SAFETY DATA SHEET

Raltegravir Pediatric Formulation

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Raltegravir Pediatric Formulation

Manufacturer or supplier's details
Company : MSD
Address : Avenida Tanner de Melo, Quadra 10 Lote 4A, Galpão A Parque Industrial Vice Presidente José Alencar Aparecida de Goias – GO, Brazil
Telephone : 908-740-4000
Emergency telephone : 1-908-423-6000
E-mail address : EHSDATASTEWARD@msd.com

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
Serious eye damage : Category 1
Reproductive toxicity : Category 2
Specific target organ toxicity - single exposure : Category 3

GHS label elements in accordance with ABNT NBR 14725 Standard
Hazard pictograms :  
Signal Word : Danger
Hazard Statements : H318 Causes serious eye damage. H335 May cause respiratory irritation. H361d Suspected of damaging the unborn child.

Precautionary Statements : Prevention:
P201 Obtain special instructions before use. P261 Avoid breathing dust. P280 Wear protective gloves/ protective clothing/ eye protection/ face protection.
Response: P304 + P340 + P312 IF INHALED: Remove person to fresh air
and keep comfortable for breathing. Call a POISON CENTER/ doctor if you feel unwell.
P305 + P351 + P338 + P310 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a POISON CENTER/ doctor.
P308 + P313 IF exposed or concerned: Get medical advice/ attention.

Other hazards which do not result in classification
Contact with dust can cause mechanical irritation or drying of the skin.
May form explosive dust-air mixture during processing, handling or other means.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mixture</td>
<td>Mixture</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Classification</th>
<th>Concentration (% w/w)</th>
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<tbody>
<tr>
<td>Raltegravir</td>
<td>871038-72-1</td>
<td>Acute toxicity (Oral), Category 5</td>
<td>&gt;= 20 - &lt; 25</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Serious eye damage, Category 1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Reproductive toxicity, Category 2</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Specific target organ toxicity - single exposure, Category 3</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Short-term (acute) aquatic hazard, Category 3</td>
<td></td>
</tr>
</tbody>
</table>

SECTION 4. FIRST AID MEASURES

General advice : In the case of accident or if you feel unwell, seek medical advice immediately. When symptoms persist or in all cases of doubt seek medical advice.

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

In case of skin contact : In case of contact, immediately flush skin with soap and plenty of water. Remove contaminated clothing and shoes. Get medical attention. Wash clothing before reuse. Thoroughly clean shoes before reuse.

In case of eye contact : In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. If easy to do, remove contact lens, if worn. Get medical attention immediately.

If swallowed : If swallowed, DO NOT induce vomiting. Get medical attention.
Most important symptoms and effects, both acute and delayed:

- Causes serious eye damage.
- May cause respiratory irritation.
- Suspected of damaging the unborn child.
- Contact with dust can cause mechanical irritation or drying of the skin.

Protection of first-aiders:

First Aid responders should pay attention to self-protection, and use the recommended personal protective equipment when the potential for exposure exists (see section 8).

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:

Avoid generating dust; fine dust dispersed in air in sufficient concentrations, and in the presence of an ignition source is a potential dust explosion hazard. Exposure to combustion products may be a hazard to health.

Hazardous combustion products:

- Carbon oxides
- Nitrogen oxides (NOx)
- Fluorine compounds
- Chlorine compounds
- Sulfur oxides
- Metal 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:

In the event of fire, wear self-contained breathing apparatus. Use personal protective equipment.

SECTION 6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures:

Use personal protective equipment. Follow safe handling advice (see section 7) and personal protective equipment recommendations (see section 8).

Environmental precautions:

Avoid release to the environment. Prevent further leakage or spillage if safe to do so. 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:

Sweep up or vacuum up spillage and collect in suitable container for disposal. Avoid dispersal of dust in the air (i.e., clearing dust surfaces...
with compressed air). Dust deposits should not be allowed to accumulate on surfaces, as these may form an explosive mixture if they are released into the atmosphere in sufficient concentration. 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: Static electricity may accumulate and ignite suspended dust causing an explosion. Provide adequate precautions, such as electrical grounding and bonding, or inert atmospheres.

Local/Total ventilation: If sufficient ventilation is unavailable, use with local exhaust ventilation.

Advice on safe handling: Avoid breathing dust. Do not swallow. Do not get in eyes. Avoid prolonged or repeated contact with skin. Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment. Keep container tightly closed. Already sensitized individuals should consult their physician regarding working with respiratory irritants or sensitizers. Minimize dust generation and accumulation. Keep container closed when not in use. Keep away from heat and sources of ignition. Take precautionary measures against static discharges. 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.

