

VI.2 Elements for a Public Summary

[Product Name] 40 mg/ml oral suspension

VI.2.1 Overview of disease epidemiology

Fungi (yeasts) are small organisms that feed by breaking down tissue. In humans, fungi typically attack skin, hair and nails. Fungal spores can be spread through human-to-human contact, but also through contact with infected animals, objects (e.g. towels) or soil. In general, elderly patients, those with suppressed immune system, with type 1 diabetes, who are overweight and who have poor circulation are at a higher risk of fungal infections.

Invasive aspergillosis

Aspergillosis is an infection caused by mold *Aspergillus*. The symptoms resulting from aspergillosis infection usually affect the breathing system (such as lungs). In some people, *Aspergillus* triggers an allergic reaction. The most serious form of aspergillosis, invasive aspergillosis, occurs when the infection spreads to blood vessels and to other body parts.

Fusariosis

Fusariosis is caused by fungi of the *Fusarium* family and typically affects the skin. It is common in cancer patients who are immunocompromised due to anti-cancer medication.

Chromoblastomycosis and mycetoma

Mycetoma typically affects the skin; feet are the most common site of infection. It is typically chronic and may, in severe cases, result in amputation of the infected body part. It is typically found in India, Mexico, Saudi Arabia, Venezuela and Sub-Saharan Africa. Mycetoma is seen most frequently in men between the ages of 20 and 40 years and is found in farmers and workers in rural areas.

Chromoblastomycosis is also a skin infection. It is usually chronic, slowly progressive and localised, most frequent in the foot. Crusted lesions typically appear at the infection site. It is more common in tropical regions (e.g. Madagascar).

Coccidioidomycosis

Also known as valley fever, coccidioidomycosis is caused by fungus *Coccidioides*, found in the soil in North and South America. The infection may cause fever, chest pain and coughing.

Oropharyngeal candidiasis

Candidiasis (thrush) is an infection caused by *Candida* species (most often *Candida albicans*). Symptoms include white spots in the mouth, redness in the mouth and taste loss / unpleasant feeling in the mouth. *Candida* species are the most common cause of fungal infections in the patients having an impaired immune system. Candidal infections are also one of the most common infections acquired in hospital.

VI.2.2 Summary of treatment benefits

[Product Name] contains a medicine called posaconazole. This belongs to a group of medicines called “antifungals”. It is used to prevent and treat many different fungal infections.

This medicine works by killing or stopping the growth of some types of fungi that can cause infections.

[Product Name] can be used in adults to treat the following types of fungal infections when other antifungal medicines have not worked or you have had to stop taking them:

- 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;
- infections caused by fungi of the *Fusarium* family that have not improved during treatment with amphotericin B or when amphotericin B has had to be stopped;
- infections caused by fungi that cause the conditions known as “chromoblastomycosis” and “mycetoma” that have not improved during treatment with itraconazole or when itraconazole has had to be stopped;
- infections caused by a fungus called *Coccidioides* that have not improved during treatment with one or more of amphotericin B, itraconazole or fluconazole or when these medicines have had to be stopped.
- Infections in the mouth or throat area (known as “thrush”) caused by fungi called *Candida*, which were not previously treated.

This medicine can also be used to prevent fungal infections in adults who are at high risk of getting a fungal infection, such as:

- patients who have a weak immune system due to having chemotherapy for “acute myelogenous leukemia” (AML) or “myelodysplastic syndromes” (MDS)
- patients having “high-dose immunosuppressive therapy” after “hematopoietic stem cell transplant” (HSCT).

