SAFETY DATA SHEET

Palonosetron Formulation

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Palonosetron Formulation

Manufacturer or supplier’s details

Company : MSD
Address : 855 Leandro N. Alem St., 8 Floor
Buenos Aires, Argentina C1001AFB

Telephone : 908-740-4000
Emergency telephone : 1-908-423-6000
E-mail address : EHSDATASTEWARD@msd.com
Telefax : 908-735-1496

Recommended use of the chemical and restrictions on use

Recommended use : Pharmaceutical

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification
Not a hazardous substance or mixture.

GHS label elements
Not a hazardous substance or mixture.

Other hazards which do not result in classification
None known.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture

Components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palonosetron Hydrochloride</td>
<td>135729-62-3</td>
<td>&lt; 0.1</td>
</tr>
</tbody>
</table>

SECTION 4. FIRST AID MEASURES

If inhaled : If inhaled, remove to fresh air.
Get medical attention if symptoms occur.

In case of skin contact : Wash with water and soap as a precaution.
Get medical attention if symptoms occur.

In case of eye contact : Flush eyes with water as a precaution.
Get medical attention if irritation develops and persists.

If swallowed : If swallowed, DO NOT induce vomiting.
Get medical attention if symptoms occur.
Rinse mouth thoroughly with water.
SECTION 5. FIRE-FIGHTING MEASURES

Suitable extinguishing media : Water spray
Alcohol-resistant foam
Carbon dioxide (CO2)
Dry chemical

Unsuitable extinguishing media : None known.

Specific hazards during firefighting : Exposure to combustion products may be a hazard to health.

Hazardous combustion products : Carbon oxides

Specific extinguishing methods : Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.
Use water spray to cool unopened containers.
Remove undamaged containers from fire area if it is safe to do so.
Evacuate area.

Special protective equipment for fire-fighters : Wear self-contained breathing apparatus for firefighting if necessary.
Use personal protective equipment.

SECTION 6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures : Follow safe handling advice and personal protective equipment recommendations.

Environmental precautions : Discharge into the environment must be avoided.
Prevent further leakage or spillage if safe to do so.
Prevent spreading over a wide area (e.g., by containment or oil barriers).
Retain and dispose of contaminated wash water.
Local authorities should be advised if significant spillages cannot be contained.

Methods and materials for containment and cleaning up : Soak up with inert absorbent material.
For large spills, provide diking or other appropriate containment to keep material from spreading. If diked material can be pumped, store recovered material in appropriate container.
Clean up remaining materials from spill with suitable absorbent.
Local or national regulations may apply to releases and disposal of this material, as well as those materials and items employed in the cleanup of releases. You will need to determine which regulations are applicable.
Sections 13 and 15 of this SDS provide information regarding...
certain local or national requirements.

SECTION 7. HANDLING AND STORAGE

Technical measures: See Engineering measures under EXPOSURE CONTROLS/PERSONAL PROTECTION section.
Local/Total ventilation: Use only with adequate ventilation.
Advice on safe handling: Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment. Take care to prevent spills, waste and minimize release to the environment.
Conditions for safe storage: Keep in properly labeled containers.
Materials to avoid: Do not store with the following product types: Strong oxidizing agents.

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Ingredients with workplace control parameters

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters / Permissible concentration</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palonosetron Hydrochloride</td>
<td>135729-62-3</td>
<td>TWA</td>
<td>0.4 µg/m3 (OEB 5)</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wipe limit</td>
<td>4 µg/100 cm²</td>
<td>Internal</td>
</tr>
</tbody>
</table>

Engineering measures: Use closed processing systems or containment technologies to control at source (e.g., glove boxes/isolators) and to prevent leakage of compounds into the workplace. All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment. No open handling permitted. Totally enclosed processes and materials transport systems are required. Operations require the use of appropriate containment technology designed to prevent leakage of compounds into the workplace.

