SAFETY DATA SHEET

Palonosetron Formulation

SECTION 1. IDENTIFICATION

Product name: Palonosetron Formulation
Other means of identification: No data available

Manufacturer or supplier’s details
Company name of supplier: Merck & Co., Inc
Address: 2000 Galloping Hill Road
Kenilworth - New Jersey - U.S.A. 07033
Telephone: 908-740-4000
Telefax: 908-735-1496
Emergency telephone: 1-908-423-6000
E-mail address: EHSDATASTEWARD@merck.com

Recommended use of the chemical and restrictions on use
Recommended use: Pharmaceutical

SECTION 2. HAZARDS IDENTIFICATION

GHS classification in accordance with the Hazardous Products Regulations
Not a hazardous substance or mixture.

GHS label elements
Not a hazardous substance or mixture.

Other hazards
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>&gt;= 0 - &lt; 0.1</td>
</tr>
</tbody>
</table>

Actual concentration or concentration range is withheld as a trade secret

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.
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Date of first issue: 08/02/2019

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
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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.
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.

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</td>
<td>No data available</td>
</tr>
<tr>
<td>range</td>
<td></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</td>
<td>No data available</td>
</tr>
<tr>
<td>flammability limit</td>
<td></td>
</tr>
<tr>
<td>Lower explosion limit / Lower</td>
<td>No data available</td>
</tr>
<tr>
<td>flammability limit</td>
<td></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>
<tr>
<td>Density</td>
<td>1.015 g/cm³</td>
</tr>
<tr>
<td>Solubility(ies)</td>
<td></td>
</tr>
<tr>
<td>Water solubility</td>
<td>No data available</td>
</tr>
</tbody>
</table>
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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.
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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:**

<table>
<thead>
<tr>
<th>Routes of exposure</th>
<th>Target Organs</th>
<th>Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ingestion</td>
<td>Gastrointestinal tract, Kidney, Central nervous system, Testis</td>
<td>May cause damage to organs through prolonged or repeated exposure.</td>
</tr>
</tbody>
</table>

Repeated dose toxicity

Components:

**Palonosetron Hydrochloride:**

<table>
<thead>
<tr>
<th>Species</th>
<th>NOAEL</th>
<th>LOAEL</th>
<th>Application Route</th>
<th>Exposure time</th>
<th>Target Organs</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mouse</td>
<td>60 mg/kg</td>
<td>150 mg/kg</td>
<td>Oral</td>
<td>3 Months</td>
<td>Kidney, male reproductive organs</td>
<td>May cause damage to organs.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>NOAEL</th>
<th>LOAEL</th>
<th>Application Route</th>
<th>Exposure time</th>
<th>Target Organs</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat</td>
<td>18 mg/kg</td>
<td>&gt; 60 mg/kg</td>
<td>Oral</td>
<td>3 Months</td>
<td>male reproductive organs, Liver</td>
<td>Significant toxicity observed in testing</td>
</tr>
</tbody>
</table>
**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
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

TDG
Not regulated as a dangerous good

SECTION 15. REGULATORY INFORMATION

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

AICS : not determined

DSL : not determined

IECSC : not determined

SECTION 16. OTHER 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

Sources of key data used to compile the Material Safety Data Sheet:

Revision Date: 08/29/2019

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 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.

CA / Z8