1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Raltegravir / Lamivudine Formulation

Manufacturer or supplier’s details
Company: MSD
Address: Briahnager - Off Pune Nagar Road, Wagholi - Pune - India 412 207
Telephone: 908-740-4000
Emergency telephone number: 1-908-423-6000
E-mail address: EHSDATASTEWARD@msd.com
Telefax: 908-735-1496

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

2. HAZARDS IDENTIFICATION

Manufacture, Storage and Import of Hazardous Chemicals Rules 1989

Classification
Not classified as hazardous according to criteria laid down in Part I of Schedule-1.

GHS Classification
Acute toxicity (Oral): Category 5
Serious eye damage/eye irritation: Category 1
Reproductive toxicity: Category 2
Specific target organ toxicity - single exposure: Category 3
Specific target organ toxicity - repeated exposure (Oral): Category 2 (Blood)
Short-term (acute) aquatic hazard: Category 3

GHS label elements
Hazard pictograms:
Signal word : Danger

Hazard statements :
- H303 May be harmful if swallowed.
- H318 Causes serious eye damage.
- H335 May cause respiratory irritation.
- H361d Suspected of damaging the unborn child.
- H373 May cause damage to organs (Blood) through prolonged or repeated exposure if swallowed.
- 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.
- P260 Do not breathe 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:
- P301 + P312 IF SWALLOWED: Call a POISON CENTER/ doctor if you feel unwell.
- 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

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>Raltegravir</td>
<td>871038-72-1</td>
<td>&gt;= 50 - &lt; 70</td>
</tr>
<tr>
<td>Lamivudine</td>
<td>134678-17-4</td>
<td>&gt;= 20 - &lt; 30</td>
</tr>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>&gt;= 10 - &lt; 20</td>
</tr>
</tbody>
</table>
### 4. FIRST AID MEASURES

<table>
<thead>
<tr>
<th>General advice</th>
<th>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.</th>
</tr>
</thead>
<tbody>
<tr>
<td>If inhaled</td>
<td>If inhaled, remove to fresh air. Get medical attention.</td>
</tr>
<tr>
<td>In case of skin contact</td>
<td>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.</td>
</tr>
<tr>
<td>In case of eye contact</td>
<td>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.</td>
</tr>
<tr>
<td>If swallowed</td>
<td>If swallowed, DO NOT induce vomiting. Get medical attention. Rinse mouth thoroughly with water.</td>
</tr>
<tr>
<td>Most important symptoms and effects, both acute and delayed</td>
<td>May be harmful if swallowed. Causes serious eye damage. May cause respiratory irritation. Suspected of damaging the unborn child. May cause damage to organs through prolonged or repeated exposure if swallowed. Contact with dust can cause mechanical irritation or drying of the skin.</td>
</tr>
<tr>
<td>Protection of first-aiders</td>
<td>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).</td>
</tr>
<tr>
<td>Notes to physician</td>
<td>Treat symptomatically and supportively.</td>
</tr>
</tbody>
</table>

### 5. FIREFIGHTING MEASURES

<table>
<thead>
<tr>
<th>Suitable extinguishing media</th>
<th>Water spray</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Alcohol-resistant foam</td>
</tr>
<tr>
<td></td>
<td>Carbon dioxide (CO2)</td>
</tr>
<tr>
<td></td>
<td>Dry chemical</td>
</tr>
<tr>
<td>Unsuitable extinguishing media</td>
<td>None known.</td>
</tr>
<tr>
<td>Specific hazards during firefighting</td>
<td>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.</td>
</tr>
<tr>
<td>Hazardous combustion products</td>
<td>Carbon oxides</td>
</tr>
<tr>
<td></td>
<td>Nitrogen oxides (NOx)</td>
</tr>
<tr>
<td></td>
<td>Fluorine compounds</td>
</tr>
<tr>
<td></td>
<td>Metal oxides</td>
</tr>
</tbody>
</table>
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 and personal protective equipment recommendations.

Environmental precautions: Discharge into the environment must be avoided. 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.

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: Do not breathe 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>
<tr>
<td>Lamivudine</td>
<td>134678-17-4</td>
<td>TWA</td>
<td>150 µg/m³ (OEB 2)</td>
<td>Internal</td>
</tr>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>557-04-0</td>
<td>TWA (Inhalable particulate matter)</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Respirable particulate matter)</td>
<td>3 mg/m³</td>
<td>ACGIH</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
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.

