# SUMMARY OF PRODUCT CHARACTERISTICS

## 1. NAME OF THE MEDICINAL PRODUCT

PALOX (Palonosetron hydrochloride Injection 0.25 mg/5 mL)

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 mL contains palonosetron hydrochloride equivalent to palonosetron 0.25 mg.

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Solution for injection.

A clear colourless solution in a 5 mL Type I clear tubular glass vial with 20 mm grey bromobutyl rubber stopper and 20 mm violet colour flip-off aluminium seal.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Palonosetron hydrochloride Injection is indicated in adults for:

- the prevention of acute nausea and vomiting associated with highly emetogenic cancer chemotherapy;
- the prevention of nausea and vomiting associated with moderately emetogenic cancer chemotherapy.

Palonosetron hydrochloride Injection is indicated in paediatric patients 1 month of age and older for:

- the prevention of acute nausea and vomiting associated with highly emetogenic cancer chemotherapy and prevention of nausea and vomiting associated with moderately emetogenic cancer chemotherapy.

### 4.2 Posology and method of administration

Palonosetron hydrochloride Injection should be used only before chemotherapy administration. This medicinal product should be administered by a healthcare professional under appropriate medical supervision.

Adults: 250 micrograms palonosetron administered as a single intravenous bolus approximately 30 minutes before the start of chemotherapy. Palonosetron hydrochloride Injection should be injected over 30 seconds.

The efficacy of Palonosetron hydrochloride Injection in the prevention of nausea and vomiting induced by highly emetogenic chemotherapy may be enhanced by the addition of a corticosteroid administered prior to chemotherapy.

Elderly people: No dose adjustment is necessary for the elderly.

Paediatric population: Children and adolescents aged 1 month to 17 years: 20 micrograms/kg (maximum total dose should not exceed 1500 micrograms) palonosetron administered as a single 15-minute intravenous infusion beginning approximately 30 minutes before the start of chemotherapy. The safety and efficacy in children aged less than 1 month have not been established. There are limited data on use in children under 2 years of age.

Hepatic impairment: No dose adjustment is necessary for patients with impaired hepatic function.

Renal impairment: No dose adjustment is necessary for patients with impaired renal function. No data are available for patients with end stage renal disease undergoing haemodialysis.

Method of administration: For intravenous use.

**4.3 Contraindications**

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

**4.4 Special warnings and precautions for use**

As palonosetron may increase large bowel transit time, patients with a history of constipation or signs of subacute intestinal obstruction should be monitored following administration. Two cases of constipation with faecal impaction requiring hospitalisation have been reported in association with palonosetron 750 micrograms.

At all dose levels tested, palonosetron did not induce clinically relevant prolongation of the QTc interval. A specific thorough QT/QTc study was conducted in healthy volunteers for definitive data demonstrating the effect of palonosetron on QT/QTc (see section 5.1). However, as for other 5-HT3 antagonists, caution should be exercised in patients who have or are likely to develop prolongation of the QT interval, including patients with a personal or family history of QT prolongation, electrolyte abnormalities, congestive heart failure, bradyarrhythmias, conduction disturbances and patients taking anti-arrhythmic agents or other medicinal products that lead to QT prolongation or electrolyte abnormalities. Hypokalaemia and hypomagnesaemia should be corrected prior to 5-HT3 antagonist administration.

There have been reports of serotonin syndrome with the use of 5-HT3 antagonists either alone or in combination with other serotonergic drugs, including SSRIs and SNRIs. Appropriate observation of patients for serotonin syndrome-like symptoms is advised.

Palonosetron hydrochloride Injection should not be used to prevent or treat nausea and vomiting in the days following chemotherapy if not associated with another chemotherapy administration. This medicinal product contains less than 1 mmol sodium (23 mg) per vial, i.e. essentially sodium-free.

**4.5 Interaction with other medicinal products and other forms of interaction**

Palonosetron is mainly metabolised by CYP2D6, with minor contribution by CYP3A4 and CYP1A2 isoenzymes. Based on in vitro studies, palonosetron does not inhibit or induce cytochrome P450 isoenzyme at clinically relevant concentrations.

Chemotherapeutic agents: In preclinical studies, palonosetron did not inhibit the antitumour activity of cisplatin, cyclophosphamide, cytarabine, doxorubicin and mitomycin C.

Metoclopramide: No significant pharmacokinetic interaction was shown between a single intravenous dose of palonosetron and steady-state oral metoclopramide, a CYP2D6 inhibitor.

