## PART III: CONSUMER INFORMATION

**POSANOL®**
**(posaconazole)**

**Solution for Injection 300 mg/vial (18 mg/mL)**

**Delayed-Release Tablets 100 mg**

**Oral Suspension 40 mg/mL**

This leaflet is part III of a three-part "Product Monograph" published when POSANOL® was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about POSANOL®. Contact your doctor or pharmacist if you have any questions about the drug.

Read all of this leaflet carefully before you start taking this medicine. Keep this leaflet; you may need to read it again. This medicine has been prescribed for you personally and you should not pass it on to others. It may harm them, even if their symptoms are the same as yours.

## ABOUT THIS MEDICATION

**What the medication is used for**:

- POSANOL® Solution for Injection, Delayed-Release Tablets and Oral Suspension can be used to prevent invasive fungal infections caused by *Aspergillus* and *Candida* in patients whose immune systems may be weakened due to other medicines or diseases.

- POSANOL® Solution for Injection, Delayed-Release Tablets and Oral Suspension can be used to treat the following types of fungal infections:
  - Infections caused by fungi of the *Aspergillus* family that have not improved during treatment with the anti-fungal medicines amphotericin B or itraconazole or when these medicines have had to be stopped.

- POSANOL® Oral Suspension can be used to treat infections in the mouth or throat area known as "thrush", caused by fungi called *Candida*.

POSANOL® Solution for Injection can be used in patients 18 years of age and older.

POSANOL® Delayed-Release Tablets and Oral Suspension can be used in patients 13 years of age and older.

**What it does**:
POSANOL® belongs to a group of medicines called triazole antifungal agents. These medicines are used to treat a wide variety of fungal infections. POSANOL® works by killing or stopping the growth of some types of fungi that can cause infections in humans.

**When it should not be used**:

- If you are hypersensitive (allergic) to posaconazole or to any of the excipients (see *What the important nonmedicinal ingredients are* section).

- If you are taking the following medicines, as they may interact with POSANOL®:
  - ergot alkaloids
  - cisapride*
  - pimozide
  - quinidine
  - terfenadine*
  - astemizole*
  - certain statin medicines that lower cholesterol (atorvastatin, lovastatin, simvastatin)
  - sirolimus (used in transplant patients)

  *No longer marketed in Canada

**What the medicinal ingredient is**:
Posaconazole

**What the important nonmedicinal ingredients are**:
**POSANOL® Solution for Injection:**
Betadex Sulfobutyl Ether Sodium (SBECD), edetate disodium, hydrochloric acid, sodium hydroxide, and water for injection

**POSANOL® Delayed-Release Tablets:**
Croscarmellose sodium, hydroxypropylcellulose, hypromellose acetate succinate, magnesium stearate, microcrystalline cellulose, Opadry† II Yellow [consists of the following ingredients: polyvinyl alcohol partially hydrolyzed, Macrogol/PEG 3350 (polyethylene glycol 3350), titanium dioxide, talc, and iron oxide yellow], and silicon dioxide.

**POSANOL® Oral Suspension:**
Artificial cherry flavor, citric acid monohydrate, glycerin, liquid glucose, polysorbate 80, purified water, simethicone, sodium benzoate, sodium citrate dihydrate, titanium dioxide, and xanthan gum.

**What dosage forms it comes in**:
**POSANOL® Solution for Injection:**

- Each vial contains 18 mg of posaconazole per mL (300 mg/vial).
- POSANOL® Solution for Injection is a clear, colourless to yellow liquid. Variations of color within this range do not affect the quality of the product.
- This medicine is available in a single use glass vial closed with bromobutyl rubber stopper and aluminium seal.

**POSANOL® Delayed-Release Tablets:**

- Are yellow, coated, capsule-shaped tablets with "100" debossed on one side of the tablet.

**POSANOL® Oral Suspension:**

- Comes in a 40 mg/mL Oral Suspension
- Is a white, cherry-flavored, 105 mL oral suspension packaged in amber glass bottles. A measuring spoon is provided with each bottle for measuring 2.5 and 5 mL doses of the drug product. It is recommended that the spoon is rinsed with water after each administration and before storage.

