Paloron

Palonosetron USP

Description
Palonosetron **(Paloron)** is a highly potent, selective, second generation Serotonin sub-type 3 (5-HT_3) receptor antagonist with a 5-HT_3 receptor binding affinity that is ≥ 100 folds higher than other 5-HT_3 recptor antagonists.

Composition
Paloron 0.5 mg Tablet: Each film-coated tablet contains Palonosetron Hydrochloride USP equivalent to Palonosetron 0.5 mg.
Paloron 0.5 mg ODT: Each orally dispersible tablet contains Palonosetron Hydrochloride USP equivalent to Palonosetron 0.5 mg.
Paloron 0.25 mg Injection: Each 5 ml vial contains Palonosetron Hydrochloride USP equivalent to Palonosetron 0.25 mg.
Paloron 0.075 mg Injection: Each 1.5 ml vial contains Palonosetron Hydrochloride USP equivalent to Palonosetron 0.075 mg.

Mode of Action
Palonosetron is a 5-HT_3 receptor antagonist with a strong binding affinity for this receptor and little or no affinity for other receptors. It is thought that chemotherapeutic agents produce nausea and vomiting by releasing serotonin from the enterochromaffin cells of the small intestine and that the released serotonin then activates 5-HT_3 receptors that are located on the nerve terminals of the vagus in the periphery and centrally in the chemoreceptor trigger zone of the area postrema, to initiate the vomiting reflex. Postoperative nausea and vomiting is influenced by multiple patient, surgical and anesthesia related factorcs and is triggered by release of 5-HT_3 in a cascade of neuronal event involving both the central nervous system and the gastrointestinal tract.
The 5-HT_3 receptor has been demonstrated to selectively participate in the emetic response. Palonosetron works by blocking the actions of Serotonin, associated with nausea and vomiting, at 5-HT_3 receptor. It is likely that Palonosetron works in the small intestine but it may also work in the brain.

Pharmacokinetics
Palonosetron exhibits linear dose-proportional pharmacokinetics over the dose-range 1-90 µg/kg in healthy subjects and in patients with cancer. In cancer patients receiving single intravenous doses of Palonosetron in this dose range, the mean maximum plasma concentration (C_{max}) ranges from 0.89 to 336 ng/ml and the area under the plasma concentration-time curve from zero to infinity (AUC_{0-}) ranges from 13.8 to 957 ng.h/ml. Palonosetron has a volume of distribution of approximately 6.9-7.9 L/kg, with approximately 62% bound to plasma proteins. Approximately 50% of Palonosetron is metabolized into two inactive metabolites that exhibit <1% of the 5-HT_3 receptor antagonist activity. Approximately 40% of the drug is metabolised via kidney, 50% by liver CYP2D6 (mainly), CYP3A4 and CYP1A2 isoenzymes. About 50% of the drug goes under metabolism. After a single intravenous dose, approximately 40% is excreted as unchanged drug in the urine after 144 hours. Total body clearance of Palonosetron is 160±35 ml/h/kg, and renal clearance is 66.5±18.2 ml/h/kg in healthy subjects. Palonosetron exhibits a longer half-life (40 hours) and has a greater 5-HT_3 receptor binding affinity.

Indications
Acute and delayed nausea and vomiting; Uncontrolled nausea and vomiting; Chemotherapy-induced nausea and vomiting (CINV): Acute CINV resulting in on the day of treatment with certain types of chemotherapy; Delayed CINV resulting in on days later with certain types of chemotherapy; Radiotherapy-induced nausea and vomiting (RINV); Post-operative & Post-discharge nausea and vomiting (PONV & PDNV).

Dosage and Administration
Usual dosage: Adult tablet dosage: 0.5 mg (01 tablet) daily.
Paediatric tablet dosage (1 month to 17 years): 0.25 mg/day (Half orally dispersible tablet).
Adult IV dosage: A single IV dose of 0.075 mg should be administered over 10 seconds.
Chemotherapy-induced nausea and vomiting: Adult tablet dosage: 0.5 mg (01 tablet) administered approximately 1 hour prior to the start of chemotherapy. Adult IV dosage: A single IV dose of 0.25 mg should be administered over 30 seconds approximately 30 minutes before the start of chemotherapy.
Radiotherapy-induced nausea and vomiting: A single IV dose of 0.25 mg should be administered over 30 seconds approximately 30 minutes before each week of radiation fraction. ***Post-operative nausea and vomiting:*** A single IV dose of 0.075 mg should be administered over 10 seconds immediately before induction of anesthesia.
Paediatric dosage (1 month to 17 years): A single IV dose at 20 mcg/kg body weight. Maximum dose limit is 1.5 mg.

Paloron ODT tablet
1. When taking the orally dispersible tablet out of its package, peel the foil back. Don't try to push the tablet through the foil. This step will help keep the tablet from breaking.
2. Place the ODT tablet on your tongue. Leave it there for a few seconds to allow it to dissolve, and then swallow.

Side-effects
The most common adverse reactions are headache and constipation.

Contra-indications
Palonosetron is contra-indicated in patients known to have hypersensitivity to the drug or any of its components.

Drug Interactions
In controlled clinical trials, Palonosetron injection has been safely administered with corticosteroids, analgesics, antiemetics/antinauseants, antispasmodics and anticholinergic agents. Palonosetron did not inhibit the antitumor activity of cisplatin, cyclophosphamide, cytarabine, doxorubicin and mitomycin C in murine tumor models. Concomitant administration of Palonosetron and metoclopramide has no significant pharmacokinetic interactions. In vitro studies indicated that palonosetron is not inhibitor of CYP1A2, CYP2A6, CYP2B6, CYP2C9, CYP2D6, CYP2E1 & CYP3A4/5 (CYP2C19 was not investigated) nor does it induce the activity of CYP1A2, CYP2D6 or CYP3A4/5. Therefore, the potential for clinically significant drug interactions with Palonosetron appears to be low.

Use in pregnancy and lactation
Pregnancy category 'B'. It is not known whether Palonosetron is excreted in breast milk.

Use in elderly patients
No dosage adjustment is recommended in elderly patients ≥65 years of age.

Use in Children & adolescent
Safe and effective in child patients from 28 days of age has been established by clinical trial.

Use in patients with impaired renal and hepatic function
No dosage adjustment is recommended in patients with renal and hepatic dysfunction.

Overdosage
There is no known antidote to Palonosetron. Overdose should be managed with supportive care.

Storage
Do not store above 25^{0}C. Protect from light & keep in a dry place. Protect injectable from freezing. Keep out of reach of children.

Packaging
Paloron 0.5 mg Tablet: Each box contains 3x10's tablets in blister pack.
Paloron 0.5 mg ODT: Each box contains 3×10's ODT in blister pack.
Paloron 0.25 mg Injection: Each box contains 4 vials of 5 ml each in separate inner carton.
Paloron 0.075 mg Injection: Each box contains 4 vials of 1.5 ml each in separate inner carton.

Manufactured by
ZISKA PHARMA
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