PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

Diflucan® 50 mg/5 ml

Powder for preparing 35 ml oral suspension

Each 5 ml contains: Fluconazole 50 mg

For a list of inactive and allergenic ingredients in the preparation, please see section 6 ''Further Information".

Read the leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

This medicine has been prescribed to treat you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours.

1. WHAT IS THE MEDICINE INTENDED FOR?

Adults

Diflucan 50 mg/5 ml is intended for treating 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 originating in the blood stream, body organs (e.g., heart, lungs) or urinary tract
- Oral thrush – infection affecting the lining of the oral cavity, throat and dentures
- Genital thrush – infection of the vagina or penis
- Skin fungus, including athlete's foot, fungus in the groin area, pityriasis versicolor, nail fungus and skin inflammations caused by *Candida*.

The medicine is also intended for:

- Preventing cryptococcal meningitis from coming back
- Preventing oral thrush from coming back
- Reducing the recurrence of vaginal thrush
- Stopping 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)

Diflucan 50 mg/5 ml is intended for treating the following types of fungal infections:

- Oral thrush – infection affecting the lining of the oral cavity and throat
- Infections caused by *Candida* and originating in the blood stream, body organs (e.g., heart, lungs) or urinary tract
- Cryptococcal meningitis – a fungal infection in the brain.

The medicine is also intended for:

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

Therapeutic group:

Antifungal from the azole group.

Diflucan 50 mg/5 ml belongs to a group of medicines called "antifungals". The active substance is fluconazole.

Fluconazole is intended for use in infections caused by fungi and also for the prevention of infections caused by *Candida*.
The most common cause of fungal infections is a type of yeast called *Candida*.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- You are sensitive (allergic) to fluconazole, to other medicines you have taken to treat fungal infections or to any of the ingredients of the medicine (listed in section 6). The symptoms may include itching, reddening of the skin or difficulty in breathing
- You are taking astemizole, terfenadine (antihistamines for treating allergy)
- You are taking cisapride (for treating stomach upsets)
- You are taking pimozide (for treating mental illness)
- You are taking quinidine (for treating heart arrhythmias)
- You are taking erythromycin (an antibiotic for treating infections)

Special warnings regarding use of the medicine
Before treatment with Diflucan, tell the doctor if:

- You have liver or kidney problems
- You suffer from heart disease, including heart rhythm problems
- You have abnormal levels of potassium, calcium or magnesium in the blood
- You develop severe skin reactions (itching, reddening of the skin or difficulty in breathing)
- You develop symptoms of 'adrenal insufficiency'. In this condition, the adrenal glands do not produce adequate amounts of hormones such as cortisol (chronic, or long-lasting fatigue, muscle weakness, loss of appetite, weight loss, abdominal pain)
- You have ever developed a severe skin rash or skin peeling, blistering and/or mouth sores after taking fluconazole.

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

Tell your doctor if the fungal infection does not improve, as alternative antifungal therapy may be needed.

Other medicines and Diflucan
If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.
Tell your doctor immediately if you are taking: astemizole, terfenadine (an antihistamine for treating allergy) or cisapride (for stomach upsets) or pimozide (for treating mental illness) or quinidine (for treating arrhythmias) or erythromycin (an antibiotic for treating infections), as these medicines must not be taken with Diflucan (see section: "Do not use the medicine if").

There are certain medicines that could interact with Diflucan. Make sure your doctor knows if you are taking any of the following medicines, as a dose adjustment or monitoring may be required to check that the medicines are still having the desired effect:

- Rifampicin or rifabutin (antibiotics for treating infections)
- Alfentanil, fentanyl (used as anesthetic)
- Amitriptyline, nortriptyline (for treating depression)
- Amphotericin B, voriconazole (antifungals)
- 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 and phenytoin (for treating fits)