Personal protective equipment

Respiratory protection: No personal respiratory protective equipment normally required.
Hand protection

Material: Chemical-resistant gloves
Remarks: Consider double gloving.
Eye protection

: Wear safety glasses with side shields or goggles.
: If the work environment or activity involves dusty conditions, mists or aerosols, wear the appropriate goggles.
**SAFETY DATA SHEET**

**Palonosetron Formulation**

<table>
<thead>
<tr>
<th>Version</th>
<th>Revision Date:</th>
<th>SDS Number:</th>
<th>Date of last issue:</th>
<th>Date of first issue:</th>
</tr>
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<td>1.2</td>
<td>08/29/2019</td>
<td>4720319-00003</td>
<td>14.08.2019</td>
<td>02.08.2019</td>
</tr>
</tbody>
</table>

**Skin and body protection**

- Work uniform or laboratory coat.
- Additional body garments should be used based upon the task being performed (e.g., sleevelets, apron, gauntlets, disposable suits) to avoid exposed skin surfaces.
- Use appropriate degowning techniques to remove potentially contaminated clothing.

**Hygiene measures**

- If exposure to chemical is likely during typical use, provide eye flushing systems and safety showers close to the working place.
- When using do not eat, drink or smoke.
- Wash contaminated clothing before re-use.
- The effective operation of a facility should include review of engineering controls, proper personal protective equipment, appropriate degowning and decontamination procedures, industrial hygiene monitoring, medical surveillance and the use of administrative controls.

**SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>Aqueous solution</td>
</tr>
<tr>
<td>Color</td>
<td>clear</td>
</tr>
<tr>
<td>Odor</td>
<td>No data available</td>
</tr>
<tr>
<td>Odor Threshold</td>
<td>No data available</td>
</tr>
<tr>
<td>pH</td>
<td>4,5 - 5,5</td>
</tr>
<tr>
<td>Melting point/freezing point</td>
<td>No data available</td>
</tr>
<tr>
<td>Initial boiling point and boiling range</td>
<td>No data available</td>
</tr>
<tr>
<td>Flash point</td>
<td>No data available</td>
</tr>
<tr>
<td>Evaporation rate</td>
<td>No data available</td>
</tr>
<tr>
<td>Flammability (solid, gas)</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Flammability (liquids)</td>
<td>No data available</td>
</tr>
<tr>
<td>Upper explosion limit / Upper flammability limit</td>
<td>No data available</td>
</tr>
<tr>
<td>Lower explosion limit / Lower flammability limit</td>
<td>No data available</td>
</tr>
<tr>
<td>Vapor pressure</td>
<td>No data available</td>
</tr>
<tr>
<td>Relative vapor density</td>
<td>No data available</td>
</tr>
<tr>
<td>Relative density</td>
<td>No data available</td>
</tr>
</tbody>
</table>
Density : 1,015 g/cm³

Solubility(ies)
  Water solubility : No data available

Partition coefficient: n-octanol/water : Not applicable

Autoignition temperature : No data available

Decomposition temperature : No data available

Viscosity
  Viscosity, kinematic : No data available

Explosive properties : Not explosive

Oxidizing properties : The substance or mixture is not classified as oxidizing.

Molecular weight : No data available

Particle size : Not applicable

SECTION 10. STABILITY AND REACTIVITY

Reactivity : Not classified as a reactivity hazard.
Chemical stability : Stable under normal conditions.
Possibility of hazardous reac-tions : Can react with strong oxidizing agents.
Conditions to avoid : None known.
Incompatible materials : Oxidizing agents
Hazardous decomposition products : No hazardous decomposition products are known.

SECTION 11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure : Inhalation
  Skin contact
  Ingestion
  Eye contact

Acute toxicity
Not classified based on available information.

Components:

Palonosetron Hydrochloride:
Acute oral toxicity : LDLo (Rat): 250 mg/kg
  LDLo (Mouse): 100 mg/kg
  LDLo (Dog): 50 mg/kg
Skin corrosion/irritation
Not classified based on available information.

