Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

The medicine is dispensed with a doctor's prescription only

VFEND® 50 mg film-coated tablets
VFEND® 200 mg film-coated tablets
VFEND® 40 mg/ml powder for oral suspension

Film-coated tablets: voriconazole 50 mg, 200 mg
Each ml of reconstituted suspension contains: voriconazole 40 mg

Inactive ingredients and allergens: see section 2 under "Important information about some of this medicine's ingredients" and section 6 "Further information".

Read the entire leaflet carefully before using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.
This medicine has been prescribed for 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 THIS MEDICINE INTENDED FOR?

VFEND is a broad-spectrum antifungal preparation intended for the treatment of:
- invasive aspergillosis (a fungal infection caused by *Aspergillus sp.*)
- *Candida* infections in the blood system (candidemia) in non-neutropenic patients
- invasive infections of *Candida* that are resistant to fluconazole (another antifungal medicine), including *C. krusei*
- severe fungal infections caused by *Scedosporium* and *Fusarium* type of fungi.

VFEND is intended for patients with severe, possibly life-threatening, fungal infections.
VFEND is intended for the prevention of invasive fungal infections in high-risk bone marrow transplant recipients.

Therapeutic group:
Antifungal from the triazole group. It works by killing or stopping the growth of different fungi that cause infections.

2. BEFORE USING THIS MEDICINE

Do not use this medicine if:

- You are sensitive (allergic) to the active ingredient or to any of the additional ingredients in this medicine (see section 6).
- Do not take this medicine with terfenadine (for allergy), astemizole (for allergy), cisapride (for stomach problems), pimozide (for mental problems), quinidine (for heart rate problems), ivabradine (for treating chronic heart failure), rifabutin (for treating tuberculosis), rifampicin (for treating tuberculosis), carbamazepine (for treating seizures), phenobarbital (for treating seizures and severe insomnia), ergot derivatives (ergotamine, dihydroergotamine; for treating migraines), sirolimus (for transplant patients), efavirenz, at a dosage of 400 mg and more once a day (for treating HIV), ritonavir at dosages given twice a day of 400 mg and more each time (for treating HIV), the Hypericum herb (St. John's Wort), naloxegol (for treating constipation caused mainly by the use of opioid painkillers (such as morphine, oxycodone, fentanyl, tramadol, codeine)), tolvaptan (used to treat hyponatremia (low sodium in the blood) or to slow kidney function decline in patients with polycystic kidney disease), lurasidone (for treating depression), finerenone (for treating chronic kidney disease), venetoclax (for treating patients with chronic lymphocytic leukaemia - CLL).

Before treatment with VFEND, tell your doctor if:

- you suffer, or have suffered in the past, from an allergic reaction to preparations from the azole group.
- you suffer from a disease of the heart muscle (cardiomyopathy), irregular or slow heart rate or an abnormality in the electrocardiogram (ECG) called 'long QTc syndrome'.
- you suffer, or have suffered in the past, from a liver disease. The doctor will monitor your liver function by performing blood tests.

Special warnings regarding use of the medicine

- Avoid any sunlight and sun exposure while using the medicine. It is important to cover sun exposed areas of skin and to use sunscreen with a high sun protection factor (SPF), as an increased sensitivity of the skin to the sun's UV rays may occur. This may be further increased by other medicines that sensitise the skin to sunlight, like methotrexate. This warning is also applicable to children.
- While using the medicine, tell the doctor immediately if you develop sunburn, a severe skin rash or blisters, bone pain.
  If one of these skin effects occurs, the doctor may refer you to a dermatologist. There is a small chance of developing skin cancer upon long-term use of VFEND.
- If you develop signs of 'adrenal insufficiency', a medical condition in which the adrenal glands do not produce adequate amounts of certain steroid

hormones such as cortisol, which may lead to symptoms such as: chronic, or long-lasting fatigue, muscle weakness, loss of appetite, weight loss, abdominal pain, please tell your doctor.
- If you develop symptoms of "Cushing syndrome", in which your body produces too much of the hormone cortisol, which may lead to symptoms such as: weight gain, fatty tissue between your shoulders, round face, darkening of the skin on your abdomen, thighs, breasts and arms, thin skin, tendency to bruise easily, high blood sugar, excessive hair, excessive sweating, please tell your doctor.
- The doctor will monitor liver and kidney function by performing blood tests during the course of treatment with VFEND.
- Before starting and during the course of treatment, monitor for disturbances in electrolyte levels, such as low levels of potassium, magnesium, and calcium.

