VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Palonosetron 250 micrograms solution for injection is a medicine that is used to prevent nausea (feeling sick) and vomiting caused by chemotherapy (medicines to treat cancer) in adults.

The so called chemotherapy-induced nausea and vomiting (CINV) is distressing for patients and may discourage them from continuing with chemotherapy. In case CINV becomes serious loss of fluid, metabolic disturbances and inflammation of the lung may occur. As a consequence, control of nausea and vomiting plays an important part in the overall treatment success for cancer patients.

CINV are common adverse effects of chemotherapy that may occur in 30% to > 90% of patients within the first 24 hours of the start of a chemotherapy that is either a moderate or a strong trigger of nausea and vomiting. Available data showed that patients that suffered from nausea and vomiting after one chemotherapy dose are at increased risk of subsequent CINV.

VI.2.2 Summary of treatment benefits

Palonosetron solution for injection has been studied in three main studies involving 1,842 adults receiving chemotherapy that was a strong or a moderate trigger of nausea and vomiting. Palonosetron injected at two different doses, was compared with ondansetron and dolasetron (other medicines of the same type).

All of the studies measured the number of patients who did not vomit after receiving chemotherapy.

Palonosetron was as effective as the comparator medicines. With chemotherapy that was a strong trigger of nausea and vomiting, 59% of the patients receiving palonosetron did not vomit in the 24 hours after chemotherapy (132 out of 223), compared with 57% of the patients receiving ondansetron (126 out of 221). With chemotherapy that was a moderate trigger of nausea and vomiting, 81% of the adults receiving palonosetron did not vomit in the 24 hours after chemotherapy (153 out of 189) compared with 69% of those receiving ondansetron (127 out of 185). When it was compared with dolasetron, these values were 63% for palonosetron (119 patients out of 189) and 53% for dolasetron (101 patients out of 191).

Palonosetron solution for injection has also been investigated in one study involving 502 children aged 64 days to 16.9 years, receiving chemotherapy that was a strong or a moderate trigger of nausea and vomiting, where palonosetron was compared with ondansetron. In this study, 59% of the children receiving palonosetron solution for injection at a dose of 20 micrograms/kilogram did not vomit in the 24 hours after chemotherapy (98 out of 165), which was the same percentage as seen in adult patients receiving ondansetron (95 out of 162).

VI.2.3 Unknowns relating to treatment benefits

It is not known whether palonosetron will cause any harmful effects when used during pregnancy. Therefore palonosetron should not be used in pregnant woman unless considered essential by the physician.

It is unknown if palonosetron is found in breast milk. Thus, breast feeding should be discontinued during therapy.

The safety and efficacy of palonosetron in children aged less than 1 month have not been established. No data are available. There are limited data on the use of palonosetron in the prevention of nausea and vomiting in children under 2 years of age.

There are no data concerning the effect of palonosetron on fertility.

No data are available for patients with end stage renal disease undergoing haemolysis.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Increased large bowel transit time (Sever constipation impaction)	Two cases of constipation with faecal impaction requiring hospitalisation have been reported in association with palonosetron 750 micrograms. Constipation is a common side effect that may affect up to 1 in 10 people.	Before starting palonosetron, patients should tell their physician if they have acute bowel obstruction or a history of repeated constipation. After initiation of treatment, these patients should be monitored.
Severe allergic reaction (Severe hypersensitivity reaction)	Allergic reactions to palonosetron are very rare adverse reactions that affect less than 1 in 10,000 patients.	Palonosetron should not be used if a patient is allergic to palonosetron or any of the other ingredients in this medicine.

Important potential risks

Risk	What is known	Preventability
Life-threatening excess of the substance serotonin in the central nervous and/or peripheral nervous system (serotonin syndrome)	There have been reports of serotonin syndrome following administration of drugs that block the action of the chemical serotonin (serotonin antagonists) when given either alone or concomitantly to other serotonergic drugs. Symptoms of severe serotonin syndrome are high fever, convulsions, irregular heartbeat and unconsciousness.	Before starting palonosetron, patients should tell their physician if they are taking, have recently taken or might take any other medicines, including drugs called selective serotonin reuptake inhibitors (SSRIs) used to treat depression and/or anxiety such as fluoxetine, paroxetine, sertraline, fluvoxamine, citalopram, escitalopram or drugs called serotonin noradrenaline reuptake inhibitors (SNRIs) used to treat depression and/or anxiety such as venlafaxine, duloxetine. An appropriate observation of patients for symptoms indicative for an excess of serotonin in the body is advised.

Risk	What is known	Preventability
Electrocardiogram abnormalities (QT/QTc prolongation)	Alterations in heart rhythm due to prolongation of a certain part of the heart beating cycle, the so called QT-interval, is an uncommon side effect that may affect up to 1 in 100 people.	Before starting palonosetron, patients should tell their physician if they are taking other medicines that may induce an abnormal heart rhythm (such as amiodarone, nicardipine, quinidine, moxifloxacin, erythromycin, haloperidol, chlorpromazine, quetiapine, thioridazine, domperidone), if they have a personal or family history of alterations in heart rhythm (QT prolongation), if they have other heart problems or if they have an imbalance of certain minerals in their blood such as potassium and magnesium which has not been treated. It is advised that an imbalance of certain minerals such as hypokalaemia and hypomagnesaemia (blood level of potassium or magnesium too low) should be corrected prior to administration of palonosetron.

Missing information

Risk	What is known
Use during pregnancy and breast-feeding	Pregnancy: It is not known whether palonosetron will cause any harmful effects when used by pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy or development of the baby. If a patient is pregnant or thinks she might be, it is recommended not to administer palonosetron unless it is clearly necessary. Breast-feeding: It is not known if palonosetron is found in breast milk. If a patient is breast-feeding, it is recommended to ask the doctor or pharmacist for advice before using palonosetron.
Effect in children aged less than 1 month (potential off-label use for CINV prevention)	The safety and efficacy of palonosetron in children aged less than 1 month have not been established. No data are available.
Effect on fertility	It is not known whether palonosetron has any harmful effects on reproduction (fertility).

Risk	What is known
Use in patients with end stage kidney disease undergoing haemodialysis	No recommendation on posology can be made for patients with end stage renal disease undergoing haemodialysis.

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.

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

Not applicable