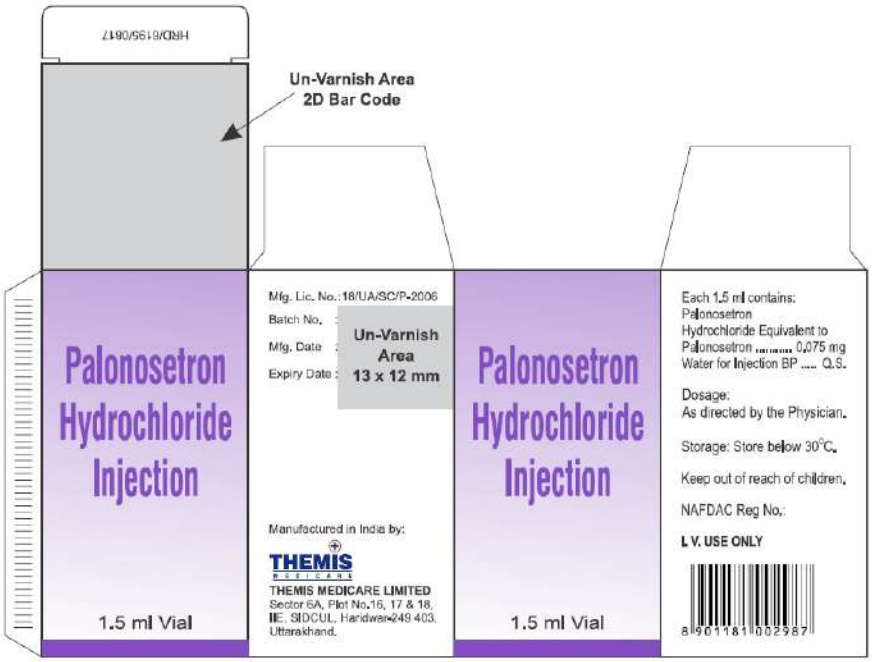
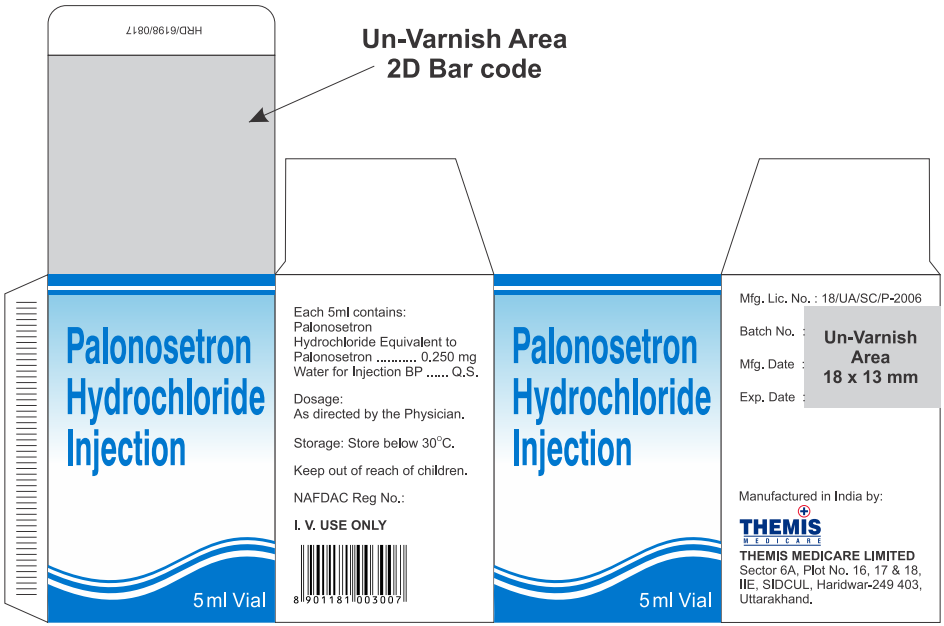

HRD/619S/0617
Un-Varnish Area
2D Bar Code
Palonosetron Hydrochloride Injection
1.5 ml Vial
Mfg. Lic. No.: 18/UA/SC/P-2006
Batch No.
Mfg. Date
Expiry Date
Un-Varnish Area 13 x 12 mm
Manufactured in India by:
THEMIS MEDICARE
THEMIS MEDICARE LIMITED
Sector 6A, Plot No.16, 17 & 18,
IIE, SIDCUL, Haridwar-249 403,
Uttarakhand.
Palonosetron Hydrochloride Injection
1.5 ml Vial
Each 1.5 ml contains:
Palonosetron
Hydrochloride Equivalent to
Palonosetron ..... 0.075 mg
Water for Injection BP ..... Q.S.
Dosage:
As directed by the Physician.
Storage: Store below 30°C.
Keep out of reach of children.
NAFDAC Reg No.:
I. V. USE ONLY
8 901181 002987