Children and adolescents
This medicine is not intended for children and infants under the age of two years.

Tests and Follow-up
As VFEND affects the liver and the kidney, the doctor will monitor the function of your liver and kidney by performing blood tests. Please tell the doctor if you experience abdominal pain or if your stools have a different consistency.

Other medicines and VFEND
If you are taking or have recently taken other medicines, including nonprescription medicines and dietary supplements, tell your doctor or pharmacist. Particularly if you are taking:
Medicines, whose administration in combination with VFEND should be avoided if possible, and a dosage adjustment is required if given together:
- Phenytoin (to treat epilepsy). If you are taking this medicine, the blood level of phenytoin should be monitored.
- Ritonavir (to treat HIV) at a low dosage of 100 mg twice a day. Certain dosages of ritonavir cannot be taken with VFEND, see “Do not use the medicine if”, in this section.
- Glasdegib (to treat cancer) - If you need to use both medicines, your doctor will monitor your heart rhythm more frequently.

Medicines, when combined with VFEND, may require a dosage adjustment and monitoring that the medicines and/or VFEND are still having the desired effect:
- Warfarin and other anticoagulants (e.g., phenprocoumon, acenocoumarol)
- Ciclosporin, tacrolimus (for transplant patients)
- Sulfonylureas (e.g., tolbutamide, glipizide, and glyburide) (to treat diabetes)
- Statins (e.g., atorvastatin, simvastatin, lovastatin) (for lowering cholesterol levels)

- Benzodiazepines (e.g., midazolam, alprazolam, and triazolam) (for severe insomnia and as a tranquilizer)
- Omeprazole (to treat peptic ulcer)
- Oral contraceptives (side effects such as nausea and menstrual disorders may occur)
- Vinca alkaloids (e.g., vincristine and vinblastine) (to treat cancer)
- Tyrosine kinase inhibitors (e.g., axitinib, bosutinib, cabozantinib, ceritinib, cobimetinib, dabrafenib, dasatinib, nilotinib, sunitinib, ibrutinib, ribociclib) (to treat cancer)
- Tretinoin (to treat leukaemia)
- Indinavir and other HIV protease inhibitors (to treat HIV)
- NNRTI medicines to treat HIV, e.g., delavirdine, nevirapine, efavirenz (some dosages of efavirenz cannot be taken with VFEND; see “Do not use the medicine if” in this section)
- Methadone (to treat addiction)
- Short-acting opiates (e.g., alfentanil, fentanyl, sufentanil) (painkillers for surgical procedures)
- Oxycodone and hydrocodone (to relieve moderate to severe pain)
- Non-steroidal anti-inflammatory drugs (e.g., ibuprofen and diclofenac) (to treat pain and inflammation)
- Fluconazole (to treat fungal infections)
- Everolimus (to treat advanced kidney cancer and in transplant patients)
- Letermovir (for preventing cytomegalovirus (CMV) disease after bone marrow transplant)
- Ivacaftor (to treat cystic fibrosis (CF))
- Flucloxacillin (antibiotic used against bacterial infections)

For a list of medicines not to be taken concomitantly with VFEND, please see “Do not use the medicine if” in this section.

Pregnancy and breastfeeding
Do not use this medicine if you are pregnant, unless you have received an explicit instruction from the doctor. Women of childbearing age must use effective contraceptives when using the medicine. Refer to your doctor immediately if you become pregnant while taking VFEND.

If you are pregnant or breastfeeding, think you are pregnant or are planning a pregnancy, ask your doctor for advice before taking this medicine.

Driving and using machines
VFEND may cause blurring of vision or sensitivity to light. If you are affected by it, do not drive or operate dangerous machines.
Caution children against riding a bicycle or playing near the road and the like.

Important information about some of this medicine’s ingredients
Suspension

- This medicine contains sucrose; therefore, if you were told by a doctor that you have an intolerance to certain sugars, refer to a doctor before taking the medicine. This should be taken into account in patients with diabetes mellitus. May also be harmful to the teeth.
- This medicine contains less than 1 mmol (23 mg) sodium per 5 ml of suspension, i.e., it is considered essentially “sodium-free”.
- The suspension contains sodium benzoate.

Film-coated tablets
- The tablets contain lactose; therefore, if you have been told by a doctor that you have an intolerance to certain sugars, refer to a doctor before taking the medicine.
- A 50 mg or a 200 mg tablet contains less than 1 mmol (23 mg) sodium per tablet, i.e., it is considered essentially “sodium-free”.

