1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Palonosetron Formulation

Manufacturer or supplier's details
Company name of supplier: MSD
Address: Kumagaya, Saitama Prefecture, Xicheng 810 MSD Co., Ltd.
Menuma factory
Telephone: 048-588-8411
E-mail address: EHSDATATESTA@msd.com
Emergency telephone number: 1-908-423-6000

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

2. HAZARDS IDENTIFICATION

GHS Classification
Not a hazardous substance or mixture according to the Globally Harmonised System (GHS).

GHS label elements
Not a hazardous substance or mixture according to the Globally Harmonised System (GHS).

Other hazards which do not result in classification
None known.

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>
<th>ENCS No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palonosetron Hydrochloride</td>
<td>135729-62-3</td>
<td>&lt; 0.1</td>
<td></td>
</tr>
</tbody>
</table>

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: None known.
and effects, both acute and delayed
Protection of first-aiders : No special precautions are necessary for first aid responders.
Notes to physician : Treat symptomatically and supportively.

5. FIREFIGHTING 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 firefighters : Wear self-contained breathing apparatus for firefighting if necessary.
Use personal protective equipment.

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 dyking or other appropriate containment to keep material from spreading. If dyked 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.
7. HANDLING AND STORAGE

Handling

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.
Avoidance of contact: Oxidizing agents
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.

Storage

Conditions for safe storage: Keep in properly labelled containers.
Store in accordance with the particular national regulations.
Materials to avoid: Do not store with the following product types:
Strong oxidizing agents
Packaging material: Unsuitable material: None known.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Threshold limit value and permissible exposure limits for each component in the work environment

<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 workshop.
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.

### 9. PHYSICAL AND CHEMICAL PROPERTIES

**Appearance** : Aqueous solution

**Colour** : clear

**Odour** : No data available

**Odour 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

**Vapour pressure** : No data available
Relative vapour 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
Auto-ignition 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

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.

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 sensitisation**

**Skin sensitisation**
Not classified based on available information.

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

STOT - single exposure
Not classified based on available information.

STOT - repeated exposure
Not classified based on available information.

Components:

Palonosetron Hydrochloride:

Exposure routes: 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
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Date of first issue: 2019/08/02

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
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, Diarrhoea, Dizziness, Weakness, anxiety
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

Hazardous to the ozone layer
Not applicable

Other adverse effects
No data available

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.

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.

National Regulations
Refer to section 15 for specific national regulation.
15. REGULATORY INFORMATION

Related Regulations

Fire Service Law
Not applicable to dangerous materials / designated flammables.

Chemical Substance Control Law
Not applicable for Specified Chemical Substance, Monitoring Chemical Substance and Priority Assessment Chemical Substance.

Industrial Safety and Health Law

Harmful Substances Prohibited from Manufacture
Not applicable

Harmful Substances Required Permission for Manufacture
Not applicable

Substances Prevented From Impairment of Health
Not applicable

Circular concerning Information on Chemicals having Mutagenicity - Annex 2: Information on Existing Chemicals having Mutagenicity
Not applicable

Circular concerning Information on Chemicals having Mutagenicity - Annex 1: Information on Notified Substances having Mutagenicity
Not applicable

Substances Subject to be Notified Names
Not applicable

Substances Subject to be Indicated Names
Not applicable

Ordinance on Prevention of Hazards Due to Specified Chemical Substances
Not applicable

Ordinance on Prevention of Lead Poisoning
Not applicable

Ordinance on Prevention of Tetraalkyl Lead Poisoning
Not applicable

Ordinance on Prevention of Organic Solvent Poisoning
Not applicable

Enforcement Order of the Industrial Safety and Health Law - Attached table 1 (Dangerous Substances)
Not applicable

Poisonous and Deleterious Substances Control Law
Not applicable

Act on Confirmation, etc. of Release Amounts of Specific Chemical Substances in the Environment and Promotion of Improvements to the Management Thereof
Not applicable
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High Pressure Gas Safety Act
Not applicable

Explosive Control Law
Not applicable

Vessel Safety Law
Not regulated as a dangerous good

Aviation Law
Not regulated as a dangerous good

Marine Pollution and Sea Disaster Prevention etc Law
Bulk transportation: Not classified as noxious liquid substance
Pack transportation: Not classified as marine pollutant

Narcotics and Psychotropics Control Act
Narcotic or Psychotropic Raw Material (Export / Import Permission)
Not applicable

Specific Narcotic or Psychotropic Raw Material (Export / Import permission)
Not applicable

Waste Disposal and Public Cleansing Law
Industrial waste

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

<table>
<thead>
<tr>
<th>Inventory</th>
<th>Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>AICS</td>
<td>not determined</td>
</tr>
<tr>
<td>DSL</td>
<td>not determined</td>
</tr>
<tr>
<td>IECSC</td>
<td>not determined</td>
</tr>
</tbody>
</table>

16. OTHER INFORMATION

Further information
Sources of key data used to compile the Safety Data Sheet

Date format: yyyy/mm/dd

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
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.

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