1. INDICATIONS AND USAGE

Palonosetron Hydrochloride Injection is indicated for the prevention of nausea and vomiting associated with initial and subsequent courses of highly emetogenic chemotherapy (HEC) in adults and pediatric patients 1 month to 17 years of age. (1)

2. DOSAGE AND ADMINISTRATION

2.1 Induction Therapy

For a dose of 0.25 mg, use the entire contents (5 mL) of the prefilled single-dose prefilled syringe (3).

3. PRECAUTIONS

3.1 Hypersensitivity Reactions

Palonosetron Hydrochloride Injection is contraindicated in patients with known hypersensitivity to other selective serotonin (5-HT3) receptor antagonists.

4. CONTRAINDICATIONS

Palonosetron Hydrochloride Injection is contraindicated in patients with a history of hypersensitivity to other selective serotonin (5-HT3) receptor antagonists.

5. WARNINGS

5.1 Serotonin Syndrome

Serotonin syndrome (including altered mental status, autonomic instability, rigidity, myoclonus, hyperreflexia, and incoordination) and a severe life-threatening condition has been associated with the concomitant use of Palonosetron Hydrochloride Injection with other 5-HT3 receptor agonists (e.g., dexamethasone, ondansetron, and alizapride), certain antibiotics (e.g., linezolid and tetracyclines), and other drugs that interfere with serotonin function (e.g., selective serotonin reuptake inhibitors (SSRIs) or serotonin-norepinephrine reuptake inhibitors (SNRIs)).

6. ADVERSE REACTIONS

6.1 Clinical Trials Experience

In clinical trials, the most frequent adverse reactions associated with the use of Palonosetron Hydrochloride Injection were constipation, dizziness, headache, and acneiform rash.

6.2 Postmarketing Experience

In postmarketing experience, the following adverse reactions have been reported in patients receiving Palonosetron Hydrochloride Injection:

- Nervous System: headache, dizziness, insomnia
- Gastrointestinal: constipation, nausea, vomiting
- Respiratory: cough
- Cardiac: palpitations, angina pectoris
- Endocrine: hyperglycemia, hypoglycemia
- Metabolic: weight increased, weight decreased
- Skin: rash, pruritus
- General: fatigue, asthenia

7. DRUG INTERACTIONS

7.1 General Information

Pharmacokinetic studies have been conducted to assess the impact of concomitant medications on the pharmacokinetics of palonosetron and the impact of palonosetron on the pharmacokinetics of concomitant medications. The potential for drug interactions due to altered pharmacokinetics of palonosetron and other drugs should be considered.

8. DOSAGE FORMS AND STRENGTHS

Palonosetron Hydrochloride Injection is available as a 5 mL single-dose prefilled syringe (3).

9. HOW SUPPLIED/STORAGE AND HANDLING

Palonosetron Hydrochloride Injection is supplied in single-dose prefilled syringes (3) and should be stored at room temperature.

10. OVERDOSAGE

In a pediatric clinical trial, 163 pediatric cancer patients with a mean age of 13 years received up to 60 mg/kg/day (1,894 times the recommended human intravenous dose in rats and rabbits, respectively) for 5 days without apparent toxicity.

11. CLINICAL STUDIES

Clinical studies have demonstrated that pediatric patients require a higher palonosetron dose than adults, and therefore, they should be dosed accordingly.

12. CLINICAL PHARMACOLOGY

12.1 Pharmacokinetics

After single doses of Palonosetron Hydrochloride Injection, palonosetron is rapidly absorbed and completely bioavailable. Palonosetron is not metabolized to any significant extent in humans.

12.2 Pharmacodynamics

Palonosetron is a potent antagonist at the 5-HT3 receptor. It has been shown to be efficacious in the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC) and highly emetogenic cancer chemotherapy (HEC).

12.3 Pharmacogenomics

The pharmacogenomic basis for individual variation in response to selective serotonin (5-HT3) receptor antagonists is not well understood and is currently being investigated.

13. NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No carcinogenic potential was detected in male and female rats treated orally for 2 years with doses up to 10 mg/kg/day (305 times the recommended human intravenous dose in rats and rabbits, respectively).

13.2 Pharmacology

In vitro studies have demonstrated that palonosetron is not a substrate for CYP1A2, CYP2C9, or CYP2C19. In vitro studies have also demonstrated that palonosetron is not an inhibitor of CYP1A2, CYP2C9, or CYP2C19.

14. CLINICAL STUDIES

14.1 Prevention of Nausea and Vomiting Associated with Initial and Subsequent Courses of Highly Emetogenic Chemotherapy

In double-blind randomized clinical trials for the prevention of nausea and vomiting associated with initial and subsequent courses of highly emetogenic chemotherapy, 1,374 adult patients received oral aprepitant and 2,025 patients receivedPalonosetron Hydrochloride Injection.

15. PATIENT FOCUS

15.1 Patient Instructions

Patients should be instructed to follow the dosage and administration instructions provided in this labeling.

16. DESCRIPTION

Palonosetron Hydrochloride Injection contains palonosetron as anhydrous 5-hydroxyindole-2-carboxylic acid (1-azabicyclo[2.2.2]oct-3-yl)-2,3,3a,4,5,6-hexahydro-1-oxo-1H-benz[d]imidazol(1,2-a)isoindole-1-carboxylic acid Hydrochloride. (3)

17. HOW SUPPLIED

Palonosetron Hydrochloride Injection is supplied in single-dose prefilled syringes (3) and is available in the following strengths:

- 0.25 mg
- 20 micrograms per mL

18. CLINICAL PHARMACOLOGY

18.1 Pharmacokinetics

After single doses of Palonosetron Hydrochloride Injection, palonosetron is rapidly absorbed and completely bioavailable. Palonosetron is not metabolized to any significant extent in humans.

