SECTION 1: Identification of the substance/mixture and of the company/undertaking

1.1 Product identifier
Trade name: Raltegravir Pediatric Granules Formulation

1.2 Relevant identified uses of the substance or mixture and uses advised against
Use of the Substance/Mixture: Pharmaceutical

1.3 Details of the supplier of the safety data sheet
Company: MSD
Shotton Lane
NE23 3JU Cramlington NU - Great Britain

Telephone: 44 1 670 59 30 00
Telefax: 908-735-1496
E-mail address of person responsible for the SDS: EHSDATASTEWARD@msd.com

1.4 Emergency telephone number
1-908-423-6000

SECTION 2: Hazards identification

2.1 Classification of the substance or mixture
Classification (REGULATION (EC) No 1272/2008)
Serious eye damage, Category 1 H318: Causes serious eye damage.
Reproductive toxicity, Category 2 H361d: Suspected of damaging the unborn child.
Specific target organ toxicity - single exposure, Category 3 H335: May cause respiratory irritation.

2.2 Label elements
Labelling (REGULATION (EC) No 1272/2008)
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.

Hazardous components which must be listed on the label:
Raltegravir

2.3 Other hazards
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

3.2 Mixtures

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>EC-No.</th>
<th>Index-No.</th>
<th>Registration number</th>
<th>Classification</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raltegravir</td>
<td>871038-72-1</td>
<td></td>
<td></td>
<td></td>
<td>Eye Dam.1; H318 Repr.2; H361d STOT SE3; H335</td>
<td>&gt;= 20 - &lt; 30</td>
</tr>
<tr>
<td>Ammonium hydroxide</td>
<td>1336-21-6</td>
<td>215-647-6</td>
<td>007-001-01-2</td>
<td></td>
<td>Acute Tox.4; H302 Skin Corr.1B; H314 Eye Dam.1; H318 Aquatic Acute1; H400</td>
<td>&gt;= 0,1 - &lt; 0,25</td>
</tr>
</tbody>
</table>

For explanation of abbreviations see section 16.

SECTION 4: First aid measures

4.1 Description of 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.
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).

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.

4.2 Most important symptoms and effects, both acute and delayed

Risks: 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.

4.3 Indication of any immediate medical attention and special treatment needed

Treatment: Treat symptomatically and supportively.

SECTION 5: Firefighting measures

5.1 Extinguishing media

Suitable extinguishing media: Water spray
Alcohol-resistant foam
Carbon dioxide (CO2)
Dry chemical

Unsuitable extinguishing media: None known.

5.2 Special hazards arising from the substance or mixture

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.

**5.3 Advice for firefighters**

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

**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.

**SECTION 6: Accidental release measures**

**6.1 Personal precautions, protective equipment and emergency procedures**
- **Personal precautions**
  - Use personal protective equipment.
  - Follow safe handling advice and personal protective equipment recommendations.

**6.2 Environmental precautions**
- **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.

**6.3 Methods and material for containment and cleaning up**
- **Methods for 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.

**6.4 Reference to other sections**
- See sections: 7, 8, 11, 12 and 13.
SECTION 7: Handling and storage

7.1 Precautions for safe handling

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 sensitisers. 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.

7.2 Conditions for safe storage, including any incompatibilities

Requirements for storage areas and containers: 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.

Advice on common storage: Do not store with the following product types: Strong oxidizing agents.

7.3 Specific end use(s)

Specific use(s): No data available

SECTION 8: Exposure controls/personal protection

8.1 Control parameters

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters</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>
8.2 Exposure controls

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

Eye protection: Wear the following personal protective equipment:
Chemical resistant goggles must be worn.
If splashes are likely to occur, wear:
Face-shield
Equipment should conform to NS EN 166

Hand protection

Material: 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.

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).

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 (P)

SECTION 9: Physical and chemical properties

9.1 Information on basic physical and chemical properties

Appearance: powder
Colour: off-white
Odour: odourless
Odour 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 : No data available
Flammability (solid, gas) : May form explosive dust-air mixture during processing, handling or other means.
Upper explosion limit / Upper flammability limit : No data available
Lower explosion limit / Lower flammability limit : No data available
Vapour pressure : No data available
Relative vapour density : No data available
Relative density : No data available
Solubility(ies)
   Water solubility : No data available
Partition coefficient: n-octanol/water : No data available
Auto-ignition temperature : No data available
Decomposition temperature : No data available
Viscosity
   Viscosity, kinematic : No data available
Explosive properties : Not explosive
Oxidizing properties : The substance or mixture is not classified as oxidizing.

9.2 Other information
   Flammability (liquids) : No data available
   Molecular weight : No data available
   Particle size : No data available

SECTION 10: Stability and reactivity

10.1 Reactivity
    Not classified as a reactivity hazard.

10.2 Chemical stability
    Stable under normal conditions.

10.3 Possibility of hazardous reactions
    Hazardous reactions : May form explosive dust-air mixture during processing, handling or other means.
Can react with strong oxidizing agents.

10.4 Conditions to avoid
Conditions to avoid: Heat, flames and sparks.
Avoid dust formation.

10.5 Incompatible materials
Materials to avoid: Oxidizing agents

10.6 Hazardous decomposition products
No hazardous decomposition products are known.

SECTION 11: Toxicological information

11.1 Information on toxicological effects

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

Ammonium hydroxide:
Acute oral toxicity: LD50 (Rat): 350 mg/kg
Acute inhalation toxicity: Assessment: Corrosive to the respiratory tract.

Skin corrosion/irritation
Not classified based on available information.

