SAFETY DATA SHEET

Raltegravir Adult Formulation

SECTION 1. IDENTIFICATION

Product name : Raltegravir Adult Formulation

Manufacturer or supplier’s details

Company : MSD
Address : 855 Leandro N. Alem St., 8 Floor
           Buenos Aires, Argentina  C1001AFB
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

Serious eye damage : Category 1
Reproductive toxicity : Category 2
Specific target organ toxicity - single exposure : Category 3
Short-term (acute) aquatic hazard : 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.
                   H402 Harmful to aquatic life.
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.
P273 Avoid release to the environment.
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.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Raltegravir</td>
<td>871038-72-1</td>
<td>&gt;= 30 -&lt; 50</td>
</tr>
<tr>
<td></td>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>&gt;= 10 -&lt; 20</td>
</tr>
<tr>
<td></td>
<td>Magnesium stearate</td>
<td>557-04-0</td>
<td>&gt;= 1 -&lt; 5</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. Rinse mouth thoroughly with water. 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 Metal oxides Oxides of phosphorus Nitrogen oxides (NOx) Fluorine compounds 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.
SECTION 7. HANDLING AND STORAGE

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 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

<table>
<thead>
<tr>
<th>Ingredients with workplace control parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Components</td>
</tr>
<tr>
<td>------------</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>
SAFETY DATA SHEET

Raltegravir Adult Formulation

<table>
<thead>
<tr>
<th>Material</th>
<th>TWA (Inhalable particulate matter)</th>
<th>TWA (Respirable particulate matter)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raltegravir</td>
<td>1000 µg/m³</td>
<td>3 mg/m³</td>
</tr>
<tr>
<td>Cellulose</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
</tbody>
</table>

Further information: A4 - Not classifiable as a human carcinogen

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).

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.
SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance: powder

Color: No data available

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 range: No data available

Flash point: No data available

Evaporation rate: Not applicable

Flammability (solid, gas): May form explosive dust-air mixture during processing, handling or other means.

Flammability (liquids): No data available

Self-ignition: 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

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, dynamic: No data available

Viscosity, kinematic: No data available

Flow time: 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

Cellulose:
Acute oral toxicity : LD50 (Rat): > 5.000 mg/kg
Acute inhalation toxicity : LC50 (Rat): > 5.8 mg/l
Exposure time: 4 h
Test atmosphere: dust/mist
Acute dermal toxicity : LD50 (Rabbit): > 2.000 mg/kg

Magnesium stearate:
Acute oral toxicity: LD50 (Rat): > 2,000 mg/kg  
Method: OECD Test Guideline 423  
Assessment: The substance or mixture has no acute oral toxicity  
Remarks: Based on data from similar materials

Acute dermal toxicity: LD50 (Rabbit): > 2,000 mg/kg  
Remarks: Based on data from similar materials

**Skin corrosion/irritation**  
Not classified based on available information.

**Components:**

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

Magnesium stearate:
- Species: Rabbit  
- Result: No skin irritation  
- Remarks: Based on data from similar materials

**Serious eye damage/eye irritation**  
Causes serious eye damage.

**Components:**

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

Magnesium stearate:
- Species: Rabbit  
- Result: No eye irritation  
- Remarks: Based on data from similar materials

**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
Magnesium stearate:
Test Type: Maximization Test
Routes of exposure: Skin contact
Species: Guinea pig
Method: OECD Test Guideline 406
Result: negative
Remarks: Based on data from similar materials

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

Cellulose:
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES)
Result: negative
Test Type: In vitro mammalian cell gene mutation test
Result: negative

Genotoxicity in vivo: Test Type: Mammalian erythrocyte micronucleus test (in vivo cytogenetic assay)
Species: Mouse
Application Route: Ingestion
Result: negative

Magnesium stearate:
Genotoxicity in vitro: Test Type: In vitro mammalian cell gene mutation test
Result: negative
Remarks: Based on data from similar materials
Test Type: Chromosome aberration test in vitro
Method: OECD Test Guideline 473
Result: negative
Remarks: Based on data from similar materials

Test Type: Bacterial reverse mutation assay (AMES)
Result: negative
Remarks: Based on data from similar materials

Carcinogenicity
Not classified based on available information.

Components:

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

Cellulose:
Species: Rat
Application Route: Ingestion
Exposure time: 72 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.