- Nifedipine, isradipine, amlodipine, verapamil, felodipine and losartan (for treating hypertension)
- Olaparib (for treating ovarian cancer)
- Ciclosporin, everolimus, sirolimus, tacrolimus (to prevent organ transplant rejection)
- Cyclophosphamide or vincristine, vinblastine or similar medicines for treating cancer
- Halofantrine (for treating malaria)
- Statins (atorvastatin, simvastatin, fluvastatin or similar medicines) for reducing high cholesterol levels
- Methadone (for treating pain)
- Celecoxib, flurbiprofen, naproxen, ibuprofen, lornoxicam, meloxicam, diclofenac (nonsteroidal anti-inflammatory drugs (NSAIDs))
- Oral contraceptive pills
- Prednisone (steroid)
- Zidovudine, saquinavir (for treating HIV-infected patients)
- Anti-diabetes medicines such as chlorpropamide, glibenclamide, glipizide or tolbutamide
- Theophylline (for treating asthma)
- Tofacitinib (for treating rheumatoid arthritis)
- Tolvaptan (for treating hyponatremia [low levels of sodium in the blood] or to slow kidney function decline)
- Vitamin A (a nutritional supplement)
- Ivacaftor (alone or combined with other drugs for treating cystic fibrosis)
- Amiodarone (for treating heart arrhythmias)
- Hydrochlorothiazide (a diuretic)
- Ibrutinib (for treating blood cancer)
- Lurasidone (used to treat schizophrenia)

Use of the medicine and food
The medicine can be taken with or without food.

Pregnancy and breastfeeding
If you are pregnant or breastfeeding, think you are pregnant or are planning to become pregnant, consult with a doctor before taking this medicine.
Do not take Diflucan if you are pregnant, think you may be pregnant, are planning to become pregnant, unless your doctor has told you otherwise.
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 trimester of pregnancy may increase the risk of miscarriage.
Fluconazole taken 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.

You can continue breastfeeding after taking a single dose of fluconazole at a dosage of up to 150 mg.
Do not breastfeed if you are taking a repeated dose of Diflucan.

Driving and operating machinery
The use of this medicine can sometimes cause dizziness or fits and therefore requires caution when driving a vehicle and operating machinery.

Important information about some of the ingredients of the medicine
The medicine contains sucrose, sodium benzoate and sodium (salt)
- The medicine contains sucrose; therefore, if you have been told by the doctor that you have an intolerance to certain sugars, contact the doctor before taking this medicine.
- Doses of 10 ml contain 5.5 gram or more of sugar. Take this into consideration in patients with diabetes mellitus.

- When using for more than two weeks, the medicine may be harmful to teeth.
- The medicine contains 83 mg sodium benzoate per bottle (60 ml), which is equivalent to 2.37 mg sodium benzoate per 1 ml suspension. Sodium benzoate may increase the risk for jaundice (yellowing of the skin and eyes) in newborns (up to 4 weeks old).
- After preparation, this medicine contains 1.13 mg sodium per 1 ml suspension. This is equivalent to 4.5% of the recommended maximum dietary intake of sodium for an adult per day.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the preparation according to the doctor's instructions.
Check with the doctor or pharmacist if you are unsure about the dosage and treatment regimen of the preparation.

The dosage and treatment regimen will be determined by the doctor only. The usual dose generally depends on the type of infection that you have.

Elderly
A similar dose to that generally given to adults unless you have kidney problems.

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

Do not exceed the recommended dosage!

It is recommended to take the medicine at a set time each day, irrespective of food.

Preparation instructions:
The pharmacist will prepare the suspension before dispensing. Preparation instructions are detailed at the end of this leaflet in section "The following information is intended for healthcare professionals".

How to use: Shake the closed bottle of suspension each time, before use.

- Use the measuring spoon intended for measuring the correct amount of the medicine. Do not use a household teaspoon to measure the amount of medicine. Household teaspoons vary in size, and you may not receive the correct amount of medicine.

If you accidentally take a higher dosage
If you took an overdose, or if a child has accidentally swallowed the medicine, refer immediately to a doctor or proceed to a hospital emergency room, and bring the package of the medicine with you. Taking an overdose may cause you to feel unwell.

Symptoms of an overdose may include: hearing, seeing or feeling things that do not exist in reality, including unrealistic thoughts (hallucinations and paranoid behavior). You may need treatment in such situations.

If you forgot to take the medicine at the required time
Do not take a double dose to make up for the forgotten dose. If you forget to take a dose, take it as soon as you remember. If it is almost time for your next dose, do not take the forgotten dose.
Adhere to the treatment regimen as recommended by the doctor.
Even if there is an improvement in your health, do not stop treatment with the medicine without consulting a doctor.

Do not take medicines in the dark! Check the label and the dose <u>each time</u> you take a medicine. Wear glasses if you need them.