9. PHYSICAL AND CHEMICAL PROPERTIES

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>powder</td>
</tr>
<tr>
<td>Colour</td>
<td>green</td>
</tr>
<tr>
<td>Odour</td>
<td>No data available</td>
</tr>
<tr>
<td>Odour Threshold</td>
<td>No data available</td>
</tr>
<tr>
<td>pH</td>
<td>No data available</td>
</tr>
<tr>
<td>Melting point/freezing point</td>
<td>No data available</td>
</tr>
<tr>
<td>Initial boiling point and boiling range</td>
<td>No data available</td>
</tr>
<tr>
<td>Flash point</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Evaporation rate</td>
<td>No data available</td>
</tr>
<tr>
<td>Flammability (solid, gas)</td>
<td>May form explosive dust-air mixture during processing, handling or other means.</td>
</tr>
<tr>
<td>Flammability (liquids)</td>
<td>No data available</td>
</tr>
<tr>
<td>Upper explosion limit / Upper flammability limit</td>
<td>No data available</td>
</tr>
<tr>
<td>Lower explosion limit / Lower flammability limit</td>
<td>No data available</td>
</tr>
<tr>
<td>Vapour pressure</td>
<td>No data available</td>
</tr>
<tr>
<td>Relative vapour density</td>
<td>No data available</td>
</tr>
</tbody>
</table>
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
May be harmful if swallowed.

Product:
Acute oral toxicity: Acute toxicity estimate: 4,931 mg/kg
Method: Calculation method

Components:
Raltegravir:
Acute oral toxicity: LD50 (Mouse, male and female): > 2,000 mg/kg

**Lamivudine:**
- Acute oral toxicity: LD50 (Rat): > 2,000 mg/kg
  - LD50 (Mouse): 4,000 mg/kg
  - Remarks: No mortality observed at this dose.
- Acute toxicity (other routes of administration): LD50 (Rat): > 2,000 mg/kg
  - Application Route: Intravenous

**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

**Lamivudine:**
- Species: Rabbit
- Result: Mild 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

Lamivudine:
Species: Rabbit
Result: No eye irritation

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

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

Lamivudine:
Exposure routes: Dermal
Species: Guinea pig
Result: Not a skin sensitizer.

Magnesium stearate:
Test Type: Maximisation Test
Exposure routes: 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
### Genotoxicity in vivo

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Method</th>
<th>Result</th>
<th>Species</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkaline elution assay</td>
<td></td>
<td>negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chromosomal aberration</td>
<td>OECD Test Guideline 473</td>
<td>negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>In vivo micronucleus test</td>
<td>Mouse</td>
<td>negative</td>
<td></td>
<td>Oral</td>
</tr>
<tr>
<td>Chromosomal aberration</td>
<td>OECD Test Guideline 475</td>
<td>negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Micronucleus test</td>
<td>Rat</td>
<td>negative</td>
<td>Oral</td>
<td></td>
</tr>
<tr>
<td>Unscheduled DNA synthesis (UDS) test</td>
<td>with mammalian liver cells in vivo</td>
<td>negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mammalian erythrocyte micronucleus test</td>
<td>(in vivo cytogenetic assay)</td>
<td>negative</td>
<td>Mouse</td>
<td>Ingestion</td>
</tr>
</tbody>
</table>

### Lamivudine:

<table>
<thead>
<tr>
<th>Genotoxicity in vitro</th>
<th>Test Type</th>
<th>Method</th>
<th>Result</th>
<th>Species</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial reverse mutation assay (AMES)</td>
<td></td>
<td></td>
<td>negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mouse Lymphoma</td>
<td></td>
<td></td>
<td>equivocal</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Genotoxicity in vivo</th>
<th>Test Type</th>
<th>Method</th>
<th>Result</th>
<th>Species</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Micronucleus test</td>
<td>Rat</td>
<td></td>
<td>negative</td>
<td>Oral</td>
<td></td>
</tr>
<tr>
<td>Unscheduled DNA synthesis (UDS) test</td>
<td>with mammalian liver cells in vivo</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Cellulose:

<table>
<thead>
<tr>
<th>Genotoxicity in vitro</th>
<th>Test Type</th>
<th>Method</th>
<th>Result</th>
<th>Species</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial reverse mutation assay (AMES)</td>
<td></td>
<td></td>
<td>negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>In vitro mammalian cell gene mutation test</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Genotoxicity in vivo</th>
<th>Test Type</th>
<th>Method</th>
<th>Result</th>
<th>Species</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mammalian erythrocyte micronucleus test</td>
<td>(in vivo cytogenetic assay)</td>
<td></td>
<td>negative</td>
<td>Mouse</td>
<td></td>
</tr>
<tr>
<td>Ingestion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Magnesium stearate:

<table>
<thead>
<tr>
<th>Genotoxicity in vitro</th>
<th>Test Type</th>
<th>Result</th>
<th>Remarks</th>
<th>Mutagenicity test</th>
</tr>
</thead>
<tbody>
<tr>
<td>In vitro mammalian cell gene mutation test</td>
<td></td>
<td>negative</td>
<td>Based on data from similar materials</td>
<td>Negative chromosome aberration test in vitro</td>
</tr>
</tbody>
</table>
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  

Lamivudine:  
Species: Rat  
Exposure time: 2 Years  
Result: negative  
Species: Mouse  
Exposure time: 2 Years  
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 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
Reproductive toxicity - Assessment: Some evidence of adverse effects on development, based on animal experiments.