Components:

Palonosetron Hydrochloride:
Remarks: No skin irritation

Serious eye damage/eye irritation
Not classified based on available information.

Respiratory or skin sensitization

Skin sensitization
Not classified based on available information.

Respiratory sensitization
Not classified based on available information.

Germ cell mutagenicity
Not classified based on available information.

Components:

Palonosetron Hydrochloride:
Genotoxicity in vitro:
Test Type: Ames test
Result: negative

Test Type: DNA damage and repair, unscheduled DNA synthesis in mammalian cells (in vitro)
Result: negative

Test Type: In vitro mammalian cell gene mutation test
Test system: Chinese hamster ovary cells
Result: negative

Test Type: Chromosome aberration test in vitro
Test system: Chinese hamster cells
Result: positive

Genotoxicity in vivo:
Test Type: In vivo micronucleus test
Species: Mouse
Result: negative

Carcinogenicity
Not classified based on available information.

Reproductive toxicity
Not classified based on available information.

Components:

Palonosetron Hydrochloride:
Effects on fertility:
Test Type: Fertility
Species: Rat, male
Application Route: Intravenous
Fertility: NOAEL: 10 mg/kg body weight  
Symptoms: No adverse effects.

Test Type: Fertility  
Species: Rat  
Application Route: Oral  
Fertility: NOAEL: > 30 mg/kg body weight  
Symptoms: No effects on fertility.

Effects on fetal development:  
Test Type: Development  
Species: Rat  
Application Route: Oral  
Developmental Toxicity: NOAEL: 18 mg/kg body weight  
Embryo-fetal toxicity: LOAEL: > 60 mg/kg body weight  
Symptoms: Reduced body weight, No effects on fetal development, Reduced fetal weight.

Test Type: Development  
Species: Rabbit  
Application Route: Oral  
General Toxicity Maternal: LOAEL: 120 mg/kg body weight  
Developmental Toxicity: NOAEL: 90 mg/kg body weight  
Symptoms: No effects on fetal development.

**STOT-single exposure**
Not classified based on available information.

**STOT-repeated exposure**
Not classified based on available information.

**Components:**

**Palonosetron Hydrochloride:**
Routes of exposure: Ingestion  
Target Organs: Gastrointestinal tract, Kidney, Central nervous system, Testis  
Assessment: May cause damage to organs through prolonged or repeated exposure.

**Repeated dose toxicity**

**Components:**

**Palonosetron Hydrochloride:**
Species: Mouse  
NOAEL: 60 mg/kg  
LOAEL: 150 mg/kg  
Application Route: Oral  
Exposure time: 3 Months  
Target Organs: Kidney, male reproductive organs  
Remarks: May cause damage to organs.

Species: Rat  
NOAEL: 18 mg/kg  
LOAEL: > 60 mg/kg  
Application Route: Oral
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Exposure time: 3 Months
Target Organs: male reproductive organs, Liver
Remarks: Significant toxicity observed in testing

Species: Dog
LOAEL: 20 mg/kg
Application Route: Oral
Exposure time: 3 Months
Target Organs: Central nervous system, Testis
Remarks: Significant toxicity observed in testing

Species: Rat
NOAEL: 7 mg/kg
Application Route: Intravenous
Exposure time: 6 Months
Target Organs: Central nervous system, Gastrointestinal tract
Remarks: Significant toxicity observed in testing

Species: Dog
NOAEL: 6 mg/kg
Application Route: Intravenous
Exposure time: 9 Months
Target Organs: Central nervous system, Gastrointestinal tract
Symptoms: Vomiting
Remarks: Significant toxicity observed in testing

**Aspiration toxicity**
Not classified based on available information.

**Components:**

Palonosetron Hydrochloride:
Not applicable

**Experience with human exposure**

**Components:**

Palonosetron Hydrochloride:

Ingestion: Symptoms: The most common side effects are:, Headache, Diarrhea, Dizziness, Weakness, anxiety