Conditions for safe storage: Keep in properly labeled containers. Store locked up. Keep tightly closed. Keep in a cool, well-ventilated place. 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 Control parameters / Permissible)</th>
<th>Basis</th>
</tr>
</thead>
</table>

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**Engineering measures**

Minimize workplace exposure concentrations. Apply measures to prevent dust explosions. Ensure that dust-handling systems (such as exhaust ducts, dust collectors, vessels, and processing equipment) are designed in a manner to prevent the escape of dust into the work area (i.e., there is no leakage from the equipment). If sufficient ventilation is unavailable, use with local exhaust ventilation.

**Personal protective equipment**

**Respiratory protection**

If adequate local exhaust ventilation is not available or exposure assessment demonstrates exposures outside the recommended guidelines, use respiratory protection.

- **Filter type**: Particulates type

**Hand protection**

Material: Chemical-resistant gloves

Remarks: Choose gloves to protect hands against chemicals depending on the concentration specific to place of work. Breakthrough time is not determined for the product. Change gloves often! For special applications, we recommend clarifying the resistance to chemicals of the aforementioned protective gloves with the glove manufacturer. Wash hands before breaks and at the end of workday.

**Eye protection**

Wear the following personal protective equipment:

- Chemical resistant goggles must be worn.
- If splashes are likely to occur, wear: Face-shield

**Skin and body protection**

Select appropriate protective clothing based on chemical resistance data and an assessment of the local exposure potential. Skin contact must be avoided by using impervious protective clothing (gloves, aprons, boots, etc).

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**SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES**

- **Appearance**: powder
- **Color**: yellow-orange
- **Odor**: No data available
- **Odor Threshold**: No data available
- **pH**: No data available
- **Melting point/freezing point**: No data available
- **Initial boiling point and boiling**: No data available
SAFETY DATA SHEET

Raltegravir Pediatric 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>
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<tr>
<td>4.4</td>
<td>16.10.2020</td>
<td>20355-00016</td>
<td>23.03.2020</td>
<td>09.10.2014</td>
</tr>
</tbody>
</table>

range

Flash point : No data available
Evaporation rate : No data available
Flammability (solid, gas) : May form explosive dust-air mixture during processing, handling or other means.
Flammability (liquids) : No data available
Upper explosion limit / Upper flammability limit : No data available
Lower explosion limit / Lower flammability limit : No data available
Vapor pressure : No data available
Relative vapor density : No data available
Relative density : No data available
Solubility(ies)
   Water solubility : No data available
Partition coefficient: n-octanol/water : No data available
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 : No data available

SECTION 10. STABILITY AND REACTIVITY

Reactivity : Not classified as a reactivity hazard.
Chemical stability : Stable under normal conditions.
Possibility of hazardous reactions
   May form explosive dust-air mixture during processing, handling or other means.
   Can react with strong oxidizing agents.
Conditions to avoid
   Heat, flames and sparks.
   Avoid dust formation.
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.

Product:
- Acute oral toxicity: Acute toxicity estimate: > 5.000 mg/kg
  Method: Calculation method

Components:
Raltegravir:
- Acute oral toxicity: LD50 (Mouse, male and female): > 2.000 mg/kg

Skin corrosion/irritation
Not classified based on available information.

Components:
Raltegravir:
- Species: Rabbit
  Result: No skin irritation

Serious eye damage/eye irritation
Causes serious eye damage.

Components:
Raltegravir:
- Species: Bovine cornea
  Result: Severe irritation

Respiratory or skin sensitization

Skin sensitization
Not classified based on available information.

Respiratory sensitization
Not classified based on available information.

Components:
Raltegravir:
- Test Type: Local lymph node assay (LLNA)
  Species: Mouse
  Result: negative
Germ cell mutagenicity
Not classified based on available information.

Components:
Raltegravir:
Genotoxicity in vitro:
- Test Type: reverse mutation assay
  Result: negative
- Test Type: Alkaline elution assay
  Test system: rat hepatocytes
  Result: negative
- Test Type: Chromosomal aberration
  Method: OECD Test Guideline 473
  Result: negative

Genotoxicity in vivo:
- Test Type: In vivo micronucleus test
  Species: Mouse
  Result: negative
- Test Type: Chromosomal aberration
  Method: OECD Test Guideline 475
  Result: negative

Carcinogenicity
Not classified based on available information.

Components:
Raltegravir:
Species: Mouse, male and female
Exposure time: 104 weeks
Result: negative

Reproductive toxicity
Suspected of damaging the unborn child.

