Sudden wheezing, difficulty breathing or tightness in the chest,
- Swelling of the eyelids, face or lips,
- Itching, reddening or itchy red spots on the whole body,
- Skin rash,
- Severe skin reactions such as rash (which may also affect the mouth and tongue) causing swelling (severe skin reactions are more likely in patients with AIDS)
- If you are experiencing any of the symptoms such as a serious disease (toxic epidermal

necrolysis) with liquid-filled blisters on the skin, immediately inform your doctor.

- Decrease in the number of white blood cells
- Decrease in the number of platelets-blood platelets
- High cholesterol
- High triglycerides
- If the blood potassium level is above normal
- Trembling
- QT prolongation
- Life-threatening irregular heart rhythm (Torsades de pointes)
- Liver-related toxicity, also rarely leading to death
- Liver failure
- Liver inflammation
- Jaundice
- Damage and death of liver tissues
- Inflammation with blood, swelling and redness on the skin and around the eyes (Stevens-Johnson syndrome)
- Acute widespread rash skin diseases including inflamed blisters marked by redness or blistering on the skin.
- Edema o 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.

If you experience any side effect not mentioned in this patient information leaflet, inform your doctor or your pharmacist.

Reporting of the side effects:

If you get any side effects not listed in this leaflet, talk to your doctor or pharmacist. You can also report side effects directly to your doctor or pharmacist. You can also report side effects directly to your country's related health authority. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store SELFLEKS FLUKOSEL

Keep SELFLEKS FLUKOSEL out of the sight and reach of children, and in its packaging.

Store at room temperature below 25°C, within its original packaging. Do not use if the solution is not clear, contains particles, or the bag is damaged. The rest of the solution, some of which has been spent, is not used again.

It should be used immediately after opening.

Use in compliance with the expiry date.

Do not use SELFLEKS FLUKOSEL after the expiration date stated on the packaging.

Marketing Authorization Holder:

HAVER FARMA İlaç A.Ş.
Akbaba Mah. Maraş Cad. No:52/2/1
Beykoz /İSTANBUL
Tel : (0216) 324 38 38
Fax : (0216) 317 04 98

Manufacturing Site:

Osel İlaç San. ve Tic. A.Ş.
Akbaba Mah. Maraş Caddesi No:52
34820 Beykoz / İstanbul
Tel : (0216) 320 45 50
Fax : (0216) 320 45 56

This patient information leaflet was approved on .../.../...

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THE FOLLOWING INFORMATION IS FOR MEDICAL PERSONNEL WHO WILL ADMINISTER THIS MEDICINE

Fluconazole is administered both orally and in the form of an intravenous infusion at a rate not exceeding 10 ml per minute. The method of administration depends on the clinical condition of the patient. There is no need to change the daily dose when switching from intravenous to oral or otherwise.

SELFLEKS FLUKOSEL injectable form is formulated in 0.9% sodium chloride solution and each 200 mg (100 mL PVC bag) contains 15 mmol Na^+ and the same amount of Cl^-. Since SELFLEKS FLUKOSEL contains a dilute salt solution, attention should be paid to the rate of fluid administration in patients requiring sodium or water restriction. SELFLEKS FLUKOSEL intravenous infusion is compatible with the following administration fluids.

a) 20% Dextrose
b) Ringer's solution
c) Hartmann solution
d) Potassium chloride in dextrose
e) 4.2% Sodium bicarbonate
f) Aminofusin
g) Physiological saline

SELFLEKS FLUKOSEL may be infused in one of the above fluids from an existing IV set. Although no specific incompatibility has been observed, mixing it with any other drug before infusion is not recommended.

Parenteral preparation products before use, the solution and packaging should be checked to see if they contain as many particulates as permitted and if the color is impaired (see precautions).

Do not use products that are not clear and unpacked.

To open: tear the outer packaging from the top and remove the solution container. Some opacity can be seen on the plastic due to the absorption of moisture during the sterilization process. This is normal and does not affect the quality and reliability of the solution. Opacity will disappear over time.

Preparation for administration: (use aseptic technique)

1- Turn off the current control lock (clamp) of the administration set.
2- Remove the lid from the exit hole under the medicine bag.
3- Insert the needle of the administration set into the hole until the set is firmly seated.
4- Hang the bag on the suspension.
5- Tighten and release the chamber where the drop flows to ensure smooth fluid flow in the chamber.
6- Open the Flow Control Lock and remove the air from the set. Close the lock.
7- Connect the set to the venipuncture device. If the serum is not flowing, adjust the venipuncture.
8- Adjust administration speed with Flow Control Lock.

ATTENTION:
DO NOT USE FLEXIBLE BAGS IN MULTIPLE CONNECTIONS.
FOR SINGLE-DOSE USE.
I.V. USE
DO NOT ADD ADDITIVES TO THIS SOLUTION.
USE ONLY CLEAR SOLUTION AND UNOPENED PACKAGE.