CYP2D6 inducers and inhibitors: Population pharmacokinetic analysis showed no significant effect on palonosetron clearance when co-administered with CYP2D6 inducers or inhibitors including dexamethasone, rifampicin, amiodarone, celecoxib,

chlorpromazine, cimetidine, doxorubicin, fluoxetine, haloperidol, paroxetine, quinidine, ranitidine, ritonavir, sertraline or terbinafine.

Corticosteroids: Palonosetron has been administered safely with corticosteroids.

Serotonergic drugs: There have been reports of serotonin syndrome following concomitant use of 5-HT3 antagonists and serotonergic drugs including SSRIs and SNRIs.

Other medicinal products: Palonosetron has been administered safely with analgesics, antiemetics/antinauseants, antispasmodics and anticholinergic medicinal products.

### 4.6 Fertility, pregnancy and lactation

Pregnancy: No clinical data on exposed pregnancies are available. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development. Palonosetron should not be used in pregnant women unless considered essential by the physician.

Breast-feeding: As there are no data concerning palonosetron excretion in breast milk, breast-feeding should be discontinued during therapy.

Fertility: There are no data concerning the effect of palonosetron on fertility.

### 4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. Since palonosetron may induce dizziness, somnolence or fatigue, patients should be cautioned when driving or operating machines.

### 4.8 Undesirable effects

In clinical studies in adults at a dose of 250 micrograms (total 633 patients) the most frequently observed adverse reactions at least possibly related to Palonosetron hydrochloride Injection were headache (9%) and constipation (5%).

In clinical studies, adverse reactions were classified as common (≥1/100 to <1/10) or uncommon (≥1/1,000 to <1/100). Very rare (<1/10,000) adverse reactions were reported post-marketing.

| System organ class | Common ARs (≥1/100 to <1/10) | Uncommon ARs (≥1/1,000 to <1/100) | Very rare ARs (<1/10,000) |
|---|---|---|---|
| Immune system disorders | | | Hypersensitivity, anaphylaxis, anaphylactic/anaphylactoid reactions and shock |
| Metabolism and nutrition disorders | | Hyperkalaemia, metabolic disorders, hypocalcaemia, hypokalaemia, anorexia, hyperglycaemia, appetite decreased | |
| Psychiatric disorders | | Anxiety, euphoric mood | |
| Nervous system disorders | Headache; Dizziness | Somnolence, insomnia, paraesthesia, hypersomnia, peripheral sensory neuropathy | |
| Eye disorders | | Eye irritation, amblyopia | |
| Ear and labyrinth disorders | | Motion sickness, tinnitus | |

| | | | |
|---|---|---|---|
| Cardiac disorders | | Tachycardia, bradycardia, extrasystoles, myocardial ischaemia, sinus tachycardia, sinus arrhythmia, supraventricular extrasystoles | |
| Vascular disorders | | Hypotension, hypertension, vein discolouration, vein distended | |
| Respiratory, thoracic and mediastinal disorders | | Hiccups | |
| Gastrointestinal disorders | Constipation; Diarrhoea | Dyspepsia, abdominal pain, abdominal pain upper, dry mouth, flatulence | |
| Hepatobiliary disorders | | Hyperbilirubinaemia | |
| Skin and subcutaneous tissue disorders | | Dermatitis allergic, pruritic rash | |
| Musculoskeletal and connective tissue disorders | | Arthralgia | |
| Renal and urinary disorders | | Urinary retention, glycosuria | |
| General disorders and administration site conditions | | Asthenia, pyrexia, fatigue, feeling hot, influenza-like illness | Injection site reaction* |
| Investigations | | Elevated transaminases, electrocardiogram QT prolonged | |

° From post-marketing experience. *Includes burning, induration, discomfort and pain.

***Paediatric population***

In paediatric clinical trials for the prevention of nausea and vomiting induced by moderately or highly emetogenic chemotherapy, 402 patients received a single dose of palonosetron (3, 10 or 20 mcg/kg). The following common or uncommon adverse reactions were reported; none were reported at a frequency of >1%.

| **System organ class** | **Common ARs (≥1/100 to <1/10)** | **Uncommon ARs (≥1/1,000 to <1/100)** |
|---|---|---|
| Nervous system disorders | Headache | Dizziness, dyskinesia |
| Cardiac disorders | Electrocardiogram QT prolonged | Conduction disorder, sinus tachycardia |
| Respiratory, thoracic and mediastinal disorders | | Cough, dyspnoea, epistaxis |
| Skin and subcutaneous tissue disorders | | Dermatitis allergic, pruritus, skin disorder, urticaria |
| General disorders and administration site conditions | | Pyrexia, infusion site pain, infusion site reaction, pain |

Adverse reactions were evaluated in paediatric patients receiving palonosetron for up to 4 chemotherapy cycles.