3. HOW TO USE THIS MEDICINE?

Always use this medicine according to your doctor’s instructions.
Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the medicine.
The dosage and treatment regimen will be determined by your doctor only.
The dosage will be determined depending on your weight and the type of your infection.

Depending on your response to treatment, the doctor may increase or decrease your daily dosage.

If you have liver disease, the doctor may decrease your dose.

Do not exceed the recommended dose!

If you or your child are taking VFEND to prevent fungal infections, your doctor may stop the treatment if you or your child develop treatment-related side effects.

- Tablets should only be given if the child is capable of swallowing tablets.

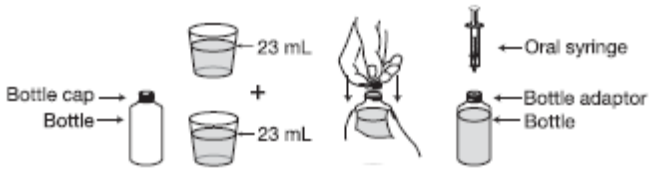
Film-coated tablets: Take the tablet at least one hour before or one hour after a meal.
Swallow the tablet whole with a little water.
Do not crush/halve/chew, since the tablet is coated.

Suspension: Take the suspension at least one hour before or two hours after a meal.
Do not mix the suspension with any other medicine and do not dilute the reconstituted suspension with water or any other liquid.

Instructions for preparation of the suspension:

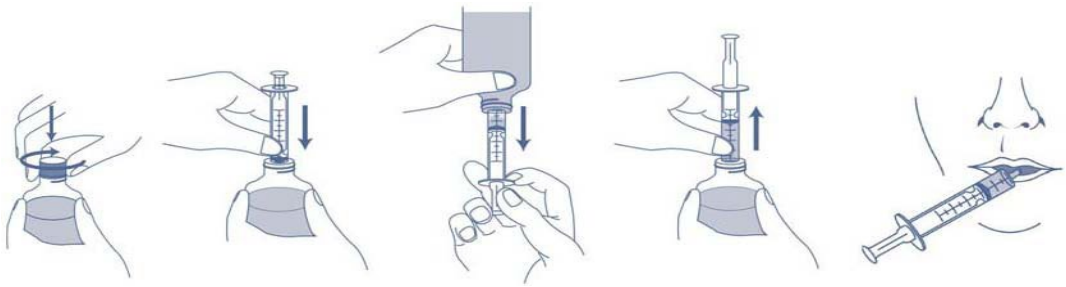
The pharmacist will prepare the suspension before dispensing.
The suspension is ready for use if it is in liquid form. If the powder looks dry, prepare the suspension according to the instructions below.

1. Tap the bottle to release the powder.
2. Remove the cap.
3. Add 2 measuring cups (a measuring cup is enclosed inside the package) of water (total of 46 ml) to the bottle. Fill the measuring cup up to the marked line, then add the water to the bottle. Always add a total of 46 ml of water, regardless of the dosage you are taking.
4. Replace the cap and shake the bottle vigorously for one minute. After reconstitution, the total volume of the suspension must be 75 ml.
5. Remove the cap. Press the bottle adaptor (enclosed inside the package) into the neck of the bottle (as shown in the figure below). The adaptor is supplied to enable the filling of the syringe with medicine from the bottle. Replace the cap on the bottle.
6. Write the expiry date of the reconstituted suspension on the bottle label. Use the reconstituted suspension within 14 days.
   Discard all remnants of the suspension after this date.



Instructions for use:

1. Use the oral syringe (enclosed inside the package) to measure the medicine dose. Shake the reconstituted suspension in the closed bottle for approximately 10 seconds before each use. Remove the cap.
2. Place the bottle on a flat surface and insert the tip of the syringe into the hole in the bottle adaptor.
3. Turn the bottle upside down while holding the syringe in place. Slowly pull back the plunger of the syringe to the graduation mark appropriate for your dose.
4. If you notice large bubbles, slowly push the plunger of the syringe back into the syringe, so that the suspension of the medicine is returned to the bottle. Repeat step no. 3.
5. Turn the bottle back upright with the syringe still in place. Remove the syringe.
6. Put the tip of the syringe into your mouth. **Slowly** push down on the plunger of the syringe to instill the suspension into your mouth (toward the inner cheek). Do not push quickly to eject the medicine. If the suspension is given to a child, make sure the child is sitting, or is held upright before administration.
7. Close the bottle with the cap; the bottle adaptor remains in place.
8. Wash the syringe after each use. Clean both parts of the syringe in soapy water and rinse with water. Dry both parts. Keep the syringe in a clean place next to the medicine.



