Vancomycin Orion

18.1.2016, Version 2

Public Summary of the Risk Management Plan

VI.2 Elements for a Public Summary

Vancomycin Orion is intravenously administered glycopeptide antibiotic. It is indicated in the treatment of severe, potentially life-threatening infections caused by microorganisms which can resist other effective antimicrobial medicines (such as penicillins and cephalosporins), or which have failed to respond to such treatment.

The use of vancomycin should be restricted to cases with a specific indication, to minimize the risk of resistance development.

Vancomycin is used to treat various severe infections of the lining or valves of the heart, lungs, bone or soft tissue (flesh) caused by susceptible microorganisms. It can also be given to before some surgical procedures to prevent infections.

Vancomycin Orion is a generic medicine. Its benefits and risks are taken as being the same as the reference medicine's.

VI.2.1 Overview of disease epidemiology

Endocarditis, also called infective endocarditis, is an inflammation of the inner lining or valves of the heart. The most common type, bacterial endocarditis, occurs when microbes enter the heart. These microbes come through bloodstream from another part of the body, often the mouth. Bacterial endocarditis can damage heart valves. If the condition is untreated, it can be life-threatening. It is rare in healthy hearts. Risk factors include having an abnormal or damaged heart valve, an artificial heart valve or congenital heart defects.

Like other parts of the body, bones can get infected. The infections are usually bacterial, but can also be fungal. They may spread to the bone from nearby skin or muscles, or from another part of the body through the bloodstream. People who are at risk for bone infections include those with diabetes, poor circulation, or recent injury to the bone or patients going through hemodialysis.

Pneumonia is an infection in one or both of the lungs. Many microbes, such as bacteria, viruses, and fungi, can cause pneumonia. Symptoms of pneumonia vary from mild to severe.
People most at risk are older than 65 or younger than 2 years of age, or patients who already have health problems.

Infection of the skin and underlying soft tissue is called cellulitis. The infection is usually caused by bacteria, such as staphylococci or streptococci that are commonly present on the skin or inner surface of the nose or mouth of otherwise normal and healthy people. The infection develops when there is a break in the skin, such as a wound or injury, which may be minor or even unnoticed. This allows bacteria to enter the skin and grow, causing infection and swelling. Many cases of cellulitis are mild and heal completely with antibiotic treatment. However, some cases of cellulitis can be severe and lead to generalized infection.

VI.2.2 Summary of treatment benefits

Vancomycin helps to fight severe and life-threatening bacterial infections which cannot be treated with other antibiotics or which have failed to respond to such treatment. Vancomycin kills bacteria by inhibiting bacteria's cell-wall biosynthesis. It also impairs permeability of the bacterial cell membrane and RNA synthesis.

VI.2.3 Unknowns relating to treatment benefits

Not applicable.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	**What is known**	**Preventability**
Important identified risks:		
Toxic effects on ears (Ototoxicity)	Toxic effect on ears, which may be transient or permanent, has been reported in patients with prior deafness; patients who have received excessive intravenous doses of vancomycin; or in patients who receive concomitant treatment with some other medicine with toxic effects on ears, such as an aminoglycoside antibiotic. Deafness may be preceded by tinnitus (ringing in ears). Experience with other antibiotics suggests that deafness may be progressive despite treatment cessation.	To reduce the risk of ototoxicity, blood levels should be determined periodically, and periodic testing of auditory function is recommended. Vancomycin should be avoided in patients with previous hearing loss. Older patients are particularly susceptible to auditory (hearing) damage and should undergo s tests for auditory function before and after the treatment. Concurrent or sequential use of other neurotoxic substances should be avoided.
Toxic effects on kidneys (Nephrotoxicity)	Intravenously administered vancomycin is excreted mostly with urine. Adverse effects on kidney have been reported, such as kidney function disorder manifested primarily by increased serum creatinine or serum urea concentrations and, rarely, certain type of inflammation in kidneys (interstitial nephritis) and acute kidney failure. The risk of toxicity is increased by high concentrations of vancomycin in blood or long-term therapy	The dose should be reduced according to the degree of kidney impairment. Kidney function tests should be performed regularly. Regular monitoring of the blood levels of vancomycin is indicated in high dose therapy and long-term use, particularly in patients with kidney dysfunction, as well as in concurrent administration of nephrotoxic substances,

