RMP version 1.1

Part VI: Summary of risk management plan

Palonosetron Fresenius Kabi 250 micrograms, solution for injection Palonosetron Fresenius Kabi 250 micrograms, solution for injection in pre-filled syringe

This is a summary of the RMP for Palonosetron Fresenius Kabi. The RMP details important risks of Palonosetron how these risks can be minimised, and how more information will be obtained about Palonosetron risks and uncertainties (missing information).

Palonosetron SmPC and its PL give essential information to healthcare professionals and patients on how Palonosetron should be used.

Important new safety concerns or changes to the current ones will be included in updates of the Palonosetron RMP.

I. The medicine and what it is used for

Palonosetron Fresenius Kabi 250 micrograms solution for injection

Palonosetron is authorized in adults for:

- the prevention of acute nausea and vomiting associated with highly emetogenic cancer chemotherapy
- the prevention of nausea and vomiting associated with moderately emetogenic cancer chemotherapy.

Palonosetron is authorized in paediatric patients 1 month of age and older for:

- the prevention of acute nausea and vomiting associated with highly emetogenic cancer chemotherapy and prevention of nausea and vomiting associated with moderately emetogenic cancer chemotherapy.

Palonosetron Fresenius Kabi 250 micrograms solution for injection in pre-filled syringe

Palonosetron is authorized in adults for:

- the prevention of acute nausea and vomiting associated with highly emetogenic cancer chemotherapy
- the prevention of nausea and vomiting associated with moderately emetogenic cancer chemotherapy.

It contains palonosetron (as hydrochloride) as active substance and it is administered by intravenous route only.

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of Palonosetron Fresenius Kabi, together with measures to minimise such risks and the proposed studies for learning more about Palonosetron Fresenius Kabi risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the PL and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute *routine risk minimisation* measures.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including PSUR assessment so that immediate action can be taken as necessary. These measures constitute routine pharmacovigilance activities.

If important information that may affect the safe use of Palonosetron is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Palonosetron Fresenius Kabi are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Palonosetron. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine).

List of important risks and missing information	
Important identified risks	- Severe constipation - Severe hypersensitivity reactions
Important potential risks	- QT/ QTc prolongation - Convulsive events - Serotonin syndrome
Missing information	- Effect in pregnancy - Effect in lactating women - Effects on fertility - Use in paediatric population - Effects in patients with end stage renal disease undergoing haemodialysis

II.B Summary of important risks

Important identified risk – Severe constipation	
Evidence for linking the risk to the medicine	Reports of constipation from Palonosetron have been derived from sources such as spontaneous data sources including published literature
Risk factors and risk groups	Patients with a history of constipation or signs of subacute intestinal obstruction.
Risk minimization measures	Routine risk minimisation measures Guidance and safety information in product label of Palonosetron Additional risk minimisation measures Not applicable

Important identified risk – Severe hypersensitivity reactions	
Evidence for linking the risk to the medicine	Reports of severe hypersensitivity reactions have been derived from sources such as spontaneous data sources, including published literature.
Risk factors and risk groups	Patients with history of allergic reaction or patients who are hypersensitive to the active substance or to any of the excipients.
Risk minimization measures	Routine risk minimisation measures Guidance and safety information in product label of Palonosetron Additional risk minimisation measures Not applicable

Important Potential Risk – QT/ QTc prolongation	
Evidence for linking the risk to the medicine	Reports of QT/ QTc prolongation from Palonosetron Kabi have been derived from multiple sources such as non-clinical findings confirmed by clinical data and published literature.
Risk factors and risk groups	In patients with a personal or family history of QT prolongation, electrolyte abnormalities, congestive heart failure, bradyarrhythmias, conduction disturbances and in patients taking anti-arrhythmic agents or other medicinal products that lead to QT prolongation or electrolyte abnormalities.
Risk minimization measures	Routine risk minimisation measures Guidance and safety information in product label of Palonosetron Additional risk minimisation measures Not applicable

Important Potential Risk – Convulsive events	
Evidence for linking the risk to the medicine	In few cases, seizure has occurred after the injection of 5-HT3 receptor antagonists, which was reported to be suspected as the cause of the seizure. Although rare, there is a risk of seizure by the administration of 5-HT3 receptor antagonists. Even though seizure seems to be a temporary benign complication, it may cause a severe problem in some patients including cardiopulmonary compromised patients. Reports of convulsive events with Palonosetron have been derived from published literature.
Risk factors and risk groups	Patients with history of epilepsy, elderly age, blood-brain barrier dysfunction and several concomitant neurological diseases
Risk minimization measures	Routine risk minimisation measures Guidance and safety information in product label of Palonosetron Additional risk minimisation measures Not applicable

Important Potential Risk – Serotonin syndrome	
Evidence for linking the risk to the medicine	As per RSI, there have been reports of serotonin syndrome with the use of 5-HT3 antagonists either alone or in combination with other serotonergic drugs (including selective serotonin reuptake inhibitors (SSRI) and serotonin noradrenaline reuptake inhibitors (SNRIs). Reports of serotonin syndrome with Palonosetron have been derived from published literature.
Risk factors and risk groups	Concomitant use of 5-HT3 antagonists and other serotonergic drugs including: • SSRIs (selective serotonin reuptake inhibitors) used to treat depression and/or anxiety including fluoxetine, paroxetine, sertraline, fluvoxamine, citalopram, escitalopram; • SNRIs (serotonin noradrenaline reuptake inhibitors) used to treat depression and/or anxiety including venlafaxine, duloxetine
Risk minimization measures	Routine risk minimisation measures Guidance and safety information in product label of Palonosetron Additional risk minimisation measures Not applicable

Missing information – Effect in pregnancy	
Risk minimization measures	Routine risk minimisation measures Guidance and safety information in product label of Palonosetron Additional risk minimisation measures Not applicable

Missing information – Effect in lactating women	
Risk minimization measures	Routine risk minimisation measures Guidance and safety information in product label of Palonosetron Additional risk minimisation measures Not applicable

Missing information – Effects on fertility	
Risk minimization measures	Routine risk minimisation measures Guidance and safety information in product label of Palonosetron Additional risk minimisation measures Not applicable

Missing information – Use in paediatric population	
Risk minimization measures	Routine risk minimisation measures Guidance and safety information in product label of Palonosetron Additional risk minimisation measures Not applicable

Missing information – Effects in patients with end stage renal disease undergoing	
Risk minimization measures	Routine risk minimisation measures Guidance and safety information in product label of Palonosetron Additional risk minimisation measures Not applicable

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of Palonosetron Fresenius Kabi.

II.C.2 Other studies in post-authorisation development plan

There are no on-going or closed studies for Palonosetron Fresenius Kabi.