Specification Box

Market : Export (Nigeria Phillips)

Item : Carton

New Code : HRD/6198/0817

Ref. Code : HRD/5796/0217

Product Name : Palonosetron Hydrochloride Injection (5ml)

Material : 300 GSM FBB with Aqua Varnish

Artist : Shrikant

Size : 30 x 29 x 46 mm (LxWxH)

Varnish : Un-Varnish Area for batch details

Location : Haridwar

TP :

Item Code : PP09PEXP0024

Date : 22.08.2017

Color : PANTONE 2195 C Pantone 295 C Pantone 185 C Black

Prepared by Packaging Development	Approved by Packaging Development	Approved by RA	Approved by Marketing	Approved by Medical	Approved by Plant head	Approved by QA Head

Additional Comments : For DRA Registration - Nigeria Phillips

Path : D:\ Shrikant Artwork \ DRA \ Nigeria\ Nigeria Phillips \ Palonosetron Hydrochloride Injection (5ml)

2.16 SUMMARY PRODUCT CHARACTERISTICS (SPC):

2.16.1 PRODUCT INFORMATION FOR HEALTH PROFESSIONALS:

<table>
<tr><td>1</td><td>Name of the Finished Medicinal Product:</td></tr>
<tr><td>1.1</td><td>Product Name:
Palonosetron Hydrochloride Injection 0.075 mg/1.5ml</td></tr>
<tr><td>1.2</td><td>Strength : 0.075 mg/1.5ml</td></tr>
<tr><td>1.3</td><td>Pharmaceutical Form: Injection</td></tr>
<tr><td>2</td><td>Qualitative and Quantitative Compositions:</td></tr>
<tr><td></td><td>Qualitative Declaration:
Active component
INN Name: Palonosetron Hydrochloride
Quantitative Declaration:
Each 1.5ml contains:
Palonosetron Hydrochloride equivalent to Palonosetron …0.075 mg
Water For Injection BP .....Q.S.
<table>
<tr><th>Sr. No.</th><th>Content Name</th><th>Quality Standard</th><th>Qty per mg/ml</th></tr>
<tr><td>1.</td><td>Palonosetron Hydrochloride</td><td>IH</td><td>0.056</td></tr>
<tr><td>2.</td><td>Disodium EDTA</td><td>BP</td><td>1.00</td></tr>
<tr><td>3.</td><td>Mannitol</td><td>BP</td><td>41.50</td></tr>
<tr><td>4.</td><td>Anhydrous Citric Acid</td><td>BP</td><td>0.50</td></tr>
<tr><td>5.</td><td>Trisodium Citrate Dihydrate</td><td>BP</td><td>0.25</td></tr>
<tr><td>6.</td><td>Sodium Hydroxide</td><td>BP</td><td>qs#</td></tr>
<tr><td>7.</td><td>Hydrochloric Acid</td><td>BP</td><td>qs#</td></tr>
<tr><td>8.</td><td>Water For Injection</td><td>BP</td><td>q.s. to 1.00 ml</td></tr>
</table>
IH- In-house Specification
BP- British Pharmacopoeia
Note: The quantity of Palonosetron Hydrochloride (0.056mg) is equivalent to 0.050mg of Palonosetron.
Only for pH adjustment.</td></tr>
<tr><td>3</td><td>Pharmaceutical form: Injection
Description: Clear colourless liquid.</td></tr>
</table>