18.2 Pharmacodynamics

Palonosetron is a potent antagonist at the 5-HT3 receptor. It has been shown to be efficacious in the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC) and highly emetogenic cancer chemotherapy (HEC).

19. NONCLINICAL TOXICOLOGY

19.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

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19.2 Pharmacology

In vitro studies have demonstrated that palonosetron is not a substrate for CYP1A2, CYP2C9, or CYP2C19. In vitro studies have also demonstrated that palonosetron is not an inhibitor of CYP1A2, CYP2C9, or CYP2C19.

20. CLINICAL STUDIES

20.1 Prevention of Nausea and Vomiting Associated with Initial and Subsequent Courses of Highly Emetogenic Chemotherapy

In double-blind randomized clinical trials for the prevention of nausea and vomiting associated with initial and subsequent courses of highly emetogenic chemotherapy, 1,374 adult patients received oral aprepitant and 2,025 patients received Palonosetron Hydrochloride Injection.

21. PATIENT FOCUS

21.1 Patient Instructions

Patients should be instructed to follow the dosage and administration instructions provided in this labeling.

22. DESCRIPTION

Palonosetron Hydrochloride Injection contains palonosetron as anhydrous 5-hydroxyindole-2-carboxylic acid (1-azabicyclo[2.2.2]oct-3-yl)-2,3,3a,4,5,6-hexahydro-1-oxo-1H-benz[d]imidazol(1,2-a)isoindole-1-carboxylic acid Hydrochloride. (3)
11. SIDE EFFECTS

The most common side effects in adults

- headache
- drowsiness
- constipation
- diarrhea

The most common side effects in pediatric patients

- headache
- drowsiness
- constipation
- diarrhea

Other side effects reported include:

- blurred vision
- changes in taste
- changes in appetite

Side effects may occur anytime during treatment or shortly afterward. Stop taking Palonosetron Hydrochloride Injection and call your doctor if:

- you have any side effects that bother you or that do not go away
- you or anyone else in your family has any side effects from taking Palonosetron Hydrochloride Injection that you think may be serious

Tell your doctor about any side effects that you experience during Palonosetron Hydrochloride Injection treatment.

12. DRUG INTERACTIONS

- Certain drugs, food, or other substances can affect the way Palonosetron Hydrochloride Injection works. These include:

  - Seizure Medications: Certain medicines to treat epilepsy may increase the risk of seizures when taken with Palonosetron Hydrochloride Injection. Your doctor will adjust your dosing and treatment plan to reduce this risk.
  - Other Medicines: Certain other medicines, such as those that cause serotonin problems, may increase the risk of serotonin problems when taken with Palonosetron Hydrochloride Injection.

- Talk to your doctor before taking Palonosetron Hydrochloride Injection if you are taking or have taken any of the following medicines:

  - Other cancer medicines (chemotherapy)
  - Certain other medicines, such as those that cause serotonin problems

- Certain foods or drinks may increase the risk of certain side effects when taken with Palonosetron Hydrochloride Injection. These include:

  - Food and drinks that contain large amounts of caffeine

Tell your doctor about the medicines you take. Keep a list of all of the medicines you take to show to your doctor and pharmacist.

13. PRECAUTIONS

- Breastfeeding: It is not known if Palonosetron Hydrochloride Injection passes into breast milk. You should not breastfeed while taking Palonosetron Hydrochloride Injection without talking to your doctor.

- Pregnancy: It is not known if Palonosetron Hydrochloride Injection can harm your unborn baby. Tell your doctor if you are pregnant or think you may be pregnant. If you become pregnant while taking Palonosetron Hydrochloride Injection, talk to your doctor about the benefits and risks.

- Children: The safety and effectiveness of Palonosetron Hydrochloride Injection in children younger than 12 years old have not been studied.

- Elderly: Older adults may be more sensitive to the effects of Palonosetron Hydrochloride Injection. Your doctor will adjust your dosing and treatment plan accordingly.

14. DIRECTIONS FOR USE

- How to use Palonosetron Hydrochloride Injection

  - Before receiving Palonosetron Hydrochloride Injection, you should receive treatment with other medications as directed by your doctor.

- After receiving Palonosetron Hydrochloride Injection, you should receive treatment with other medications as directed by your doctor.

15. INFORMATION ABOUT PATIENT SAFETY

- What to do in the event of an emergency

  - If you have an allergic reaction to Palonosetron Hydrochloride Injection, stop taking the medicine and call your doctor or get immediate medical attention.

- In case of overdose

  - There is no known specific treatment for overdose of Palonosetron Hydrochloride Injection.

- Storage

  - Keep Palonosetron Hydrochloride Injection out of the reach of children.

- Disposal

  - Do not flush Palonosetron Hydrochloride Injection down the toilet or pour it into a sink.

- Additional information

  - This Patient Information is not a complete guide to using Palonosetron Hydrochloride Injection. It does not cover all possible side effects or precautions.

- Additional information can be found in the full Prescribing Information for Palonosetron Hydrochloride Injection. You can ask your doctor or pharmacist for more information.