If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Diflucan may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

Stop taking Diflucan and see a doctor immediately if you notice any of the following symptoms:
- widespread rash, high body temperature and enlarged lymph nodes (drug reaction with eosinophilia and systemic symptoms (DRESS syndrome) or drug hypersensitivity syndrome).

Some people develop **allergic reactions** although serious allergic reactions are rare. If you develop any side effect, contact your doctor or pharmacist. This includes any side effect not listed in this leaflet.

Contact a doctor **immediately** in case of:
- Difficulty in breathing, sudden wheezing or tightness in the chest
- Swelling of the eyelids, face or lips
- Itching all over the body, reddening of the skin or itchy red areas
- Skin rash
- Severe skin reactions such as a rash that causes blistering (this can affect the mouth and tongue)

The medicine may affect your liver. Symptoms of liver problems include:
- Tiredness
- Loss of appetite
- Vomiting
- Yellowing of the skin or the eyes (jaundice)

If you experience any of these symptoms, stop using the medicine and **contact your doctor immediately**.

Additional side effects

Common side effects (occur in up to 1 in 10 people) include:
- Headache
- Abdominal discomfort, diarrhea, vomiting, nausea
- Increased level of liver enzymes in the blood
- Rash

Uncommon side effects (occur in up to 1 in 100 people) include:
- Reduction in the number of red blood cells, which could cause pale skin, weakness or breathing difficulties
- Decreased appetite
- Insomnia, feeling drowsy
- Fits, dizziness, sensation of spinning, sensation of tingling, pricking or numbness, changes in sense of taste
- Constipation, difficult digestion, wind, dry mouth
- Muscle pain
- Liver damage and yellowing of the skin or eyes (jaundice)
- Wheals, blistering of the skin (hives), itching, increased sweating
- Tiredness, general feeling of being unwell, fever

Rare side effects (occur in up to 1 in 1000 people) include:
- Decreased number of white blood cells that help deal with infections and in the number of other blood cells that help stop bleeding
- Red or purple discoloration of the skin which may be caused by a low platelet count and other blood cell changes
- Blood chemistry changes (high levels of cholesterol, fats in the blood)
- Low levels of potassium in the blood
- Shaking
- Abnormal electrocardiogram (ECG), changes in heart rhythm
- Liver failure
- Allergic reactions (sometimes severe), including the appearance of a widespread rash with skin blisters and skin peeling, severe skin reactions, swelling of the lips or face
- Hair loss

Side effects of unknown frequency (effects whose frequency has not yet been determined):
- Hypersensitivity reaction with skin rash, fever, swollen glands, an increase in a type of white blood cell (eosinophilia) and inflammation of internal organs (liver, lungs, heart, kidneys and large intestine) (DRESS).

If a side effect occurs, if one of the side effects worsens or if you suffer from a side effect not mentioned in the leaflet, consult with the doctor.

Side effects can be reported to the Ministry of Health by clicking on the link “Report Side Effects of Drug Treatment” found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link:
https://sideeffects.health.gov.il

5. HOW SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine, and any other medicine, should be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.
- Store below 30°C.
- After preparation, store the prepared suspension below 30°C and use within 14 days.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:
Sucrose, natural orange flavour, citric acid anhydrous, sodium citrate hydrous, sodium benzoate, xanthan gum, colloidal silicone dioxide, titanium dioxide.

What the medicine looks like and the contents of the package:
- The capacity of the medicine bottle is 60 ml, when containing 24.4 grams of powder. After dilution, the volume of the suspension is 35 ml.
- The powder comes in a white to off-white color. After adding the water to the powder, a white to off-white, orange flavored suspension is obtained.

License holder and address: Pfizer PFE Pharmaceuticals Israel Ltd., 9 Shenkar St., Herzeliya Pituach 46725.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 106-79-29073

Revised in 06/2022 according to MOH guidelines.

The following information is intended for healthcare professionals:

Instructions to make up the suspension:

1. Tap the bottle to release the powder.
2. Reconstitute by adding 24 ml of water and shake vigorously.
3. Shake well for 1 to 2 minutes to obtain a well-mixed suspension.
4. After preparation, there will be a usable volume of 35 ml.
5. Write the date of expiration of the reconstituted suspension on the bottle label (the shelf-life of the reconstituted suspension is 14 days).