SAFETY DATA SHEET

Palonosetron Formulation

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Palonosetron Formulation

Manufacturer or supplier’s details

Company: MSD
Address: Rua Treze de Maio, 1161
Campinas, São Paulo, Brazil 13106-054
Telephone: 908-740-4000
Emergency telephone: 55 19 3758 2000
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 in accordance with ABNT NBR 14725 Standard
Not a hazardous substance or mixture.

GHS label elements in accordance with ABNT NBR 14725 Standard
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>Classification</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palonosetron Hydrochloride</td>
<td>135729-62-3</td>
<td>Specific target organ toxicity - repeated exposure (Oral) (Gastrointestinal tract, Kidney, Central nervous system, Testis), Category 2</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.

Most important symptoms and effects, both acute and delayed: None known.

Protection of first-aiders: No special precautions are necessary for first aid responders.

Notes to physician: Treat symptomatically and supportively.

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 fire fighting: 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.

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.

Conditions for safe storage
Keep in properly labeled containers.
Store in accordance with the particular national regulations.

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.

Wear a faceshield or other full face protection if there is a potential for direct contact to the face with dusts, mists, or aerosols.

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.

**SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES**

Appearance: Aqueous solution

Color: clear

Odor: No data available

Odor Threshold: No data available

pH: 4,5 - 5,5

Melting point/freezing point: No data available

Initial boiling point and boiling range: No data available

Flash point: No data available

Evaporation rate: No data available

Flammability (solid, gas): Not applicable

Flammability (liquids): No data available

Upper explosion limit / Upper flammability limit: No data available

Lower explosion limit / Lower flammability limit: No data available
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flammability limit

Vapor pressure : No data available
Relative vapor density : No data available
Relative density : No data available
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 reactions : 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
  - **Exposure time**: 3 Months
  - **Target Organs**: Male reproductive organs, Liver
  - **Remarks**: Significant toxicity observed in testing

### Species
- **Dog**
  - **NOAEL**: 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.

Domestic regulation

ANTT
Not regulated as a dangerous good
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SECTION 15. REGULATORY INFORMATION

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

National List of Carcinogenic Agents for Humans - (LINACH) : Not applicable

Brazil. Ordinance No. 1274 on the control and monitoring of chemicals.: Not applicable

International Regulations

The ingredients of this product are reported in the following inventories:

AICS : not determined

DSL : not determined

IECSC : not determined

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 - Organization for Economic Co-operation and Develop-
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Palonosetron Formulation

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Date of first issue: 02.08.2019

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BR / Z8