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

Reporting of suspected adverse reactions: Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

### 4.9 Overdose

No case of overdose has been reported. Doses of up to 6 mg have been used in adult clinical studies; the highest dose group showed a similar incidence of adverse reactions compared to other dose groups and no dose response effects were observed. In the unlikely event of overdose, supportive care should be provided. Dialysis studies have not been performed; due to the large volume of distribution, dialysis is unlikely to be an effective treatment. No case of overdose has been reported in paediatric clinical studies.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antiemetics and antinauseants, serotonin (5HT3) antagonists. ATC code: A04AA05.

Palonosetron is a selective high-affinity receptor antagonist of the 5HT3 receptor. Palonosetron was non-inferior versus comparators in the acute phase of emesis in both moderately and highly emetogenic settings. The overall safety was maintained during up to 9 additional cycles of chemotherapy in an open-label safety study.

| Endpoint/phase | Palonosetron 250 micrograms (n=189) | Ondansetron 32 mg (n=185) | Delta | 97.5% CI / p-value |
|---|---|---|---|---|
| Complete response, 0-24 h | 81.0% | 68.6% | 12.4 | [1.8%, 22.8%] |
| Complete response, 24-120 h | 74.1% | 55.1% | 19.0 | [7.5%, 30.3%] |
| Complete response, 0-120 h | 69.3% | 50.3% | 19.0 | [7.4%, 30.7%] |
| Complete control, 0-24 h | 76.2% | 65.4% | 10.8 | NS |
| Complete control, 24-120 h | 66.7% | 50.3% | 16.4 | 0.001 |
| Complete control, 0-120 h | 63.0% | 44.9% | 18.1 | 0.001 |
| No nausea, 0-24 h | 60.3% | 56.8% | 3.5 | NS |
| No nausea, 24-120 h | 51.9% | 39.5% | 12.4 | NS |
| No nausea, 0-120 h | 45.0% | 36.2% | 8.8 | NS |

| Endpoint/phase | Palonosetron 250 micrograms (n=185) | Dolasetron 100 mg (n=191) | Delta | 97.5% CI / p-value |
|---|---|---|---|---|
| Complete response, 0-24 h | 63.0% | 52.9% | 10.1 | [-1.7%, 21.9%] |
| Complete response, 24-120 h | 54.0% | 38.7% | 15.3 | [3.4%, 27.1%] |
| Complete response, 0-120 h | 46.0% | 34.0% | 12.0 | [0.3%, 23.7%] |
| Complete control, 0-24 h | 57.1% | 47.6% | 9.5 | NS |
| Complete control, 24-120 h | 48.1% | 36.1% | 12.0 | 0.018 |
| Complete control, 0-120 h | 41.8% | 30.9% | 10.9 | 0.027 |
| No nausea, 0-24 h | 48.7% | 41.4% | 7.3 | NS |
| No nausea, 24-120 h | 41.8% | 26.2% | 15.6 | 0.001 |
| No nausea, 0-120 h | 33.9% | 22.5% | 11.4 | 0.014 |

| Endpoint/phase | Palonosetron | Ondansetron 32 | Delta | 97.5% CI / p- |
|---|---|---|---|---|

| | 250 micrograms (n=223) | mg (n=221) | | value |
|---|---|---|---|---|
| Complete response, 0-24 h | 59.2% | 57.0% | 2.2 | [-8.8%, 13.1%] |
| Complete response, 24-120 h | 45.3% | 38.9% | 6.4 | [-4.6%, 17.3%] |
| Complete response, 0-120 h | 40.8% | 33.0% | 7.8 | [-2.9%, 18.5%] |
| Complete control, 0-24 h | 56.5% | 51.6% | 4.9 | NS |
| Complete control, 24-120 h | 40.8% | 35.3% | 5.5 | NS |
| Complete control, 0-120 h | 37.7% | 29.0% | 8.7 | NS |
| No nausea, 0-24 h | 53.8% | 49.3% | 4.5 | NS |
| No nausea, 24-120 h | 35.4% | 32.1% | 3.3 | NS |
| No nausea, 0-120 h | 33.6% | 32.1% | 1.5 | NS |

The effect of palonosetron on blood pressure, heart rate and ECG parameters including QTc were comparable to ondansetron and dolasetron. A double-blind, randomised, parallel, placebo and positive controlled QT/QTc study in 221 healthy subjects demonstrated no effect on QT/QTc interval duration or other ECG intervals at doses up to 2.25 mg.

Paediatric population: The efficacy of Palonosetron hydrochloride Injection for prevention of chemotherapy-induced nausea and vomiting in paediatric cancer patients was demonstrated in a pivotal non-inferiority trial comparing a single intravenous infusion of palonosetron with intravenous ondansetron. The 20 micrograms/kg dose demonstrated non-inferiority to ondansetron.