Components:

Raltegravir:
Species: Rabbit
Result: No skin irritation

Ammonium hydroxide:
Species: Rabbit
Result: Corrosive after 3 minutes to 1 hour of exposure
Remarks: Based on harmonised classification in EU regulation 1272/2008, Annex VI

Serious eye damage/eye irritation
Causes serious eye damage.
Components:

Raltegravir:
Species: Bovine cornea
Result: Severe irritation

Ammonium hydroxide:
Result: Irreversible effects on the eye
Remarks: Based on skin corrosivity.

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

Ammonium hydroxide:
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES)
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 - Assessment: 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

SECTION 12: Ecological information

12.1 Toxicity

Components:

Raltegravir:
Toxicity to fish : LC50 (Pimephales promelas (fathead minnow)): > 100 mg/l
Exposure time: 96 h
Method: OECD Test Guideline 203
**Raltegravir Pediatric Granules Formulation**

**Toxicity to daphnia and other aquatic invertebrates**
- LC50 (Cyprinodon variegatus (sheepshead minnow)): > 100 mg/l
- Exposure time: 96 h
- Method: OECD Test Guideline 203

**Toxicity to algae/aquatic plants**
- EC50 (Daphnia magna (Water flea)): > 100 mg/l
- Exposure time: 48 h
- Method: OECD Test Guideline 202

**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

**Ammonium hydroxide**

**Toxicity to fish**
- LC50 (Pimephales promelas (fathead minnow)): 8.2 mg/l
  - Exposure time: 96 h

**Toxicity to daphnia and other aquatic invertebrates**
- EC50 (Daphnia magna (Water flea)): 0.66 mg/l
  - Exposure time: 48 h

**M-Factor (Acute aquatic toxicity)**
- 1

**Ecotoxicology Assessment**
- Chronic aquatic toxicity: This product has no known ecotoxicological effects.
12.2 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

12.3 Bioaccumulative potential

**Components:**

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

12.4 Mobility in soil

No data available

12.5 Results of PBT and vPvB assessment

Not relevant

12.6 Other adverse effects

No data available

SECTION 13: Disposal considerations

13.1 Waste treatment methods

**Product:** Dispose of in accordance with local regulations.
- According to the European Waste Catalogue, Waste Codes are not product specific, but application specific.
- Waste codes should be assigned by the user, preferably in discussion with the waste disposal authorities.

**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

14.1 UN number

Not regulated as a dangerous good

14.2 UN proper shipping name

Not regulated as a dangerous good

14.3 Transport hazard class(es)

Not regulated as a dangerous good
14.4 Packing group
Not regulated as a dangerous good

14.5 Environmental hazards
Not regulated as a dangerous good

14.6 Special precautions for user
Not applicable

14.7 Transport in bulk according to Annex II of Marpol and the IBC Code
Remarks : Not applicable for product as supplied.

SECTION 15: Regulatory information

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

REACH - Restrictions on the manufacture, placing on the market and use of certain dangerous substances, preparations and articles (Annex XVII) : Not applicable
REACH - Candidate List of Substances of Very High Concern for Authorisation (Article 59). : Not applicable
REACH - List of substances subject to authorisation (Annex XIV) : Not applicable
Regulation (EC) No 1005/2009 on substances that deplete the ozone layer : Not applicable
Regulation (EC) No 850/2004 on persistent organic pollutants : Not applicable

Other regulations:
Take note of Directive 92/85/EEC regarding maternity protection or stricter national regulations, where applicable.

The components of this product are reported in the following inventories:
AICS : not determined
DSL : not determined
IECSC : not determined

15.2 Chemical safety assessment
A Chemical Safety Assessment has not been carried out.

SECTION 16: Other information

Other information : Items where changes have been made to the previous version are highlighted in the body of this document by two vertical lines.
SAFETY DATA SHEET
according to Regulation (EC) No. 1907/2006

Raltegravir Pediatric Granules Formulation

Version 2.2 Revision Date: 09/13/2019 SDS Number: 20456-00014 Date of last issue: 24.04.2019 Date of first issue: 09.10.2014

Full text of H-Statements
H302 : Harmful if swallowed.
H314 : Causes severe skin burns and eye damage.
H318 : Causes serious eye damage.
H335 : May cause respiratory irritation.
H361d : Suspected of damaging the unborn child.
H400 : Very toxic to aquatic life.

Full text of other abbreviations
Acute Tox. : Acute toxicity
Aquatic Acute : Short-term (acute) aquatic hazard
Eye Dam. : Serious eye damage
Repr. : Reproductive toxicity
Skin Corr. : Skin corrosion
STOT SE : Specific target organ toxicity - single exposure

ADN - European Agreement concerning the International Carriage of Dangerous Goods by Inland Waterways; ADR - European Agreement concerning the International Carriage of Dangerous Goods by Road; AICS - Australian Inventory of Chemical Substances; ASTM - American Society for the Testing of Materials; bw - Body weight; CLP - Classification Labelling Packaging Regulation; Regulation (EC) No 1272/2008; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECHA - European Chemicals Agency; EC-Number - European Community number; 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; 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; IECS - 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; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; 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; RID - Regulations concerning the International Carriage of Dangerous Goods by Rail; SADT - Self-Accelerating Decomposition Temperature; SDS - Safety Data Sheet; SVHC - Substance of very high concern; TCSI - Taiwan Chemical Substance Inventory; 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

Further information
Sources of key data used to compile the Safety Data : Internal technical data, data from raw material SDSs, OECD eChem Portal search results and European Chemicals Agen-
Classification of the mixture:

- Eye Dam. 1: H318
- Repr. 2: H361d
- STOT SE 3: H335

Classification procedure:

- Calculation method

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.

NO / EN