Palonosetron Hydrochloride Injection

**ACTIONS**

**1. Mechanism of Action**

Palonosetron is a highly selective, potent, and long-acting 5-HT3 receptor antagonist. It has a high binding affinity for the 5-HT3 receptor, which is located on the surface of motoneurones in the brainstem that are responsible for mediating the emetic response to chemotherapy.

**2. Pharmacokinetics**

Palonosetron is rapidly absorbed following intravenous administration, with peak plasma concentrations occurring within 15 minutes. The drug undergoes extensive enterohepatic recirculation, with approximately 40% of the administered dose being excreted in the bile and subsequently reabsorbed into the circulation. The systemic clearance of palonosetron is primarily renal, with a mean terminal half-life of approximately 4 hours.

**3. Indications**

Palonosetron hydrochloride is indicated for the prevention of nausea and vomiting associated with cancer chemotherapy, particularly in highly emetogenic regimens. It is also approved for the prevention of nausea and vomiting following surgery.

**4. Administration**

Palonosetron is administered as an intravenous injection over 5 minutes. The recommended dose varies depending on the clinical setting and the type of chemotherapy.

**5. Adverse Reactions**

Adverse reactions associated with palonosetron administration include headache, constipation, diarrhea, and flushing. The incidence of these reactions is typically lower than with other 5-HT3 receptor antagonists.

**6. Contraindications**

Palonosetron hydrochloride is contraindicated in patients with a history of hypersensitivity to the drug or any of its components.

**7.WARNINGS AND PRECAUTIONS**

Serotonin syndrome (including altered mental status, autonomic instability, and neuromuscular symptoms) has been described following the concomitant use of 5-HT3 receptor antagonists and other serotonergic agents. Close monitoring is recommended in patients receiving concomitant therapy.

**8. Use in Special Populations**

- **Pregnancy:** Use during pregnancy only if clearly needed.
- **Lactation:** Palonosetron hydrochloride is excreted in breast milk. The benefits of breastfeeding must be weighed against the potential risks to the infant.
- **Pediatric Use:** Safety and efficacy in pediatric patients below the age of 1 month have not been established.

**9. Dose and Administration**

The recommended dose of palonosetron for adults is 0.25 mg administered intravenously. For children aged 1 month to 17 years, the recommended dose is 0.0075 mg/kg (up to a maximum of 0.25 mg).

**10. Monitoring and Follow-Up**

Regular monitoring of patients receiving palonosetron is recommended to assess for the development of adverse events and to ensure the efficacy of therapy.

**11. Supportive Measures**

Supportive measures should be initiated for patients who experience side effects such as diarrhea or constipation. In the event of an adverse reaction, discontinuation of the drug and initiation of appropriate supportive treatment is recommended.

**12. References**

For further information, please consult the full Prescribing Information provided by the manufacturer.
The primary hypothesis in Study 1 was that at least one of the three palonosetron doses were superior to placebo postoperatively. In Study 1 patients were randomized to receive palonosetron 0.025 mg, 0.050 mg or 0.075 mg or placebo, each given intravenously immediately prior to induction of anesthesia. These studies show that palonosetron was effective in the prevention of nausea and vomiting throughout the 120 hours (5 days) following initial and repeat courses of moderately emetogenic chemotherapy. In a phase 2 randomized, double-blind, multicenter, placebo-controlled, dose ranging study, palonosetron 0.075 mg was given intravenously to 160 patients, which had a CR rate of 44% versus 19% for placebo, \( p = 0.004 \). Palonosetron 0.075 mg significantly reduced the severity of nausea versus placebo, \( p = 0.009 \). Palonosetron was significantly better than placebo on delay to first response, time to next vomiting, nausea-free days, and overall activity days. These studies show that palonosetron was effective in the prevention of delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic chemotherapy. In this study, palonosetron 1 mcg/kg (approximately 0.075 mg) which had a CR rate of 44% versus 19% for placebo, \( p = 0.004 \). Palonosetron 1 mcg/kg also significantly reduced the severity of nausea versus placebo, \( p = 0.009 \). Palonosetron was significantly better than placebo on delay to first response, time to next vomiting, nausea-free days, and overall activity days. These studies were designed to show non-inferiority. A lower bound greater than -15% demonstrates non-inferiority between palonosetron and comparator. The primary efficacy measure was the proportion of patients with CR in the first 24 hours after recovery from surgery. The lowest effective dose was palonosetron 1 mcg/kg (approximately 0.075 mg). The table shows the prevention of overall nausea and vomiting (0 to 120 hours): Complete Response Rates for different doses of palonosetron and placebo.

<table>
<thead>
<tr>
<th>Palonosetron Dose (mcg/kg)</th>
<th>Placebo</th>
<th>CR Rate (0 to 48 hours)</th>
<th>CR Rate (0 to 72 hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.025</td>
<td>0.050</td>
<td>32/72 (44%)</td>
<td>34/72 (47%)</td>
</tr>
<tr>
<td>0.050</td>
<td>0.075</td>
<td>50/70 (71%)</td>
<td>52/70 (74%)</td>
</tr>
<tr>
<td>0.075</td>
<td></td>
<td>63/70 (90%)</td>
<td>65/70 (93%)</td>
</tr>
</tbody>
</table>

Palonosetron hydrochloride injection is a prescription medicine called an "antiemetic." Palonosetron hydrochloride injection is used in adults to help prevent the nausea and vomiting that happens:

- up to 24 hours while recovering from anesthesia after surgery
- due to Helsinn Healthcare SA's marketing exclusivity rights, this drug product is not labeled with that pediatric information.

You may report side effects to FDA at 1-800-FDA-1088.