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If you have accidentally taken a higher dosage
If you have taken an overdose, or if a child has accidentally swallowed some medicine, immediately go to a hospital emergency room and bring the medicine package with you. You may experience increased sensitivity to light as a result of taking an overdose.

If you forget to take the medicine
It is important that you take the medicine at the same time every day.
If you forget to take the medicine at the scheduled time, take the next dose at the usual time, but never take a double dose to compensate for a forgotten dose.

Adhere to the treatment as recommended by your doctor.

Even if your health improves, do not stop taking this medicine without consulting your doctor.

If you stop taking this medicine
Continue taking the medicine until the doctor tells you to stop. If you stop taking the medicine early, your infection may continue or recur. Patients with a weakened immune system or those with difficult infections may require long-term treatment to prevent the infection from returning.

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

If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of VFEND may cause side effects in some users. Do not be alarmed by the list of side effects; You may not experience any of them.

Serious side effects - stop taking the medicine and refer to the doctor immediately

- Rash
- Jaundice; change in blood test results for liver function
- Pancreatitis

Additional side effects

Very common side effects (may occur in more than 1 in 10 people):
- Visual impairment (change in vision including blurred vision, color alterations, increased sensitivity to light, color blindness, eye disorder, seeing a halo, night blindness, swinging vision, seeing sparks, visual aura, reduced visual acuity, blinding brightness, narrowed field of vision, blotches/spots in the field of vision)
- High fever
- Rash
- Nausea, vomiting, diarrhea
- Headache
- Swelling in the extremities
- Stomach pain
- Breathing difficulties
- Increased liver enzymes

Common side effects (may occur in up to 1 in 10 people):
- Sinusitis, inflammation of the gums, chills, weakness
- Low level, including severe, of certain red and/or white blood cells (sometimes accompanied by fever), low level of platelets that help the blood to clot
- Low blood sugar level, low blood potassium level, low blood sodium level
- Anxiety, agitation, depression, confusion, sleep difficulties, hallucinations
- Seizures, tremor or involuntary muscle movement, tingling or abnormal skin sensations, increase in muscle tone, sleepiness, dizziness
- Bleeding in the eye
- Heart rhythm problems including very fast/very slow heartbeat, fainting
- Low blood pressure, inflammation of the veins (phlebitis)
- Acute breathing difficulties, chest pain, swelling of the face (mouth, lips and around the eyes), fluid retention in the lungs
- Constipation, indigestion, inflammation of the lips
- Jaundice, inflammation of the liver (hepatitis) and liver damage
- Skin rashes which may lead to severe peeling and blistering of the skin characterized by a flat and red area on the skin covered with small confluent bumps, redness of the skin
- Itchiness
- Hair loss
- Back pain
- Kidney failure, blood in the urine, changes in kidney function tests
- Sunburn or severe skin reaction following exposure to light or sun

- Skin cancer

Uncommon side effects (may occur in up to 1 in 100 people):
- Flu-like symptoms, irritation and inflammation of the gastrointestinal tract, inflammation of the gastrointestinal tract causing diarrhea, inflammation of the lymphatic vessels
- Inflammation of the thin tissue that lines the inner wall of the abdomen and covers the abdominal cavity
- Enlarged lymph glands (sometimes painful), failure of bone marrow, increased eosinophil level in the blood
- Decreased function of the adrenal gland, underactive thyroid gland
- Abnormal brain function, Parkinson-like symptoms, nerve injury resulting in numbness, pain, tingling or burning sensation in the limbs
- Problems with balance or coordination
- Swelling of the brain
- Double vision, serious conditions of the eye including pain and inflammation of the eyes and eyelids, abnormal eye movement, damage to the optic nerve causing vision disturbance, optic disc swelling
- Decreased sensitivity to touch
- Change in sense of taste
- Hearing disturbances, ringing in the ears, vertigo (dizzy sensation)
- Inflammation of certain internal organs - pancreas and duodenum, swelling and inflammation of the tongue
- Enlarged liver, liver failure, gallstones or gallbladder disease
- Joint inflammation, inflammation of the veins accompanied by the formation of a blood clot (thrombosis)
- Inflammation of the kidney, protein in the urine, damage to the kidney
- Very fast heart rate or skipped heartbeats, sometimes accompanied by irregular electric impulses
- Changes in the electrocardiogram (ECG)
- Increase in level of blood cholesterol, increased level of blood urea
- Allergic skin reactions (sometimes severe), including life-threatening conditions of the skin, which cause onset of painful blisters, sores/warts on the skin and mucous membranes, especially in the mouth, inflammation of the skin, hives, skin redness and irritation, red or purple spots on the skin due to a decrease in the blood platelet count, eczema
- Allergic reaction or abnormal immune response
- Inflammation of the tissue surrounding the bone