## 5.2 Pharmacokinetic properties

Absorption/Exposure: Following intravenous administration, systemic exposure is generally dose-proportional over the dose range of 0.3-90 micrograms/kg in healthy subjects and in cancer patients. Following intravenous palonosetron 0.25 mg once every other day for 3 doses in 11 testicular cancer patients, the mean increase in plasma concentration from Day 1 to Day 5 was 42 ± 34%. After 0.25 mg once daily for 3 days in 12 healthy subjects, the mean increase from Day 1 to Day 3 was 110 ± 45%.

Distribution: Palonosetron at the recommended dose is widely distributed in the body with a volume of distribution of approximately 6.9 to 7.9 L/kg. Approximately 62% is bound to plasma proteins.

Biotransformation: Palonosetron is eliminated by dual route, about 40% through the kidney and approximately 50% metabolised to two primary metabolites, which have less than 1% of the 5HT3 receptor antagonist activity of palonosetron. CYP2D6 and, to a lesser extent, CYP3A4 and CYP1A2 are involved in metabolism. Palonosetron does not inhibit or induce cytochrome P450 isoenzymes at clinically relevant concentrations.

Elimination: After a single intravenous dose of 10 micrograms/kg [14C]-palonosetron, approximately 80% of the dose was recovered within 144 hours in the urine, with palonosetron representing approximately 40% of the administered dose as unchanged active substance. Total body clearance was 173 ± 73 mL/min and renal clearance was 53 ± 29 mL/min. The terminal elimination half-life was approximately 40 hours; 10% of patients have a mean terminal elimination half-life greater than 100 hours.

Special populations: Age and gender do not affect palonosetron pharmacokinetics. No dosage adjustment is necessary in elderly patients or based on gender. Mild to moderate renal impairment and hepatic impairment do not require dose adjustment. No pharmacokinetic data in haemodialysis patients are available.

| Parameter | <2 years | 2 to <6 years | 6 to <12 years | 12 to <17 years | Adults 3 µg/kg | Adults 10 µg/kg |
|---|---|---|---|---|---|---|
| AUC0-∞, h·µg/L | 69.0 (49.5) | 103.5 (40.4) | 98.7 (47.7) | 124.5 (19.1) | 35.8 (20.9) | 81.8 (23.9) |
| t1/2, hours | 24.0 | 28 | 23.3 | 30.5 | 56.4 (5.81) | 49.8 (14.4) |
| Clearance, L/h/kg | 0.31 (34.7) | 0.23 (51.3) | 0.19 (46.8) | 0.16 (27.8) | 0.10 (0.04) | 0.13 (0.05) |
| Volume of distribution, L/kg | 6.08 (36.5) | 5.29 (57.8) | 6.26 (40.0) | 6.20 (29.0) | 7.91 (2.53) | 9.56 (4.21) |

### 5.3 Preclinical safety data

Effects in non-clinical studies were observed only at exposures considered sufficiently in excess of the maximum human exposure, indicating little relevance to clinical use. Non-clinical studies indicate that palonosetron, only at very high concentrations, may block ion channels involved in ventricular de- and re-polarisation and prolong action potential duration. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development. Palonosetron is not mutagenic. High doses applied daily for two years caused an increased rate of liver tumours, endocrine neoplasms and skin tumours in rats but not in mice; these findings are not considered relevant for clinical use.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Mannitol, Edetate Disodium, Sodium citrate dihydrate, Citric acid monohydrate, Sodium hydroxide, Hydrochloric acid and Water for injection.

### 6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products.

### 6.3 Shelf life

2 years. Upon opening of the vial, use immediately and discard any unused solution.

### 6.4 Special precautions for storage

Store below 30°C.

### 6.5 Nature and contents of container

Clear tubular vials.

### 6.6 Special precautions for disposal and other handling

Single use only. Any unused solution should be discarded. Any unused product or waste material should be disposed of in accordance with local requirements.

## 7. MARKETING AUTHORISATION HOLDER AND MANUFACTURING SITE ADDRESS

| Marketing Authorisation Holder | Manufacturing Site |
|---|---|
| Hetero Labs Limited, 7-2-A2, Hetero Corporate, Industrial Estates, Sanath Nagar, Hyderabad-500018, Telangana, India. | Aspiro Pharma Limited, Survey No. 321, Biotech Park, Phase-III, Karkapatla, Markook Mandal, Siddipet District - 502281, Telangana. |

**8. MARKETING AUTHORISATION NUMBER**

H2025/CTD11097/15565

**9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

21/08/2026

**10. DATE OF REVISION OF THE TEXT**

21/08/2026