**SECTION 12. ECOLOGICAL INFORMATION**

**Ecotoxicity**

**Components:**

Palonosetron Hydrochloride:

Ecotoxicology Assessment
Acute aquatic toxicity: Toxic effects cannot be excluded, No data available
Chronic aquatic toxicity: Toxic effects cannot be excluded, No data available
Persistence and degradability
No data available

Bioaccumulative potential
No data available

Mobility in soil
No data available

Other adverse effects
No data available

SECTION 13. DISPOSAL CONSIDERATIONS

Disposal methods
Waste from residues: Dispose of in accordance with local regulations.
Contaminated packaging: Empty containers should be taken to an approved waste handling site for recycling or disposal. If not otherwise specified: Dispose of as unused product.

SECTION 14. TRANSPORT INFORMATION

International Regulations

UNRTDG
Not regulated as a dangerous good

IATA-DGR
Not regulated as a dangerous good

IMDG-Code
Not regulated as a dangerous good

Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code
Not applicable for product as supplied.

SECTION 15. REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture

Argentina. Carcinogenic Substances and Agents Registry: Not applicable

Control of precursors and essential chemicals for the preparation of drugs: Not applicable

International Regulations

The ingredients of this product are reported in the following inventories:
AICS: not determined
SAFETY DATA SHEET

Palonosetron Formulation

Version 1.2
Revision Date: 08/29/2019
SDS Number: 4720319-00003
Date of last issue: 14.08.2019
Date of first issue: 02.08.2019

SECTION 16. OTHER INFORMATION

Further information

Full text of other abbreviations

AICS - Australian Inventory of Chemical Substances; ANTT - National Agency for Transport by Land of Brazil; ASTM - American Society for the Testing of Materials; bw - Body weight; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; ELx - Loading rate associated with x% response; EmS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; ERG - Emergency Response Guide; GHS - Globally Harmonized System; GLP - Good Laboratory Practice; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; IBC - International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk; IC50 - Half maximal inhibitory concentration; ICAO - International Civil Aviation Organization; IECSC - Inventory of Existing Chemical Substances in China; IMDG - International Maritime Dangerous Goods; IMO - International Maritime Organization; ISHL - Industrial Safety and Health Law (Japan); ISO - International Organisation for Standardization; KECI - Korea Existing Chemicals Inventory; LC50 - Lethal Concentration to 50 % of a test population; LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose); MARPOL - International Convention for the Prevention of Pollution from Ships; n.o.s. - Not Otherwise Specified; Nch - Chilean Norm; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NOM - Official Mexican Norm; NTP - National Toxicology Program; NZIoC - New Zealand Inventory of Chemicals; OECD - Organisation for Economic Co-operation and Development; OPPTS - Office of Chemical Safety and Pollution Prevention; PBT - Persistent, Bioaccumulative and Toxic substance; PICCS - Philippines Inventory of Chemicals and Chemical Substances; (Q)SAR - (Quantitative) Structure Activity Relationship; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; SADT - Self-Accelerating Decomposition Temperature; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance Inventory; TDG - Transportation of Dangerous Goods; TSCA - Toxic Substances Control Act (United States); UN - United Nations; UNRTDG - United Nations Recommendations on the Transport of Dangerous Goods; vPvB - Very Persistent and Very Bioaccumulative; WHMIS - Workplace Hazardous Materials Information System

The information provided in this Safety Data Sheet is correct to the best of our knowledge, information and belief at the date of its publication. The information is designed only as a guidance for safe handling, use, processing, storage, transportation, disposal and release and shall not be considered a warranty or quality specification of any type. The information provided relates only to the specific material identified at the top of this SDS and may not be valid when the SDS material is used in combination with any other materials or in any process, unless specified in the text. Material users should review the information and recommendations in the specific

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context of their intended manner of handling, use, processing and storage, including an assessment of the appropriateness of the SDS material in the user's end product, if applicable.

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