## WARNINGS AND PRECAUTIONS

**Serious Warnings and Precautions**

- **Drug Interactions (See the *When it should not be used* section and the *Interactions With This Medication* section)**
- **Heart Effects (See the *Warnings and Precautions* section and the *Side Effects and What To Do About Them* section)**
- **Liver Problems (See the *Warnings and Precautions* section and the *Side Effects and What To Do About Them* section)**

BEFORE you use POSANOL® talk to your doctor or pharmacist if:

- You have had an allergic reaction to other antifungal medicines such as ketoconazole, fluconazole, itraconazole or voriconazole.
- You are taking certain drugs that suppress your immune system like cyclosporine and tacrolimus. Serious and rare fatal toxicity from cyclosporine has occurred when taken in combination with POSANOL®. Therefore the doctor may adjust the dosage of these immune suppressants and monitor their blood levels when taken with POSANOL®.
- You are taking vincristine (a medicine used to treat cancer). Toxicity from vincristine has occurred when taken in combination with POSANOL® and serious adverse events have occurred such as:
  - Damage to nervous tissue
  - Seizures
  - *Numbness, pain and weakness in hand and feet due to damage to nerves*
  - *Muscles cramps, nausea, vomiting and confusion can occur due to water retention in body*
  - Obstruction of the intestine (abdominal pain).
- You have or have had liver problems.
- You have kidney problems and your doctor is considering the use of the POSANOL® Solution for Injection product.
- You are taking or have taken any other medicines, even those that are obtained without a prescription. Some medicines may affect the way POSANOL® works or POSANOL® may affect the way they work. Please see the section "Interactions with this medication" for medicines which may interact with POSANOL®.
- You have any of the following conditions: history of heart disease, or an irregular beat.
- You are a nursing mother. Do not breast feed while being treated with POSANOL® unless you are told by your doctor.
- You are pregnant or planning on becoming pregnant. Do not use POSANOL® during pregnancy unless you are told by your doctor. Use effective contraception if you are a woman who could become pregnant. Contact your doctor immediately if you become pregnant while being treated with POSANOL®.
- You think you have galactose intolerance or glucose-galactose malabsorption. Please check with your doctor before starting to take POSANOL® suspension since it contains glucose.

Your doctor may ask you to have your blood tested during treatment with POSANOL®.

Do not drive or operate machinery if you experience sleepiness or blurred vision.

Contact your doctor if you develop severe diarrhea or vomiting, as these conditions may limit the effectiveness of POSANOL®.

## INTERACTIONS WITH THIS MEDICATION

Please inform your doctor or pharmacist if you are taking or have recently taken any other medicines, even those not prescribed. The following list of medicines **must not be taken** (contraindicated) during your course of POSANOL® treatment:

- vincristine (a medicine used to treat cancer)
- cisapride* (a medicine for stomach problems)
- pimozide (a medicine for treating mental illness)
- quinidine (a medicine for treating irregular heart beat)
- ergot alkaloids (a medicine to treat migraines along with other indications)
- terfenadine* (a medicine to treat allergies)
- astemizole* (a medicine to treat allergies)
- certain statin medicines that lower cholesterol (atorvastatin, lovastatin, simvastatin)
- sirolimus (used in transplant patients)

*No longer marketed in Canada

Certain medications may affect the levels of POSANOL® and these combinations should be avoided if possible. Tell your doctor if you are taking or if you plan to stop taking any of the following:

- rifabutin or rifampin (a medicine to treat bacterial infections like tuberculosis)
- phenytoin (a medicine to treat seizures)
- cimetidine (a medicine to treat stomach ulcers) - pertains only to POSANOL® Oral Suspension
- proton pump inhibitors (e.g., esomeprazole) - pertains only to POSANOL® Oral Suspension
- efavirenz (a medicine to treat HIV infection)

POSANOL® may cause changes in the blood levels of certain medications you may be using. Tell your doctor if you are taking or plan to stop taking any of the following medicines before starting treatment with POSANOL®, as dose adjustment or monitoring may be needed:

- vinca alkaloids (used to treat cancer)
- cyclosporine (used in transplant patients)
- tacrolimus (used in transplant patients)
- rifabutin (a medicine to treat bacterial infections)
- midazolam (used as a sedative to help sleep)
- statins (used to treat high cholesterol)

- calcium channel blockers (used to treat high blood pressure)
- digoxin (used to treat heart failure)

## PROPER USE OF THIS MEDICATION

POSANOL® must only be used as directed by your doctor.
Your doctor will monitor your response and condition to determine what POSANOL® dose is needed.

