VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Chemotherapy Induced Nausea and Vomiting (CINV):
Patients frequently cite nausea and vomiting as being among the most unpleasant and distressing side effects of chemotherapy (a treatment of cancer). Cancer patients who were scheduled for their first cycle of a new chemotherapy regimen were recruited. Chemotherapy-induced nausea and vomiting can be broadly categorized as acute (occurring within 24 hours of therapy), delayed (persisting for 6-7 days after therapy), or anticipatory (occurring prior to chemotherapy administration). One hundred fifty-one patients provided information for at least one cycle. During cycle 1, only 33% had neither acute nor delayed CINV. Of the 36% patients who developed acute CINV, 8% developed acute CINV only. Of the 59% who developed delayed CINV, 53% reported delayed only and 47% reported acute and delayed CINV. Chemotherapy-induced nausea and vomiting (CINV) may occur within hours of the administration of chemotherapy medicines (acute, i.e., of short duration), or their appearance may be delayed until after the first 24 h (delayed), and may persist for several days. Female patients and younger patients are at greater risk of developing nausea and vomiting following cancer chemotherapy. Inadequately-controlled CINV can cause a number of medical complications that may prove life-threatening, including dehydration and electrolyte imbalance, or cause physical damage. These complications may lead to extended hospitalization.

VI.2.2 Summary of treatment benefits

Pivotal clinical studies were not conducted for evaluating effective and safe use of Palonosetron hydrochloride QILU 250 micrograms solution for injection, considering this is a generic medicine (generic medicine means a medicine that is developed to be the same as a reference medicine that has already been authorized). The available medical literature is considered sufficient to evaluate the safety of palonosetron in the proposed therapeutic indication for Palonosetron hydrochloride QILU 250 micrograms solution for injection.

VI.2.3 Unknowns relating to treatment benefits

The safety and efficacy of palonosetron in children aged less than 1 month have not been established. There are no data available on the drug's effects on fertility or use in patients with end-stage renal disease undergoing haemodialysis.. There is no experience of palonosetron in human pregnancy. It is not known if palonosetron is found in breast milk.

VI.2.4 Summary of safety concerns

Important identified risks:

Risk	What is known	Preventability
Severe constipation	Cases of constipation following use of palonosetron have been reported commonly. Two cases of constipation requiring hospitalization have been reported in association with palonosetron 750 micrograms.	Yes, the patient should talk to the treating physician or pharmacist before using palonosetron if he or she has acute bowel obstruction or a history of repeated constipation.
Allergy problems (Severe hypersensitivity reactions)	Allergic reactions to palonosetron have been reported very rarely.	Yes, the patient should not use palonosetron hydrochloride if he or she is allergic to palonosetron or any of the other ingredients of palonosetron hydrochloride solution for injection.

Important potential risks:

Risk	What is known
Alterations in heart rhythm - QT/QTc prolongation (Electrocardiogram QT/QTc prolonged)	Electrocardiogram abnormalities like QT/QTc prolongation have been reported with palonosetron use during clinical trials; however, these abnormalities were not considered clinically relevant. The patient should talk to the treating physician or pharmacist before using palonosetron hydrochloride if he or she has a personal or family history of alterations in QT/QTc prolongation or other heart problems, or if he or she has an imbalance of certain minerals in the blood, such as potassium and magnesium, which has not been treated.
A reaction called serotonin syndrome showing symptoms like increased heart beats, shivering, sweating, dilated pupils, jerking or twitching, etc. (Serotonin syndrome)	There have been reports of serotonin syndrome with the use of 5-HT_3 antagonist types of medicines, to which palonosetron belongs, either alone or in combination with other medicines called serotonergic drugs. The patient should tell the treating physician or pharmacist if he or she is taking, has recently taken or might take any other medicines, including SSRIs (selective serotonin reuptake

Risk	What is known
	inhibitors) used to treat depression and/or anxiety including fluoxetine, paroxetine, sertraline, fluvoxamine, citalopram, escitalopram; or SNRIs (serotonin noradrenaline reuptake inhibitors) used to treat depression and/or anxiety including venlafaxine, duloxetine. Appropriate observation of patients for serotonin syndrome-like symptoms is advised.
Convulsions	There have been reports of serotonin syndrome with the use of 5-HT3 antagonist types of medicines, to which palonosetron belongs, either alone or in combination with other medicines called serotonergic drugs. Appropriate observation of patients for serotonin syndrome-like symptoms is advised.

Missing information:

Risk	What is known
Use in children aged less than 1 month (potential off-label use for CINV prevention)	The safety profile of palonosetron is consistent with the established profile in adults. However, the safety and efficacy of palonosetron in children aged less than 1 month have not been established. The treating physician should decide the dose for children depending on body weight; however the maximum recommended dose is 1500 micrograms.
Use during pregnancy	Animal studies have indicated that palonosetron does not cause harmful effects on developing animals (embryo or foetus) during pregnancy as well as following birth. Only limited data from animal studies are available regarding the transfer of the medicine in developing animals (placental transfer). There is no experience of palonosetron in human pregnancy. If the female patient is pregnant or thinks she might be, the treating physician should not administer palonosetron unless it is clearly necessary. The female patient should ask the treating physician or pharmacist for advice before using this medicine if he or she is pregnant or think she might be.

Risk	What is known
Use in breast-feeding	It is not known if palonosetron is found in breast milk. The female patient should ask the treating physician or pharmacist for advice before using palonosetron if she is breast-feeding.
Effects on fertility	There are no data available on the effect of palonosetron on fertility.
Use in patients with end-stage renal disease undergoing haemodialysis	There are no data available on the effect of palonosetron in patients with end-stage renal disease undergoing haemodialysis.

VI.2.5 Summary of additional risk minimization measures by safety concern

The Summary of Product Characteristics (SmPC) of Palonosetron hydrochloride QILU 250 micrograms solution for injection provides physicians, pharmacists and other health care professionals with details on how to use the medicine and the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PIL). All these risk minimization measures are given in the SmPC and PIL of Palonosetron hydrochloride QILU 250 micrograms solution for injection.

No additional risk minimization measures have been proposed for this generic medicine.

VI.2.6 Planned Post-Authorisation Development Plan

No post-authorisation study is planned for this product.

VI.2.7 Summary of changes to the risk management plan over time

Version	Date (dd-mm-yyyy)	Safety Concerns	Comment
02	05 Jan 2016	Some safety concerns have been updated.	As per the agency suggestions