EMA/359520/2014
EMEA/H/C/000387

EPAR summary for the public

Vfend

voriconazole

This is a summary of the European public assessment report (EPAR) for Vfend. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Vfend.

What is Vfend?

Vfend is an antifungal medicine that contains the active substance voriconazole. It is available as tablets (50 mg or 200 mg), as an oral suspension (40 mg/ml) and as a powder to be made up into a solution for infusion (drip into a vein).

What is Vfend used for?

Vfend is used for the treatment of adults and children over the age of two years who have the following fungal infections:

- invasive aspergillosis (a type of fungal infection due to *Aspergillus*);
- candidaemia (another type of fungal infection due to *Candida*) in patients with a normal white blood cell count;
- serious invasive *Candida* infections when the fungus is resistant to fluconazole (another antifungal medicine);
- serious fungal infections caused by *Scedosporium* or *Fusarium* (two different types of fungus).

When used for treatment of fungal infections, Vfend is intended mainly for patients with worsening and possibly life-threatening infections.

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Vfend is also used to prevent invasive fungal infections in patients who have had undergone haematopoietic (blood) stem-cell transplant (a transplant of a type of stem cells that can develop into blood cells) and are at high risk of infection.

The medicine can only be obtained with a prescription.

How is Vfend used?

Vfend is given twice a day at least one hour before or one hour after a meal. The dose of Vfend to use depends on the weight of the patient and on which formulation of the medicine is used.

When used to treat fungal infections, patients need to receive an initial higher dose (loading dose) on the first day. The aim of the loading dose is to reach stable blood levels. The loading dose is then followed by a maintenance dose that can be adjusted according to the patient's response. The dose may be increased or decreased according to how the patient responds and the side effects experienced respectively. Treatment duration should be as short as possible. Treatment beyond 180 days requires careful assessment to ensure that the benefits continue to outweigh the risk for the patient.

In adults, both the loading and the maintenance doses can be given by infusion or by mouth using either the tablets or the suspension, but in children it is recommended to start treatment with the infusion and to consider switching to the suspension if an improvement is seen. The tablets and suspension are to be taken at least one hour before or after a meal.

When used to prevent infections in patients who have had blood stem-cell transplantation, Vfend is given on the day of the transplantation and for up to 100 days after. Preventive treatment should last for as short a time as possible. It may be continued for a further 80 days but only if the patient's immune system is still suppressed or if they develop graft-versus-host disease (when the transplanted cells start attacking the body's own cells). Treatment should be stopped if patients experience treatment-related side effects.

For further information, see the package leaflet.

How does Vfend work?

The active substance in Vfend, voriconazole, belongs to the 'triazole' class of antifungal medicines. It works by disrupting the formation of ergosterol, which is an important component of fungal cell membranes. Without a functional cell membrane, the fungus is killed or prevented from spreading. The list of fungi against which Vfend is active can be found in the summary of product characteristics (also part of the EPAR).

How has Vfend been studied?

The study of Vfend in the treatment of invasive aspergillosis involved 277 immunocompromised patients (patients whose immune system was not working properly). Vfend was compared with amphotericin B (another antifungal medicine).

The study of Vfend in the treatment of candidaemia compared Vfend with a treatment of amphotericin B followed by fluconazole in 370 patients.

Vfend has also been studied in the treatment of serious refractory *Candida* infections in 55 patients, in scedosporiosis in 38 patients, and in fusariosis in 21 patients. 'Refractory' means that the infections were not responding to treatment. Most patients receiving Vfend treatment for these rare infections did not tolerate or did not respond to prior treatment with other antifungal medicines.

Vfend has also been studied in 285 children.

The main measure of effectiveness in all these studies was the number of patients who had a complete or partial response to treatment.

Vfend has also been studied as a preventative treatment in patients who have had blood stem-cell transplantation. In a study involving 465 patients, Vfend was compared with another antifungal medicine, itraconazole. Treatment was considered to be successful if a patient was able to continue treatment for 100 days after the transplantation and had not developed a fungal infection by day 180.

What benefit has Vfend shown during the studies?

In the treatment of invasive aspergillosis, the proportion of patients responding to treatment was higher with Vfend than with amphotericin B (53% versus 31%). The survival for voriconazole was significantly greater than that for amphotericin B.

For candidaemia, the percentage of responders to Vfend treatment at the end of therapy was the same as for the comparator (72%).

A successful outcome was seen in 44% of the patients with serious refractory *Candida* infections (24 out of 55). In most of these (15 out of 24), the response was complete.

In the treatment of scedosporiosis and fusariosis, 28 out of 59 patients had a complete or partial response to treatment.

In the study on prevention in patients who had blood stem-cell transplantation, around 49% of patients who were given Vfend (109 out of 224) had a successful treatment compared with around 33% of patients who received itraconazole (80 out of 241).

What is the risk associated with Vfend?

The most common side effects with Vfend (seen in more than 1 patient in 10) are peripheral oedema (swelling of the arms and legs), headache, visual disturbances (including blurred vision, changes in colour perception and excessive sensitivity to light), respiratory distress (difficulty breathing), abdominal pain (stomach ache), nausea (feeling sick), vomiting, diarrhoea, rash and pyrexia (fever) and abnormal liver function test results. For the full list of all side effects reported with Vfend, see the package leaflet.

Vfend must not be used in patients who are taking any of the following medicines:

- terfenadine, astemizole (commonly used for allergy – these medicines may be available without a prescription);
- cisapride (used for stomach problems);
- pimozide (used to treat mental illnesses);
- quinidine (used for irregular heart beat);
- rifampicin (used to treat tuberculosis);
- carbamazepine (used to treat seizures [fits]);
- phenobarbital (used for severe insomnia and seizures);
- ritonavir (used to treat HIV infection) at doses of 400 mg or more twice a day;
- ergot alkaloids such as ergotamine and dihydroergotamine (used to treat migraine headache);

- sirolimus (used in transplant patients);
- St John's wort (a herbal preparation used to treat depression);
- high dose efavirenz (used to treat HIV infection).

Caution is also needed when Vfend is taken at the same time as other medicines. For the full list of restrictions, see the package leaflet.

Why has Vfend been approved?

The CHMP decided that Vfend's benefits are greater than its risks and recommended that it be given marketing authorisation.

What measures are being taken to ensure the safe and effective use of Vfend?

A risk management plan has been developed to ensure that Vfend is used as safely as possible. Based on this plan, safety information has been included in the summary of product characteristics and the package leaflet for Vfend, including the appropriate precautions to be followed by healthcare professionals and patients.

Other information about Vfend

The European Commission granted a marketing authorisation valid throughout the European Union for Vfend on 19 March 2002.

The full EPAR for Vfend can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports. For more information about treatment with Vfend, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 06-2014.