Components:
Raltegravir:
Effects on fertility:
- Test Type: Fertility/early embryonic development
  Species: Rat, male and female
  Application Route: Oral
  General Toxicity Parent: NOAEL: 600 mg/kg body weight
  Result: negative

Effects on fetal development:
- Species: Rat
  Application Route: Oral
  General Toxicity Maternal: NOAEL: >= 600 mg/kg body weight
  Teratogenicity: LOAEL F1: 300 mg/kg body weight
  Symptoms: Skeletal malformations.
  Result: positive
Species: Rabbit
General Toxicity Maternal: NOAEL: >= 1.000 mg/kg body weight
Teratogenicity: NOAEL: >= 1.000 mg/kg body weight
Result: negative

Reproductive toxicity - Assessment: Some evidence of adverse effects on development, based on animal experiments.

STOT-single exposure
May cause respiratory irritation.

Components:
Raltegravir:
Routes of exposure: Inhalation
Target Organs: Respiratory Tract
Assessment: May cause respiratory irritation.

STOT-repeated exposure
Not classified based on available information.

Repeated dose toxicity
Components:
Raltegravir:
Species: Dog
NOAEL: 90 mg/kg
Application Route: Oral
Exposure time: 371 d
Symptoms: Vomiting

Species: Rat
NOAEL: 30 mg/kg
LOAEL: 120 mg/kg
Application Route: Oral
Exposure time: 189 d
Target Organs: Stomach

Species: Mouse
NOAEL: 50 mg/kg
LOAEL: 500 mg/kg
Application Route: Oral
Exposure time: 14 Weeks
Target Organs: Stomach

Species: Rat
NOAEL: 50 mg/kg
LOAEL: 200 mg/kg
Application Route: Oral
Exposure time: 8 Weeks
Target Organs: Stomach
Aspiration toxicity
Not classified based on available information.

Experience with human exposure

Components:

**Raltegravir:**
- **Ingestion:**
  - Symptoms: Nausea, Diarrhea, Headache, Fever, Rash, Skin irritation

**SECTION 12. ECOLOGICAL INFORMATION**

Ecotoxicity

Components:

**Raltegravir:**
- **Toxicity to fish:**
  - LC50 (Pimephales promelas (fathead minnow)): > 100 mg/l
  - Exposure time: 96 h
  - Method: OECD Test Guideline 203
- LC50 (Cyprinodon variegatus (sheepshead minnow)): > 100 mg/l
  - Exposure time: 96 h
  - Method: OECD Test Guideline 203
- **Toxicity to daphnia and other aquatic invertebrates:**
  - EC50 (Daphnia magna (Water flea)): > 100 mg/l
  - Exposure time: 48 h
  - Method: OECD Test Guideline 202
- **Toxicity to algae/aquatic plants:**
  - EC50 (Pseudokirchneriella subcapitata (green algae)): 66 mg/l
  - Exposure time: 96 h
  - Method: OECD Test Guideline 201
  - NOEC (Pseudokirchneriella subcapitata (green algae)): 3,8 mg/l
  - Exposure time: 96 h
  - Method: OECD Test Guideline 201
- **Toxicity to fish (Chronic toxicity):**
  - NOEC (Pimephales promelas (fathead minnow)): 9,3 mg/l
  - Exposure time: 33 d
  - Method: OECD Test Guideline 210
- **Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity):**
  - NOEC (Daphnia magna (Water flea)): 9,5 mg/l
  - Exposure time: 21 d
  - Method: OECD Test Guideline 211
- **Toxicity to microorganisms:**
  - EC50: > 1.000 mg/l
  - Exposure time: 3 h
  - Test Type: Respiration inhibition
  - Method: OECD Test Guideline 209
  - NOEC: 1.000 mg/l
  - Exposure time: 3 h
Test Type: Respiration inhibition  
Method: OECD Test Guideline 209

**Persistence and degradability**

**Components:**

**Raltegravir:**
- **Biodegradability**: Result: rapidly degradable  
  Biodegradation: 50 %  
  Exposure time: 9 d  
  Method: OECD Test Guideline 302B
- **Stability in water**: Hydrolysis: < 10 % (5 d)  
  Method: OECD Test Guideline 111

**Bioaccumulative potential**

**Components:**

**Raltegravir:**
- **Partition coefficient: n-octanol/water**: log Pow: -0.328
- **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**
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Version 4.4 Revision Date: 16.10.2020 SDS Number: 20355-00016 Date of last issue: 23.03.2020 Date of first issue: 09.10.2014

ANTT
Not regulated as a dangerous good

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. List of chemicals controlled by the Federal Police : 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

AIIC - Australian Inventory of Industrial Chemicals; 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
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