VI.2.3 Unknowns relating to treatment benefits

The safety and efficacy of posaconazole in children aged below 18 years have not been established.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
<p>Liver problems</p> <p>(Hepatic events – elevated liver enzymes, hepatotoxicity, hepatic failure, hepatitis)</p>	<p>Various liver problems may occur in patients treated with posaconazole. Elevated liver function tests were generally reversible on discontinuation of therapy and in some instances these tests normalised without interruption of therapy. Rarely, more severe liver reactions have been reported. Posaconazole should be used with caution in patients with liver impairment due to limited clinical experience and the possibility that posaconazole plasma levels may be higher in these patients.</p>	<p>Your doctor may need to perform liver function tests before and during therapy with posaconazole.</p> <p>The dose of posaconazole may need to be adjusted by your doctor based on these tests.</p>
<p>Blood coagulation disorder and haemolytic uraemic syndrome (when red blood cells breakup, which may happen with or without kidney failure)</p> <p>(Blood - thrombotic thrombocytopenic purpura, haemolytic uraemic syndrome)</p>	<p>Blood coagulation disorder (thrombotic thrombocytopenic purpura) and haemolytic uraemic syndrome (when red blood cells breakup, which may happen with or without kidney failure) may occur in up to 1 in 1000 patients treated with posaconazole.</p>	<p>Tell your doctor if you have or have ever had any blood problems.</p> <p>Inform your doctor if you notice any of the following symptoms:</p> <ul style="list-style-type: none"> • fatigue • bruising • urination problems • abdominal pain and/or diarrhoea

Abnormal heart rhythm (Cardiac – Torsades de pointes)	Torsades de pointes, an abnormal heart rhythm that can lead to serious heart problems, may occur when posaconazole is taken together with terfenadine, astemizole, cisapride, pimozide, halofantrine or quinidine.	Tell your doctor if you are taking any other drugs at the same time as [Product Name]. [Product Name] should not be co-administered with terfenadine, astemizole, cisapride, pimozide, halofantrine or quinidine.
Interactions with other drugs (General – drug interaction)	Multiple drug interactions are known for posaconazole. These may affect the level of posaconazole in your body and the effect it has on the treating disease. The risk of side effects may be increased in some cases.	Tell your doctor if you are taking any other drugs at the same time as [Product Name]. Your doctor may decide to adjust the dosage of [Product Name] or of other medicines so as to minimise the chance of adverse events.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Blood – Agranulocytosis, aplastic anaemia	Patients treated with posaconazole may be at an increased risk of developing aplastic anaemia (deficiency in all blood cell types). No further data is available. No clinical data are available for the risk agranulocytosis.
Cardiac – QTc prolongation, heart failure, myocardial infarction	Various heart problems may occur with posaconazole therapy.
Psychiatric – depression, suicide	Posaconazole therapy may lead to depression in up to 1 in 1000 patients treated with posaconazole. No further data is available. No clinical data are available for the risk suicide.
Endocrine – adrenal insufficiency	Posaconazole therapy may lead to adrenal insufficiency (adrenal glands not producing adequate amounts of steroid hormones) in up to 1 in 1000 patients treated with posaconazole. No further data is available.
CNS – convulsions, cerebral ischaemia, cerebral hemorrhage	Various central nervous system problems, such as seizures, may occur with posaconazole therapy.
Respiratory – pulmonary haemorrhage	Patients treated with posaconazole may be at an increased risk of developing bleeding from the lung. No further data is available.
Vascular – hypertension, venous thrombosis, arterial thrombosis	Various vascular problems (high blood pressure) may occur with posaconazole therapy.

Metabolism – hypokalaemia	Low potassium levels may occur in up to 1 in 10 patients treated with posaconazole.
Visual – photopsia, visual brightness, visual disturbances	Visual disturbances may occur with posaconazole therapy.
Neoplasms – Occurrence of any neoplasm/malignancy, especially: Hepatic adenoma; Hepatic neoplasm; Adrenal adenoma; Adrenal neoplasm; Pheochromocytoma	No evidence of an increased risk of neoplasms in patients using posaconazole has been established.
Infections – Fungal infections	Patients who have severe diarrhoea or vomiting should be monitored closely for breakthrough fungal infections.

Missing information

Risk	What is known
Experience in children	The safety and efficacy of posaconazole in children aged below 18 years have not been established

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

No post-authorisation studies have been imposed or are planned.

VI.2.7 Summary of changes to the Risk Management Plan over time

Not applicable.