

Posaconazole

Product:

POSACONAZOLE (Posanol®, formerly Spriafil®) 40mg/mL oral suspension

Class of drugs:

Triazole antifungal agent

Indication:

Prophylaxis treatment of *Aspergillus* and *Candida* infections; treatment of invasive aspergillosis; treatment of oropharyngeal candidiasis

Manufacturer:

Schering-Plough Canada Inc.

CED Recommendation

The CED recommended that posaconazole (Posanol) be funded through the Exceptional Access Program for the prophylaxis of *Aspergillus* and *Candida* infections according to specific criteria.

The CED recommended that posaconazole (Posanol) not be funded for the treatment of invasive aspergillosis or oropharyngeal candidiasis.

Executive Officer Decision

Based on the CED's recommendation, the Executive Officer decided to fund posaconazole (Posanol) through the Exceptional Access Program for the prophylaxis of *Aspergillus* and *Candida* infections according to specific criteria, but not to fund for the treatment of invasive aspergillosis or oropharyngeal candidiasis.

Status

Funding available through the Ontario Public Drug Programs via the Exceptional Access Program.

Highlights of Recommendation:

Posaconazole (Posanol) is an antifungal agent. In Canada, it is approved for use in three indications. The Committee considered each of these indications separately:

Prophylaxis of *Aspergillus* and *Candida* Infections

The Committee noted that posaconazole (Posanol) has been shown to be effective in the prevention of *Aspergillus* and *Candida* infections. Although posaconazole (Posanol) has not been shown to provide value for money, the Committee noted that invasive fungal infections are associated with high mortality rates and that prevention may be of value in certain high risk patient subgroups. As such, funding for posaconazole (Posanol) in the prophylaxis of *Aspergillus* and *Candida* infections was recommended through the Exceptional Access Program according to specific criteria.

Treatment of Invasive Aspergillosis

The Committee noted that there is no evidence that posaconazole (Posanol) provides any clinical advantage over less costly alternatives in the treatment of invasive aspergillosis. Therefore, it was recommended that posaconazole (Posanol) not be funded for this indication.

Treatment of Oropharyngeal Candidiasis

The Committee noted that posaconazole (Posanol) does not offer any clinical advantage over less costly alternatives in the treatment of oropharyngeal candidiasis. As such, the Committee recommended that funding not be provided for this indication.

Background:

Aspergillus and *Candida* are two types of fungi commonly found in nature. They rarely cause illness in healthy people. However, *Aspergillus* and *Candida* can cause serious infections in people with weakened immune systems due to chemotherapy, HIV infection, leukemia, organ and bone marrow transplantation, or other conditions that cause impaired immunity such as neutropenia (low white blood cell count).

Invasive aspergillosis is a very serious, sometimes fatal, infection caused by *Aspergillus* species. Invasive aspergillosis destroys vital lung tissues and can spread to other organs such as the brain and skin.

Oropharyngeal candidiasis (also called thrush) is a superficial fungal infection of the mouth and throat caused by *Candida* species. Symptoms include thick white patches on the mucous tissues of the mouth and throat, which can feel sore, painful, or burning and can limit the patient's ability to eat.

Posaconazole (Posanol) is an antifungal agent that can be used for the prophylaxis (prevention) and treatment of invasive fungal infections.

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Detailed Discussion:

The Committee reviewed posaconazole (Posanol) on two occasions, initially in February 2008 and again in September 2008.