4	**Clinical Particulars:**
4.1	**Therapeutic Indications:** Palonosetron Hydrochloride Injection 0.075 mg/1.5ml is indicated for: Prevention of postoperative nausea and vomiting (PONV) for upto 24 hours following surgery. Efficacy beyond 24 hours has not been demonstrated.
4.2	**Posology and method of administration** **Dosage for Adults** A single 0.075 mg I.V. dose administered over 10 seconds immediately before the induction of anesthesia. **Administration** Palonosetron Hydrochloride Injection is to be infused intravenously over 10 seconds. Palonosetron Hydrochloride Injection should not be mixed with other drugs. Flush the infusion line with normal saline before and after administration of Palonosetron Hydrochloride Injection. **Hepatic insufficiency:** There is no evidence that the dose needs to be modified in patients with hepatic impairment. **Renal insufficiency:** There is no evidence that the dose needs to be modified in patients with renal impairment.
4.3	**Contra-indications:** The Product is contraindicated in the following situations: patients previously sensitive to the drug components or to any of the excipients of the product.
4.4	**Special warning and precautions for use:** **General** Hypersensitivity reactions may occur in patients who have exhibited hypersensitivity to other selective 5-HT3 receptor antagonists. Although Palonosetron has been safely administered to 192 patients with pre-existing cardiac impairment in the Phase 3 studies, Palonosetron should be administered with caution in patients who have or may develop prolongation of cardiac conduction intervals, particularly QTc. These include patients with hypokalemia or hypomagnesemia, patients taking diuretics with potential for inducing electrolyte abnormalities, patients with congenital QT syndrome, patients taking anti-arrhythmic drugs or other drugs which lead to QT prolongation, and cumulative high dose anthracycline therapy. In 3 pivotal trials, ECGs were obtained at baseline and 24 hours after subjects received Palonosetron or a comparator drug. In a subset of patients ECGs were also obtained 15 minutes following dosing. The percentage of patients (<1%) with changes in QT and QTc intervals (either absolute values of > 500 msec or changes of > 60 msec from baseline) was similar to that seen with the comparator drugs.

4.5	**Interaction with other drugs, other forms of interactions:** Palonosetron is eliminated from the body through both renal excretion and metabolic pathways. Therefore, the potential for clinically significant drug interactions with Palonosetron appears to be low.
4.6	**Usage in pregnancy& Lactation** **Pregnancy:** Pregnancy category B Adequate and well controlled studies with palonosetron have not been conducted in pregnant women. The drug should be used in pregnancy, only if clearly needed. **Nursing mothers:** It is not known whether the drug gets excreted in human milk. A decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of drug to the mother.
4.7	**Effects on ability to drive and operate machine:** Not known
4.8	**Undesirable effects:** **Side Effects :** • Less Common Side Effects: • Headache • Constipation • **Rare Side Effects :** • Dizziness • Diarrhea • Fatigue • Abdominal pain • Trouble sleeping • Increase or decrease in heart rate • Increased or decreased blood pressure • Irregular heart beat • Abnormal electrocardiogram (picture of heart beat) • Stomach area pain In clinical trials, the following infrequently reported adverse reactions, assessed by investigators as treatment-related or causality unknown, occurred following administration to adult patients receiving concomitant cancer chemotherapy: **Cardiovascular:** 1%: non-sustained tachycardia, bradycardia, hypotension, < 1%: hypertension, myocardial ischemia, extrasystoles, sinus tachycardia, sinus arrhythmia, supraventricular extrasystoles and QT prolongation. In many cases, the relationship to palonosetron was unclear. **Dermatological:** < 1%: allergic dermatitis, rash.

	Hearing and Vision: < 1%: motion sickness, tinnitus, eye irritation and amblyopia. **Gastrointestinal System:** 1%: diarrhea, < 1%: dyspepsia, abdominal pain, dry mouth, hiccups and flatulence. **General:** 1%: weakness, < 1%: fatigue, fever, hot flush, flu-like syndrome. **Liver:** < 1%: transient, asymptomatic increases in AST and/or ALT and bilirubin. These changes occurred predominantly in patients receiving highly emetogenic chemotherapy. **Metabolic:** 1%: hyperkalemia, < 1%: electrolyte fluctuations, hyperglycemia, metabolic acidosis, glycosuria, appetite decrease, anorexia. **Musculoskeletal:** < 1%: arthralgia. **Nervous System:** 1%: dizziness, < 1%: somnolence, insomnia, hypersomnia, paresthesia. **Psychiatric:** 1%: anxiety, < 1%: euphoric mood. **Urinary System:** < 1%: urinary retention. **Vascular:** < 1%: vein discoloration, vein distention.
4.9	**Overdose and special antidotes :** Overdose should be managed with supportive care. **Symptoms of Overdose:** Get emergency help immediately if any of the following symptoms of overdose occur • Bluish color of fingernails, lips, skin, palms, or nail beds, collapse, gasping to breathe, paleness of skin, seizures.
5	**Pharmacological Properties:**
5.1	**Pharmacodynamic Properties:** **Pharmacotherapeutic Group (ATC Code) : A04AA05** Palonosetron is a selective 5-HT3 receptor antagonist with a strong binding affinity for this receptor and little or no affinity for other receptors. The effect of Palonosetron on blood pressure, heart rate, and ECG parameters including QTc were comparable to ondansetron and dolasetron in clinical trials. In non-clinical studies Palonosetron possesses the ability to block ion channels involved in ventricular de- and re-polarization and to prolong action potential duration. In clinical trials, the dose-response relationship to the QTc interval has not been fully evaluated.