Risk	What is known	Preventability
Heart stops beating (Cardiac arrest)	Rapid intravenous administration of this medicinal product may be associated with severely low blood pressure, which may lead to shock and in rare cases to cardiac arrest i.e. heart stops beating. Vancomycin may potentiate heart muscle depression induced by anaesthesia.	Vancomycin should be infused slowly in a dilute solution over a minimum period of 60 minutes to avoid rapidly occurring infusion-related reactions. Discontinuation of the infusion usually results in prompt cessation of these reactions. When used during anaesthesia, doses must be well-diluted and administered slowly with close heart monitoring. The patient should remain in the same posture until the infusion is completed.
Anaphylaxis	Rare cases of severe acute hypersensitivity reactions (anaphylactic reaction) have been reported. Concurrent administration of vancomycin and anaesthetic agents has been associated with redness, histamine-like flushing, and anaphylactoid reactions. These effects may be reduced by administering vancomycin over 60 minutes before induction of anaesthesia. Patients who are allergic/hypersensitive to teicoplanin (another antibiotic) may be allergic to vancomycin as well.	This medicinal product must not be given to patient who is allergic/hypersensitive to vancomycin. Caution should be administered when treating patients who are allergic to some other antibiotic, especially teicoplanin. In case of severe acute hypersensitivity reactions (e.g. anaphylaxis), the vancomycin treatment must be discontinued immediately and the usual appropriate emergency treatment (e.g. antihistamines, corticosteroids, and – if needed – artificial respiration) initiated. If the administration of vancomycin is required for surgical prophylaxis, it is advisable to administer the anaesthetic agents after completion of the vancomycin infusion.
Overgrowth of microbes (e.g. bacteria or fungi) that are not sensitive to vancomycin (Overgrowth of non-susceptible organisms)	Use of antibiotics may sometimes result in overgrowth of microbes (superinfection) that do not react to the antibiotic in concern. E.g. overgrowth of bacteria against which vancomycin has no effect.	Guidance regarding appropriate use of antibiotic should be followed. Patients should be regulatory monitored.

Risk	What is known	Preventability
		If a superinfection develops during therapy, appropriate treatment measures should be taken.
Bowel inflammation (colitis) associated with antibiotic therapy (Antibiotic associated colitis)	Antibiotic-associated bowel inflammation (pseudomembranous colitis) that might be life-threatening has been reported. Symptoms of antibiotic-associated colitis can be severe persistent diarrhoea.	It is important to contact doctor in case of diarrhoea during antibiotic therapy or soon after. Medicines that slow down bowel movements (certain medicines against diarrhoea) should not be used.
Severe skin reactions	Severe skin reactions have been reported in association with vancomycin therapy. Symptoms or signs can be e.g. progressive skin rash often with blisters or mucosal lesions. If untreated, condition can be life-threatening.	If symptoms or signs of severe skin reaction appear, vancomycin therapy should be discontinued immediately and appropriate treatment measures initiated. Doctor should be informed before treatment if the patient has a history of severe skin reactions is association with medicinal therapy.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Use in children (Pediatric patients)	Vancomycin should be used with particular caution in premature infants and children, because of their immature kidneys and the possible increase in serum vancomycin concentrations. The blood vancomycin concentrations should therefore be monitored closely. Specific dosing recommendations are given to child patients. Vancomycin passes into breast milk and can potentially affect the breastfed baby. Caution should be taken in administration of vancomycin to breast-feeding mothers because of potential adverse reactions in the infant (disturbances in the intestinal flora with diarrhoea, colonisation with yeast-like fungi and possibly sensibilisation). Discontinuation of breast-feeding should be considered.
Toxic effects on blood cells (Hematotoxicity)	Low amount of platelets and low amount/lack of blood cells are listed possible adverse drug reactions. All patients receiving vancomycin should undergo periodic blood tests.

Risk	What is known (Including reason why it is considered a potential risk)
	Especially in patients receiving vancomycin long-term, or concurrently with other medications that may cause similar kind of effects on blood cells, the white blood cell count should be monitored regularly.

Missing information

Risk	What is known
Administration during pregnancy (Pregnancy)	There are no adequate data from the use of vancomycin in pregnant patients. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity during development. Vancomycin crosses the placenta and a potential risk for unborn child cannot be excluded. Vancomycin should be given during pregnancy only if clearly needed and after a careful risk/benefit evaluation.

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) 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.

The Summary of Product Characteristics and the Package leaflet for Vancomycin Orion can be found in the authority's web page

This medicine has no additional risk minimisation measures>

VI.2.6 Planned post authorisation development plan

Not applicable.

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

Major changes to the Risk Management Plan over time

Version	Date	Safety Concerns	Comment
2	18.1.2016	Added new important identified risk: Severe skin reactions	In addition contents of the RMP have been modified based on updated SPC.