Cellulose:
Effects on fertility: Test Type: One-generation reproduction toxicity study
Species: Rat  
Application Route: Ingestion  
Result: negative

Effects on fetal development:  
Test Type: Fertility/early embryonic development  
Species: Rat  
Application Route: Ingestion  
Result: negative

Magnesium stearate:  
Effects on fertility:  
Test Type: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test  
Species: Rat  
Application Route: Ingestion  
Method: OECD Test Guideline 422  
Result: negative  
Remarks: Based on data from similar materials

Effects on fetal development:  
Test Type: Embryo-fetal development  
Species: Rat  
Application Route: Ingestion  
Result: negative  
Remarks: Based on data from similar materials

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

Cellulose:
Species: Rat
NOAEL: >= 9.000 mg/kg
Application Route: Ingestion
Exposure time: 90 Days

Magnesium stearate:
Species: Rat
NOAEL: > 100 mg/kg
Application Route: Ingestion
Exposure time: 90 Days
Remarks: Based on data from similar materials

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

**Toxicity to algae/aquatic plants**

- **EC50 (Pseudokirchneriella subcapitata (green algae)):** 66 mg/l
  - Exposure time: 96 h

**NOEC (Pseudokirchneriella subcapitata (green algae)):** 3.8 mg/l
  - Exposure time: 96 h

**Toxicity to fish (Chronic toxicity)**

- **NOEC (Pimephales promelas (fathead minnow)):** 9.3 mg/l
  - Exposure time: 33 d

**Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity)**

- **NOEC (Daphnia magna (Water flea)):** 9.5 mg/l
  - Exposure time: 21 d

**Toxicity to microorganisms**

- **EC50:** > 1.000 mg/l
  - Exposure time: 3 h
  - Test Type: Respiration inhibition

**NOEC:** 1.000 mg/l
  - Exposure time: 3 h
  - Test Type: Respiration inhibition

**Cellulose:**

**Toxicity to fish**

- **LC50 (Oryzias latipes (Japanese medaka)):** > 100 mg/l
  - Exposure time: 48 h
  - Remarks: Based on data from similar materials

**Magnesium stearate:**

**Toxicity to fish**

- **LC50 (Leuciscus idus (Golden orfe)):** > 100 mg/l
  - Exposure time: 48 h
  - Method: DIN 38412
  - Remarks: Based on data from similar materials

**Toxicity to daphnia and other aquatic invertebrates**

- **EL50 (Daphnia magna (Water flea)):** > 1 mg/l
  - Exposure time: 47 h
  - Test substance: Water Accommodated Fraction
  - Remarks: Based on data from similar materials
  - No toxicity at the limit of solubility.

**Toxicity to algae/aquatic plants**

- **EL50 (Pseudokirchneriella subcapitata (green algae)):** > 1 mg/l
  - Exposure time: 72 h
Test substance: Water Accommodated Fraction
Method: OECD Test Guideline 201
Remarks: Based on data from similar materials
No toxicity at the limit of solubility.

NOELR (Pseudokirchneriella subcapitata (green algae)): > 1 mg/l
Exposure time: 72 h
Test substance: Water Accommodated Fraction
Method: OECD Test Guideline 201
Remarks: Based on data from similar materials

Toxicity to microorganisms: EC10 (Pseudomonas putida): > 100 mg/l
Exposure time: 16 h
Test substance: Water Accommodated Fraction
Remarks: Based on data from similar materials

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

Cellulose:
Biodegradability: Result: Readily biodegradable.

Magnesium stearate:
Biodegradability: Result: Not biodegradable
Remarks: Based on data from similar materials

Bioaccumulative potential

Components:

Raltegravir:
Partition coefficient: n-octanol/water: log Pow: -0.328

Magnesium stearate:
Partition coefficient: n-octanol/water: log Pow: > 4

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.
Special precautions for user
Not applicable

SECTION 15. REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture
Argentina. Carcinogenic Substances and Agents Registry. : Not applicable
Control of precursors and essential chemicals for the preparation of drugs. : Not applicable

SECTION 16. OTHER INFORMATION

Further information

Full text of other abbreviations
ACGIH : USA. ACGIH Threshold Limit Values (TLV)
AR OEL : Argentina. Occupational Exposure Limits
ACGIH / TWA : 8-hour, time-weighted average
AR OEL / CMP : TLV (Threshold Limit Value)
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.