

Voriconazole

Product:

VORICONAZOLE (Vfend®) 50mg, 200mg oral tablet, 200mg/vial intravenous injection

Class of drugs:

Antifungal agent

Indication:

Treatment of serious or invasive *Candida* infections of the blood, skin, abdomen, urinary tract, bone and joints.

Manufacturer:

Pfizer Canada Inc.

CED Recommendation

The CED recommended that voriconazole (Vfend) be funded through the Exceptional Access Program (EAP) to treat candidemia (*Candida* infection of the blood) caused by *Candida species* with known or documented resistance to fluconazole, on the basis that patients with resistant *Candida* infections need a treatment when standard therapy is neither effective nor appropriate.

Executive Officer Decision

Based on the CED's recommendation, the Executive Officer has decided to fund voriconazole (Vfend) through EAP for the treatment of candidemia caused by *Candida species* with known or documented resistance to fluconazole, according to the specified criteria.

Status

Funding available through the Ontario Public Drug Programs under the EAP.

Highlights of Recommendation:

- ◆ Voriconazole (Vfend) is an anti-fungal drug used to treat *Candida*-related infections. *Candida*, a genus of fungus, can cause a variety of superficial and invasive fungal infections.
- ◆ Amphotericin B and fluconazole are standard treatments for serious or invasive *Candida* infection; both agents are listed on the ODB Formulary.
- ◆ Voriconazole (Vfend) is an alternative to amphotericin B and fluconazole when neither is appropriate.
- ◆ The results of a clinical trial of patients with *Candida* infections of the blood (candidemia) show that voriconazole (Vfend) is as effective as using either amphotericin B or fluconazole. Treatment with voriconazole (Vfend) is associated with fewer side effects.
- ◆ Intravenous voriconazole (Vfend) therapy costs about \$420 per day while oral voriconazole (Vfend) therapy costs about \$95 per day. Amphotericin B therapy costs about \$52 per day and fluconazole oral therapy costs about \$17.60 per day. The added cost for voriconazole (Vfend) therapy is acceptable if patients are able to leave hospital earlier.
- ◆ **Overall, the CED noted that patients with serious or invasive resistant *Candida* infections needed a treatment alternative when standard treatment was neither appropriate nor adequate.** The CED recommended voriconazole (Vfend) be funded through the Exceptional Access Program for patients meeting specific criteria. Please refer to the "Detailed Discussion" section for details of the criteria.

Background:

Candida species of fungus often cause mild fungal infections (commonly referred to as "yeast infections"). However, they can also cause serious or invasive infections in patients with a weak immune system or those who are hospitalized. Invasive *Candida* infections can affect the esophagus, bloodstream, urinary tract, abdominal cavity, bone and joints. *Candida* infection of the blood (candidemia) can be life-threatening.

In the hospital, treatment of a serious or invasive *Candida* infection involves the initial use of intravenous amphotericin B or fluconazole. This may be followed by oral fluconazole therapy when the patient is discharged from the hospital.

Voriconazole (Vfend) is an anti-fungal drug that inhibits the growth of *Candida* species. Treatment is usually started with intravenous voriconazole (Vfend). Often, as the patient is well enough to go home, treatment is continued with oral voriconazole (Vfend) tablets.

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Detailed Discussion:

- ◆ The manufacturer, Pfizer Canada Inc., requested that the Ministry of Health and Long-Term Care reimburse voriconazole (Vfend) tablets and intravenous injection on the Formulary.
- ◆ Voriconazole (Vfend) is indicated for the treatment of candidemia in non-neutropenic patients and in the following candidal infections: disseminated infections in skin and infections in abdomen, kidney, bladder wall and wounds.
- ◆ It was noted that one clinical trial (Trial 608, Kullberg et al.) demonstrated that voriconazole (Vfend) was non-inferior to amphotericin B followed by fluconazole in terms of response to therapy at 12 weeks after drug discontinuation in non-neutropenic patients with candidemia. Mortality attributed to candidemia was similar between both treatment arms.
- ◆ In the Kullberg trial, the incidence of adverse events was significantly less in the voriconazole (Vfend) treated group.
- ◆ Harms associated with voriconazole (Vfend) include hepatotoxicity, and blurred vision/photopsia (usually reversible upon discontinuation of drug). Common side effects for voriconazole (Vfend) may include visual problems, nausea, vomiting, diarrhea, rash, headache and stomach pain.
- ◆ The average drug cost (over approximately three months) with voriconazole (Vfend) was \$6,077, versus \$1,468 for amphotericin B followed by fluconazole.
- ◆ The Committee noted that the cost difference was largely offset by a reduction in the cost of shorter hospital stay with voriconazole (Vfend).
- ◆ Overall, the Committee noted that voriconazole (Vfend) was a reasonable treatment option for patients with candidemia where the fungal isolate is resistant to fluconazole. Given the concerns regarding appropriate use and the fact that there are only a small number of patients who would be considered for this type of treatment, it was suggested that reimbursement be provided through the Exceptional Access Program (EAP).

- ◆ As such, the CED recommended that voriconazole (Vfend) tablets and intravenous injection be considered for reimbursement through the EAP according to the following criteria:
 - For the treatment of patients with culture positive candidemia, due to *Candida* species, with known or documented resistance to fluconazole.
 - Therapy is to be initiated in hospital and prescribed by a hospital physician. EAP will allow for continuation of therapy in the out-patient setting.
 - If the patient has a properly functioning gastrointestinal (GI) tract, oral voriconazole (Vfend) will be authorized. If a patient does not have a properly functioning GI tract, then intravenous voriconazole (Vfend) may be authorized.

CEDAC Recommendation:

(<http://www.cadth.ca/index.php/en/cdr/recommendations>)

The Canadian Expert Drug Advisory Committee recommended that voriconazole (Vfend) be listed with criteria.



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