Lamivudine:
Effects on fertility: Test Type: Two-generation reproduction toxicity study
Species: Rat
Application Route: Oral
Fertility: NOAEL: 900 mg/kg body weight
Result: No effects on fertility and early embryonic development were detected.

Effects on foetal development: Test Type: Embryo-foetal development
Species: Rabbit
Application Route: Oral
Symptoms: Preimplantation loss, Skeletal malformations
Result: Embryotoxic effects and adverse effects on the offspring were detected.

Test Type: Embryo-foetal development
Species: Rat
Application Route: Oral
Developmental Toxicity: LOAEL: 45 mg/kg body weight
Symptoms: Effects on foetal development
Result: positive

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

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

**Components:**

**Raltegravir:**
- Exposure routes: Inhalation
- Target Organs: Respiratory Tract
- Assessment: May cause respiratory irritation.

**STOT - repeated exposure**
May cause damage to organs (Blood) through prolonged or repeated exposure if swallowed.

**Components:**

**Lamivudine:**
- Exposure routes: Ingestion
- Target Organs: Blood
- Assessment: May cause damage to organs through prolonged or repeated exposure.

**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
SAFETY DATA SHEET

Raltegravir / Lamivudine Formulation

Version: 3.3
Revision Date: 23.03.2020
SDS Number: 187397-00011
Date of last issue: 13.09.2019
Date of first issue: 17.06.2015

LOAEL: 200 mg/kg
Application Route: Oral
Exposure time: 8 Weeks
Target Organs: Stomach

Lamivudine:
Species: Rat
NOAEL: 425 mg/kg
Application Route: Oral
Exposure time: 6 Months
Target Organs: Blood
Symptoms: Gastrointestinal discomfort, Breathing difficulties, Fatality
Remarks: Significant toxicity observed in testing

Species: Dog
LOAEL: 90 mg/kg
Application Route: Oral
Exposure time: 12 Months
Target Organs: Blood, spleen, Liver
Symptoms: Salivation, Diarrhoea, Changes in the blood count, Liver disorders, Gastrointestinal disturbance

Species: Mouse
NOAEL: 500 mg/kg
Application Route: Oral
Exposure time: 1 Months
Target Organs: Blood

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, Diarrhoea, Headache, Fever, Rash, Skin irritation

Lamivudine:
Ingestion:
Symptoms: Headache, Fatigue, Respiratory disorders, Diarrhoea, Cough

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

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

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

Toxicity to fish (Chronic toxicity):
- NOEC: 9.3 mg/l
  - Exposure time: 33 d
  - Species: Pimephales promelas (fathead minnow)
  - Method: OECD Test Guideline 210

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity):
- NOEC: 9.5 mg/l
  - Exposure time: 21 d
  - Species: Daphnia magna (Water flea)
  - Method: OECD Test Guideline 211

Lamivudine:
### Toxicity to fish
- **EC50 (Pimephales promelas (fathead minnow)):** > 97.7 mg/l
  - Exposure time: 96 h
  - Method: OECD Test Guideline 203
- **EC50 (Daphnia magna (Water flea)):** > 100 mg/l
  - Exposure time: 48 h
  - Method: OECD Test Guideline 202

### Toxicity to daphnia and other aquatic invertebrates
- **EC50 (Pseudokirchneriella subcapitata (green algae)):** > 96.9 mg/l
  - Exposure time: 72 h
  - Method: OECD Test Guideline 201

### Toxicity to algae/aquatic plants
- **EC50 (Pseudokirchneriella subcapitata (green algae)):** > 96.9 mg/l
  - Exposure time: 72 h
  - Method: OECD Test Guideline 201

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

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

**Lamivudine:**
- Biodegradability: Result: Not readily biodegradable.  
  Biodegradation: 4%  
  Exposure time: 28 d

**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

**Lamivudine:**
- Partition coefficient: n-octanol/water: log Pow: -1.44

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

**Mobility in soil**

**Components:**

**Lamivudine:**
- Distribution among environmental compartments: log Koc: 2.03
SAFETY DATA SHEET

Raltegravir / Lamivudine Formulation

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 IMO instruments
Not applicable for product as supplied.

15. REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture

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 : dd.mm.yyyy
Full text of other abbreviations
ACGIH : USA. ACGIH Threshold Limit Values (TLV)
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ACGIH / TWA : 8-hour, time-weighted average

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.

IN / EN