Do not switch between POSANOL® Delayed-Release Tablets and POSANOL® Oral Suspension without talking to your doctor first, as the dosing is different for the 2 formulations.

**POSANOL® Solution for Injection:**

- This solution will be administered to you by a healthcare professional by a slow intravenous (in the vein) infusion.
- The usual dose is 300 mg twice a day on the first day, then 300 mg once a day, thereafter.
- POSANOL® Solution for Injection will be diluted to the correct concentration by your pharmacist or nurse.
- The length of treatment may depend on the type of infection that you have and may be individually adapted for you by your doctor.

**POSANOL® Delayed-Release Tablets:**

- Take POSANOL® Delayed-Release Tablets exactly as prescribed by your doctor.
- Take POSANOL® Delayed-Release Tablets for as long as your doctor tells you.
- Take POSANOL® Delayed-Release Tablets by mouth, with or without food.
- POSANOL® Delayed-Release Tablets must be swallowed whole. Use plenty of water if you have some difficulty swallowing.
- Do not crush, chew, break, or dissolve the tablets.

**POSANOL® Oral Suspension:**

- Shake POSANOL® Oral Suspension well before each use.
- Take POSANOL® Oral Suspension exactly as prescribed by your doctor.
- Take POSANOL® Oral Suspension for as long as your doctor tells you.
- Take POSANOL® Oral Suspension with a meal or nutritional supplement.

**Usual dose**:
**POSANOL® Solution for Injection:**

| Indication | Dose |
|---|---|
| Prevention of Certain Serious Fungal Infections | Take 300 mg (300 mg Solution for Injection) twice a day on the first day. After the first day, take 300 mg (300 mg Solution for Injection) once a day. |
| Treatment of Certain Refractory (not successfully treated by other therapies) Fungal Infections | Take 300 mg (300 mg Solution for Injection) twice a day on the first day. After the first day, take 300 mg (300 mg Solution for Injection) once a day thereafter. |

**POSANOL® Delayed-Release Tablets:**

| Indication | Dose |
|---|---|
| Prevention of Certain Serious Fungal Infections | Take 300 mg (three 100 mg tablets) twice a day on the first day. After the first day, take 300 mg (three 100 mg tablets) once a day. |
| Treatment of Certain Refractory (not successfully treated by other therapies) Fungal Infections | Take 300 mg (three 100 mg tablets) twice a day on the first day. After the first day, take 300 mg (three 100 mg tablets) once a day thereafter. |

**POSANOL® Oral Suspension:**
Take each dose of POSANOL® Oral Suspension with food or with a nutritional supplement if you are unable to eat a full meal, to help absorb the medicine well.

| Indication | Dose |
|---|---|
| Prevention of Certain Serious Fungal Infections | Take 200 mg (one 5 mL spoonful) three times a day with food or nutritional supplement. |
| Treatment of Certain Refractory (not successfully treated by other therapies) Fungal Infections | Take 400 mg (two 5 mL spoonfuls) of the suspension twice a day with food or with a nutritional supplement. If you are not able to take food or nutritional supplement, your doctor will tell you to take 200 mg (one 5 mL spoonful) four times a day. |
| Initial Treatment of Thrush | On the first day of treatment take 100 mg (2.5 mL) twice a day. After the first day, take 100 mg (2.5 mL) once a day. Always take with food or nutritional supplement. |

Your doctor will determine how long the duration of your treatment will be and may change your dose depending on your condition. Do not stop treatment early because your infection may not be fully cured. If you are given POSANOL® for preventing infections, take the full course as prescribed by your doctor, as your immune system may still be weakened and you may need treatment to prevent an infection from occurring even if you feel well.

**Overdose**:
Take your bottle of POSANOL® with you.

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

**Missed dose**:
If you miss taking a dose of POSANOL®, take it as soon as possible. However, if it is almost time for the next dose, skip the missed dose and go back to the regular dosing schedule. Do not take a double dose to make up for the forgotten dose.

## SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all medicines, POSANOL® can have side effects. If side effects do occur, most are likely to be minor and temporary. Please tell your doctor or healthcare professional if you experience any reaction that is continuous, bothersome or you think is serious.

**POSANOL® Solution for Injection:**
The side effects reported for POSANOL® Solution for Injection were similar to those reported for POSANOL® Oral Suspension.

The most commonly reported side effect for POSANOL® Solution for Injection was diarrhea.

