SAFETY DATA SHEET

Raltegravir Pediatric Formulation

1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Raltegravir Pediatric Formulation

Manufacturer or supplier’s details

Company : Merck & Co., Inc
Address : 2000 Galloping Hill Road
Kenilworth - New Jersey - U.S.A. 07033
Telephone : 908-740-4000
Emergency telephone number : 1-908-423-6000
E-mail address : EHSDATASTEWARD@msd.com

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

2. HAZARDS IDENTIFICATION

GHS Classification

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

GHS label elements

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.
P202 Do not handle until all safety precautions have been read and understood.
P261 Avoid breathing dust.
P271 Use only outdoors or in a well-ventilated area.
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.

Storage:
P405 Store locked up.

Disposal:
P501 Dispose of contents/container to an approved waste disposal plant.

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.

3. COMPOSITION/INFORMATION ON INGREDIENTS

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

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raltegravir</td>
<td>871038-72-1</td>
<td>&gt;= 20 -&lt; 30</td>
</tr>
</tbody>
</table>

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. Rinse mouth thoroughly with water.

Most important symptoms: Causes serious eye damage.
and effects, both acute and delayed
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.

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

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 surfac-
es, 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.

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 sensitised 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.

Conditions for safe storage: Keep in properly labelled 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

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Components 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>Raltegravir</td>
<td>871038-72-1</td>
<td>TWA</td>
<td>1,000 µg/m3</td>
<td>Internal</td>
</tr>
</tbody>
</table>

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: Chemical-resistant gloves

Remarks: Choose gloves to protect hands against chemicals depending on the concentration and quantity of the hazardous substance and 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

Protective clothing: 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).

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.

9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance: powder

Colour: yellow-orange

Odour: No data available

Odour Threshold: No data available

pH: No data available

Melting point/freezing point: No data available

Initial boiling point and boiling: No data available
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.

11. TOXICOLOGICAL INFORMATION

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

Acute toxicity
Not classified based on available information.

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 sensitisation

Skin sensitisation
Not classified based on available information.

Respiratory sensitisation
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 foetal 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 - Assesement
Some evidence of adverse effects on development, based on animal experiments.

**STOT - single exposure**
May cause respiratory irritation.

**Components:**

**Raltegravir:**
Exposure routes : 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, Diarrhoea, Headache, Fever, Rash, Skin irritation

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 (sheephead 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

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.

15. REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture
Minister of Industry Regulation No. 23/M-IND/PER/4/2013 concerning the Revision of Minister of Industry Regulation No. 87/M-IND/PER/9/2009 concerning Globally Harmonized System of Classification and Labelling of Chemicals.

Regulation of the Minister of Health No. 472 of 1996 on the Safeguarding of Substances Hazardous to Health

Hazardous substances that must be registered : Not applicable

Government Regulation No. 74 of 2001 on the Management of Hazardous and Toxic Substances

Hazardous substances approved for use : Not applicable

Prohibited substances : Not applicable

Restricted substances : Not applicable

Regulation of the Minister of Trade No. 44 of 2009 on Procurement, Distribution and Supervision of Hazardous Materials

Type of Hazardous Materials Restricted to Import, Distribution and Supervision : Not applicable

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

AICS : not determined

DSL : not determined

IECSC : not determined

16. OTHER INFORMATION

Further information


Date format : yyyy/mm/dd

Full text of other abbreviations

AIC - 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 Loading Rate; NOM - Official Mexican Norm; NTP - National Toxicology Program; NZIoC - New Zealand Inventory of Chemicals; OECD - Organization 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 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.