Rare side effects (may occur in up to 1 in 1,000 people):
- Overactive thyroid gland
- Deterioration of brain function (a serious complication of liver disease)

- Severe damage to the optic nerve, cloudy cornea, involuntary eye movement
- Appearance of blisters as a result of sensitivity/exposure to light
- A disorder in which the body's immune system attacks part of the peripheral nervous system
- Heart rhythm or conduction problems (sometimes life-threatening)
- Life-threatening allergic reaction
- Disorder of blood clotting system
- Allergic skin reactions (sometimes severe) including rapid swelling (edema) of the skin, itchy or sore patches of thick, red skin with scales, itching of the skin and mucous membranes, a life-threatening skin condition that causes large portions of the epidermis (the skin's outermost layer) to detach from the layers of skin below
- Small, dry and scaly skin patches, sometimes thickened with 'horns'

Side effects of unknown frequency (the frequency of these effects has not yet been determined):
- Freckles and pigmented spots

Side effects of unknown frequency (the frequency of these effects has not yet been determined), but are significant and need to be reported to the attending doctor immediately:
- Red and scaly areas or ring-shaped skin lesions may be a symptom of an autoimmune disease called cutaneous lupus erythematosus

There have been reports of skin cancer developing in patients who took VFEND for a long period of time.

Sunburn or a severe skin reaction, following exposure to light or sun, was observed more frequently in children. If you/your child develop skin disorders, your doctor may refer you to a dermatologist, who after consultation may decide whether it is important for you/your child to come for monitoring on a regular basis. An increase in liver enzymes has also been observed more frequently in children.

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects or by using the link: https://sideeffects.health.gov.il

5. HOW TO STORE THE MEDICINE?

- Prevent poisoning! This and any other medicine should be kept in a closed place, out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by a doctor.
- Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.

Storage conditions:

- **Film-coated tablets:** Store below 30°C.
  Suspension: Before preparation, store the powder in the refrigerator (2º-8°C).
  After preparation, store the reconstituted suspension below 30°C, not in a refrigerator or freezer. Should be used within 14 days from day of preparation.

6. FURTHER INFORMATION

In addition to the active ingredient, this medicine also contains:

Film-coated tablets:
Lactose monohydrate, pregelatinised starch, croscarmellose sodium, povidone, magnesium stearate, hypromellose, titanium dioxide, glycerol triacetate.
Suspension:
Sucrose, citric acid (anhydrous), natural orange flavour, sodium citrate dihydrate, sodium benzoate, xanthan gum, silica colloidal anhydrous, titanium dioxide.

Film-coated tablets:
Each 50 mg VFEND tablet contains 62.5 mg lactose monohydrate.
Each 200 mg VFEND tablet contains 250 mg lactose monohydrate.

Suspension:
Each 1 ml of reconstituted suspension contains 0.54 grams sucrose.
A dose of 5 ml of suspension contains 12 mg of sodium benzoate.

What the medicine looks like and contents of the pack:

VFEND 50 mg film-coated tablets: white to off-white round tablet marked with “Pfizer” on one side and “VOR 50” on the other side. Supplied in a package of 2, 10, 14, 20, 28, 30, 50, 56, 100 tablets.
VFEND 200 mg film-coated tablets: white to off-white oval-shaped tablet marked with “Pfizer” on one side and “VOR 200” on the other side. Supplied in a package of 2, 10, 14, 20, 28, 30, 50, 56, 100 tablets.
Not all package sizes may be marketed.

VFEND 40 mg/ml powder for oral suspension: white to off-white powder for preparing a white to off-white, orange-flavored suspension. Supplied in a bottle containing 45 grams of powder for preparing 75 ml suspension.

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

Registration number of the medicine in the Ministry of Health's National Drug Registry:
VFEND 50 mg film-coated tablets: 126-69-30596
VFEND 200 mg film-coated tablets: 126-70-30597
VFEND 40 mg/ml powder for oral suspension: 134-48-31157

Revised in 08/2025.