# Palon

## Palonosetron

**Composition**

**Palon Tablet:** Each tablet contains Palonosetron Hydrochloride USP equivalent to Palonosetron 0.5 mg.

**Palon 0.25 Injection:** Each ampoule contains 5 ml solution of Palonosetron Hydrochloride USP equivalent to Palonosetron 0.25 mg.

**Palon 0.075 Injection:** Each ampoule contains 1.5 ml solution of Palonosetron Hydrochloride USP equivalent to Palonosetron 0.075 mg.

**Description**

Palonosetron Hydrochloride is an antiemetic and antinauseant agent. It is a serotonin subtype 3 (5-HT3) receptor antagonists with a strong binding affinity for this receptor. The empirical formula is C19H24N2O.HCl, with a molecular weight of 332.87. Palonosetron hydrochloride is a white to off white crystalline powder. It is freely soluble in water, soluble in propylene glycol and slightly soluble in ethanol and 2-propanol.

**Pharmacology**

Mechanism of Action : Palonosetron is a 5-HT3 receptor antagonist with a strong binding affinity for this receptor and little or no affinity for other receptors.

**Pharmacokinetics**

Absorption : Following oral administration, palonosetron is well absorbed with its absolute bioavailability reaching 97%. After single oral doses using bufferedm solution mean maximum palonosetron concentrations (Cmax) and area under the concentration-time curve (AUC0-∞) were dose proportional over the dose range of 3.0 to 80 µg/kg in healthy subjects.

Metabolism : Palonosetron is eliminated by multiple routes with approximately 50% metabolized to form two primary metabolites: N-oxide-palonosetron and 6-S-hydroxy-palonosetron. These metabolites each have less than 1% of the 5-HT3 receptor antagonist activity of palonosetron. In vitro metabolism studies have suggested that CYP2D6 and to a lesser extent, CYP3A4 and CYP1A2 are involved in the metabolism of palonosetron. However, clinical pharmacokinetic parameters are not significantly different between poor and extensive metabolizers of CYP2D6 substrates.

Elimination : Following administration of a single oral 0.75 mg dose of Palonosetron to six healthy subjects, 85% to 93% of the total radioactivity was excreted in urine, and 5% to 8% was eliminated in feces. The amount of unchanged Palonosetron excreted in the urine represented approximately 40% of the administered dose.

**Pharmacodynamics**

The effect of Palonosetron on blood pressure, heart rate and ECG parameters including QTc were comparable to ondansetron and dolasetron in CINV clinical trials. In PONV clinical trials the effect of Palonosetron on the QTc interval was no different from placebo.

**Indications and Usage**

- Moderately emetogenic cancer chemotherapy-prevention of acute and delayed nausea and vomiting associated with initial and repeat courses.
- Highly emetogenic cancer chemotherapy-prevention of acute nausea and vomiting associated with initial and repeat courses.
- Prevention of postoperative nausea and vomiting (PONV) for up to 24 hours following surgery. Efficacy beyond 24 hours has not been demonstrated.

**Dosage and Administration**

Usual dosage

Adult tablet dosage: One 0.5 mg tablet/day

Adult IV dosage: A single 0.075 mg (1 vial) IV dose administered over 10 seconds.

Postoperative Nausea and Vomiting

Adult IV dosage: A single 0.075 mg IV dose administered over 10 seconds immediately before the induction of anesthesia.

Chemotherapy-Induced Nausea and Vomiting

Adults tablet dosage: One 0.5 mg tablet administered approximately one hour prior to the start of chemotherapy.

Adult 0.25 mg IV dosage: A single 0.25 mg IV dose administered over 30 seconds. Dosing should occur approximately 30 minutes before the start of chemotherapy.

Child dosage: A single 1-3 mcg/kg IV dose

**Pediatric Use**

Safety and effectiveness in patients below the age of 18 years have not been established.

**Use In Special Cases**

Renal Function Impairment : No dosage adjustments are needed with any degree of renal function impairment.

Hepatic Function Impairment: No dosage adjustments are needed with any degree of hepatic function impairment.

Elderly: No dosage adjustments or special monitoring are needed in elderly patients.

**Precaution**

Hypersensitivity reactions may occur in patients who have exhibited hypersensitivity to other 5-HT3 receptor antagonists. Hypersensitivity reactions may occur rarely for intravenous palonosetron like dyspnea, bronchospasm, swelling/edema, erythema, pruritus, rash, urticaria. No any significant hypersensitivity reactions for oral Palonosetron.

**Contraindication**

Palonosetron is contraindicated in patients known to have hypersensitivity to the drug or any of its components. Hypersensitivity reactions may occur in patients who have exhibited hypersensitivity to other selective 5-HT3 receptor antagonists.

**Adverse Effects**

The most common adverse reactions in chemotherapy-induced nausea and vomiting (incidence ≥ 5%) are headache and constipation. The most common adverse reactions in postoperative nausea and vomiting (incidence ≥ 2%) are QT prolongation, bradycardia, headache and constipation.

**Drug Interactions**

In vitro studies indicated that Palonosetron is not an inhibitor of CYP1A2, CYP2A6, CYP2B6, CYP2C9, CYP2D6, CYP2E1 and CYP3A4/5 (CYP2C19 was not investigated) nor does it induce the activity of CYP1A2, CYP2D6 or CYP3A4/5. Therefore, drug interactions with Palonosetron appear to be low. Palonosetron did not inhibit the antitumor activity of the five chemotherapeutic agents tested (cisplatin, cytarabine, doxorubicin and mitomycin C) in murine tumor models.

**Overdose**

There is no known antidote to palonosetron HCl. Overdose should be managed with supportive care. Dialysis studies have not been performed, however, due to the large volume of distribution, dialysis is unlikely to be an effective treatment for palonosetron HCl overdose. A single intravenous dose of palonosetron HCl at 30 mg/kg (947 and 474 times the human dose for rats and mice, respectively, based on body surface area) was lethal to rats and mice. The major signs of toxicity were convulsions, gasping, pallor, cyanosis and collapse.

**Use in Pregnancy and Lactation**

US FDA Pregnancy category B. It is not known whether Palonosetron is excreted in human milk.

**Storage Condition**

Store at temperature 15-30°C. Keep in a cool and dry place, away from light. Keep out of the reach of children.

**Commercial Pack**

**Palon Tablet:** Each box contains 10 tablets in Alu-Alu blister pack.

**Palon 0.25 Injection:** Each box contains one ampoule of 5 ml solution containing Palonosetron 0.25 mg.

**Palon 0.075 Injection:** Each box contains one ampoule of 1.5 ml solution containing Palonosetron 0.075 mg.

Pharmasia

* Palon Injection is manufactured by The IBN SINA Pharmaceutical Industry Ltd. for Pharmasia Ltd.

Manufactured by*
**Pharmasia Limited**
Gojariapara, Bhawal Mirzapur,
Gazipur, Bangladesh

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