**POSANOL® Delayed-Release Tablets:**
The side effects reported for POSANOL® Delayed-Release Tablets were similar to those reported for POSANOL® Oral Suspension.

The most commonly reported side effects for POSANOL® Delayed-Release Tablets were diarrhea, fever, and nausea.

**POSANOL® Oral Suspension:**
Common side effects (occurring in at least 1 in 100 patients) are: Headache; dizziness; numbness or tingling; sleepiness; feeling or being sick; loss of appetite; stomach pain; diarrhea; upset stomach; nausea; vomiting; flatulence (excessive gas in the digestive tract); dry mouth; abnormal liver function tests; rash; weakness; tiredness; a decrease in white blood cells (that can increase the risk of infections); fever; abnormal amounts of salts in the blood.

Other reported side effects include infrequent cases of liver reactions (e.g**.,** mild to moderate elevations in liver tests called ALT, AST, alkaline phosphatase, total bilirubin, and/or clinical hepatitis). The elevations in liver function tests were generally reversible when POSANOL® was stopped, and in some instances these tests went back to normal without stopping POSANOL®. These effects rarely required stopping POSANOL®. Rarely, more severe liver reactions including cholestasis (back-up of bile in the liver) or liver failure were reported in patients with serious underlying medical conditions (e.g., leukemia or other blood cancers) during treatment with POSANOL®. As POSANOL® has been known to affect the liver in patients who already have liver problems, your doctor may wish to monitor the function of your liver by doing blood tests. Some of the symptoms of liver problems include yellowing of the eyes or skin, "flu-like" feeling or feeling more tired than usual, stomach pains, light colored stools, nausea or vomiting. Please let your doctor know if you have any of these symptoms.

Uncommon and rare treatment related serious or medically significant adverse events reported during clinical trials with posaconazole have included poor functioning of the adrenal gland; heart problems including very fast heartbeat, very slow heartbeat, irregular heartbeat including Torsade de Pointes; abnormal findings on heart tests (like ECGs that show heart rhythm), severe allergic reactions, including widespread blistering rash and skin peeling. There have been rare cases of hemolytic uremic syndrome (a serious problem with the blood vessels causing low red blood cell counts and kidney failure) and thrombotic thrombocytopenic purpura (a serious blood problem causing bruising, confusion, fever, and low blood clotting cell counts), which have been reported primarily among patients who had been receiving concomitant cyclosporine or tacrolimus for management of transplant rejection or graft vs. host disease.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

**SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM**

| Symptom / effect | | Talk with your doctor or pharmacist | | Stop taking drug and seek immediate emergency medical attention |
|---|---|---|---|---|
| | | Only if severe | In all cases | |
| Common | **Blood problems**, including decreased white blood cells, and other blood cell types, with symptoms such as increased infection, fever, bleeding, bruising. | | ✓ | |
| Infrequent | **Liver problems**, including liver failure, with symptoms such as dark colored urine, pale stools, yellowing of the skin and eyes, abdominal pain, nausea, vomiting. | | | ✓ |
| Uncommon | **Heart problems** such as very slow, fast or irregular heartbeat. | | | ✓ |
| Rare | **Severe allergic reaction** with symptoms such as severe skin blistering, peeling, rash, swollen lips, mouth and throat, difficulty in breathing. | | | ✓ |

This is not a complete list of side effects. For any unexpected effects while taking POSANOL®, contact your doctor or pharmacist.

## HOW TO STORE IT

Keep out of the reach and sight of children. Do not freeze. Do not use this product after the expiry date stated on the label.

**POSANOL® Solution for Injection:**
The healthcare professional will store the POSANOL® Solution for Injection at 2 to 8°C until preparation of the infusion. After preparation, the diluted solution can be stored up to 24 hours at 2 to 8°C.

**POSANOL® Delayed-Release Tablets:**
Store at room temperature (15 to 30°C).

**POSANOL® Oral Suspension:**
Store at room temperature (15 to 30°C). Once opened, use the suspension within 4 weeks.

**REPORTING SIDE EFFECTS**

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345

*NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.*

## MORE INFORMATION

If you want more information about POSANOL®:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Consumer Information by visiting the Health Canada website or the Merck Canada website www.merck.ca or by calling Merck Canada a 1-800-567-2594

To report an adverse event related to POSANOL®, please contact 1-800-567-2594.

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