Prophylaxis of *Aspergillus* and *Candida* Infections

- ◆ Posaconazole (Posanol) is approved by Health Canada for the prophylaxis (prevention) of both *Aspergillus* and *Candida* infections in high risk patients.
- ◆ The Committee reviewed two randomized controlled studies evaluating the prophylaxis use of posaconazole (Posanol) in patients at high risk of developing invasive fungal infections.
- ◆ One study was conducted in 602 patients with chemotherapy-induced neutropenia and compared posaconazole (Posanol) with either fluconazole or itraconazole. The study reported that posaconazole (Posanol) is superior to fluconazole or itraconazole in preventing invasive fungal infections, including invasive aspergillosis. However, the Committee noted that there were too few patients randomized to receive itraconazole to allow for a meaningful comparison. Moreover, fluconazole, although the standard comparator at time the study was conducted, may not be the most appropriate comparator due to its lack of antifungal activity against *Aspergillus* species.
- ◆ The second study compared posaconazole (Posanol) to fluconazole in 600 patients who had undergone bone marrow transplant and had graft-versus-host disease. (Graft-versus-host disease is a complication that can occur after a bone marrow transplant in which the newly transplanted material attacks the transplant recipient's body.) This study reported that posaconazole (Posanol) was superior to fluconazole in preventing invasive aspergillosis.
- ◆ At the dose recommended for the prophylaxis of *Aspergillus* and *Candida* infections, posaconazole (Posanol) costs \$141 per day, which is considerably more expensive than fluconazole (\$18-80 per day) and itraconazole (\$4-18 per day). Value for money has not been demonstrated.
- ◆ **Overall, the Committee noted that posaconazole (Posanol) has been shown to be effective in the prevention of *Aspergillus* and *Candida* infections. Although posaconazole (Posanol) has not been shown to provide value for money, the Committee noted that invasive fungal infections are associated with high mortality rates and that prevention may be of value in certain high risk patient subgroups. As such, funding for posaconazole (Posanol) in the prophylaxis of *Aspergillus* and *Candida* infections was recommended through the Exceptional Access Program according to specific criteria.**

Treatment of Invasive Aspergillosis

- ◆ The Committee reviewed a single non-randomized study evaluating the use of posaconazole (Posanol) in a subgroup of 107 patients with probable invasive aspergillosis, and compared them with 86 patients matched from a historical control group (i.e. patients who had been treated with various other antifungal drugs in the past). The study found that more patients treated with posaconazole (Posanol) achieved treatment response compared to those from the historical control group. However, most of the difference in efficacy was due to a difference in partial response as opposed to a complete response. Moreover, the non-randomized design of the study and the use of a historical control group with uncertain treatment strategies make the true relative efficacy of posaconazole (Posanol) difficult to determine.
- ◆ There are no direct comparison data between posaconazole (Posanol) and other antifungal drugs (such as voriconazole) for the treatment of invasive aspergillosis.
- ◆ At the recommended dose for the treatment of invasive aspergillosis, posaconazole (Posanol) costs \$188 per day, which is significantly more expensive than voriconazole (\$190 per day for the first day followed by \$95 per day for the remainder of therapy) and itraconazole (\$16 to \$35 per day).
- ◆ **Overall, the Committee noted that there is no evidence that posaconazole (Posanol) provides any clinical advantage over less costly alternatives in the treatment of invasive aspergillosis. Therefore, it was recommended that posaconazole (Posanol) not be funded for this indication.**

Treatment of Oropharyngeal Candidiasis

- ◆ The Committee reviewed a single randomized controlled study in 350 patients with HIV/AIDS comparing posaconazole (Posanol) to fluconazole in the treatment of oropharyngeal candidiasis. The study found that the two treatments were similar in terms of efficacy and safety outcomes.
- ◆ Comparison studies between posaconazole (Posanol) and other antifungal drugs in the treatment of oropharyngeal candidiasis are not available.
- ◆ At the recommended dose for the treatment of oropharyngeal candidiasis, posaconazole (Posanol) costs \$359 for a 14-day treatment course versus \$64 for a course of fluconazole.
- ◆ **Given that there is no evidence that posaconazole (Posanol) offers any clinical advantage over less costly alternatives in the treatment of oropharyngeal candidiasis, the Committee recommended that funding not be provided for this indication.**

EAP Criteria:

The CED recommended that posaconazole (Posanol) be funded through the Exceptional Access Program (EAP) according to the following clinical criteria:

*–For the prophylaxis of *Aspergillus* and *Candida* infections in patients who have recently (within the last 3 months) undergone allogeneic bone marrow transplant.*

–Duration of treatment is limited to 4 months.

Prophylaxis of invasive fungal infection in patients who have previously (greater than 3 months) undergone an allogeneic stem cell transplant for acute lymphocytic leukemia (ALL) or acute myelogenous leukemia (AML) and are experiencing moderate to severe graft-versus-host disease will be considered on a case-by-case basis.

CEDAC Recommendation:

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

The Canadian Expert Drug Advisory Committee (CEDAC) recommended that posaconazole (Posanol) not be listed.



Ministry of
Health and Long-Term Care
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