5.2	**Pharmacokinetic Properties:** After intravenous dosing of Palonosetron in healthy subjects and cancer patients, an initial decline in plasma concentrations is followed by a slow elimination from the body. Mean maximum plasma concentration (Cmax) and area under the concentration-time curve (AUC 0-∞) are generally dose-proportional ov4er the dose range of 0.3–90 µg/kg in healthy subjects and in cancer patients. Following single IV dose of Palonosetron at 3µg/kg (or 0.21mg/70kg) to six cancer patients, mean (±SD) maximum plasma concentration was estimated to be 5.6 ± 5.5 ng/ml and mean AUC was 35.8 ± 20.9 ng hr/ml. **Distribution :** Palonosetron has a volume of distribution of approximately 8.3±2.5L /kg approximately 62% of Palonosetron is bound to plasma protein. **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 CYP2D6and to a lesser extent, CYP3A and CYP1A2are involved in the metabolism of Palonosetron. However, clinical pharmacokinetic parameter are not significantly different between poor and extensive metabolizes of CYP2D6 substrates. **Elimination :** After a single intravenous dose of 10µg/kg(14C) Palonosetron approximately 80% of the two dose was recovered with 144 hour in urine with Palonosetron representing approximately 40% of the administered dose. In healthy subjects the total body clearance of Palonosetron was 160±35mL/h/kg and renal clearance was 66.5±18.2mL/h/kg. Mean terminal elimination half -life is approximately 40hours.
5.3	**Preclinical Safety Data :** 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. Only limited data from animal studies are available regarding the placental transfer. Palonosetron is not mutagenic. High doses of Palonosetron (each dose causing at least 30 times the human therapeutic exposure) applied daily for two years caused an increased rate of liver tumours, endocrine neoplasms (in thyroid, pituitary, pancreas, adrenal medulla) and skin tumours in rats but not in mice. The underlying mechanisms are not fully understood, but because of the high doses employed and since Palonosetron is intended for single application in humans, these findings are not considered relevant for clinical use.

6	**Pharmaceuticals Particulars:**
6.1	**List of Excipients:** Disodium EDTA BP Mannitol BP Anhydrous Citric Acid BP Trisodium Citrate Dihydrate BP Sodium Hydroxide BP Hydrochloric Acid BP Water for Injection BP
6.2	**Incompatibilities:** This medicinal product must not be mixed with other medicinal products.
6.3	**Shelf life:** 24 Months
6.4	**Special precautions for storage:** Store below 30°C.
6.5	**Nature and contents of container:** Palonosetron Hydrochloride Injection 0.075mg/1.5ml is packed in 3ml USP Type I clear glass vial with grey bromo butyl rubber stopper and aluminium seal. 1 such vial is packed in a carton along with pack insert.
6.6	**Special precaution for disposal :** Not Applicable
7	**Registrant:** **Marketing Authorization Holder:** **M/s PHILLIPS PHARMACEUTICALS (NIGERIA) LTD.** Address : Afprint Industrial Estate, Plot 122-132, Apapa Oshodi Expressway Lagos. Country : Nigeria. Telephone : +234 806761764 Fax : --- E-mail : --- **Manufacturing Site Address:** **M/s THEMIS MEDICARE LIMITED** **Address :** Sector 6A,16,17 &18, IIE, SIDCUL, Haridwar, Uttarakhand-249 403. **Country :** India **Telephone :** 91-1334-239322/21 **Telefax :** 91-1334-239217 **E-Mail :** hwdgmtech@themismedicare.com

8	**Date of Revision of the Text:** Not Applicable
9	**Dosimetry (if applicable):** Not Applicable
10	**Instruction for preparations of Radiopharmaceutical (if applicable):** Not Applicable