

Raltegravir Pediatric Tablets Formulation

Version 4.4 Revision Date: 06/12/2017 SDS Number: 20384-00008 Date of last issue: 04/28/2017
Date of first issue: 10/09/2014

SECTION 1. IDENTIFICATION

Product name : Raltegravir Pediatric Tablets Formulation

Manufacturer or supplier's details

Company name of supplier : Merck & Co., Inc

Address : 2000 Galloping Hill Road
Kenilworth - New Jersey - USA 1685

Telephone : 908-740-4000

Telefax : 908-735-1496

Emergency telephone : 1-908-423-6000

E-mail address : EHSDATASTEWARD@merck.com

Recommended use of the chemical and restrictions on use

Recommended use : Pharmaceutical

SECTION 2. HAZARDS IDENTIFICATION

GHS classification in accordance with 29 CFR 1910.1200

Combustible dust

Serious eye damage : Category 1

Reproductive toxicity : Category 2

Specific target organ
systemic toxicity - single
exposure : Category 3

GHS label elements

Hazard pictograms :



Signal Word : Danger

Hazard Statements : If small particles are generated during further processing, handling or by other means, may form combustible dust concentrations in air.
H318 Causes serious eye damage.
H335 May cause respiratory irritation.
H361d Suspected of damaging the unborn child.

Precautionary Statements : **Prevention:**

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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

Contact with dust can cause mechanical irritation or drying of the skin.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture

Hazardous ingredients

Chemical name	CAS-No.	Concentration (% w/w)
Raltegravir	871038-72-1	>= 20 -< 30

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.

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- 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 : Contact with dust can cause mechanical irritation or drying of the skin.
Causes serious eye damage.
May cause respiratory irritation.
Suspected of damaging the unborn child.
- 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.
- Notes to physician : Treat symptomatically and supportively.
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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 : Exposure to combustion products may be a hazard to health.
- Hazardous combustion products : Carbon oxides
Nitrogen oxides (NO_x)
Fluorine compounds
Chlorine compounds
Sulfur oxides
Metal oxides
- Specific extinguishing methods : Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.
Use water spray to cool unopened containers.
Remove undamaged containers from fire area if it is safe to do so.
Evacuate area.
- Special protective equipment for fire-fighters : In the event of fire, wear self-contained breathing apparatus.
Use personal protective equipment.
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SECTION 6. ACCIDENTAL RELEASE MEASURES

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- 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.

SECTION 7. HANDLING AND STORAGE

- Technical measures : Static electricity may accumulate and ignite suspended dust causing an explosion. Provide adequate precautions, such as electrical grounding and bonding, or inert atmospheres.
- Local/Total ventilation : 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.
Keep container tightly closed.
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 labeled containers.
Store locked up.
Keep tightly closed.
Keep in a cool, well-ventilated place.
Store in accordance with the particular national regulations.
- Materials to avoid : Do not store with the following product types:

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Strong oxidizing agents

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Ingredients with workplace control parameters

Ingredients	CAS-No.	Value type (Form of exposure)	Control parameters / Permissible concentration	Basis
Raltegravir	871038-72-1	TWA	1,000 µg/m ³	Merck

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). Use with local exhaust ventilation. Dust formation may be relevant in the processing of this product. In addition to substance-specific OELs, general limitations of concentrations of particulates in the air at workplaces have to be considered in workplace risk assessment. Relevant limits include: OSHA PEL for Particulates Not Otherwise Regulated of 15 mg/m³ - total dust, 5 mg/m³ - respirable fraction; and ACGIH TWA for Particles (insoluble or poorly soluble) Not Otherwise Specified of 3 mg/m³ - respirable particles, 10 mg/m³ - inhalable particles.

Personal protective equipment

Respiratory protection : General and local exhaust ventilation is recommended to maintain vapor exposures below recommended limits. Where concentrations are above recommended limits or are unknown, appropriate respiratory protection should be worn. Follow OSHA respirator regulations (29 CFR 1910.134) and use NIOSH/MSHA approved respirators. Protection provided by air purifying respirators against exposure to any hazardous chemical is limited. Use a positive pressure air supplied respirator if there is any potential for uncontrolled release, exposure levels are unknown, or any other circumstance where air purifying respirators may not provide adequate protection.

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

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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 : Ensure that eye flushing systems and safety showers are located 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 : yellow-orange
- Odor : No information 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 : No data available
- Flammability (solid, gas) : May form explosive dust-air mixture during processing, handling or other means.
- Flammability (liquids) : No data available
- Upper explosion limit / Upper flammability limit : No data available
- Lower explosion limit / Lower flammability limit : No data available
- Vapor pressure : No data available

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Relative vapor density : No data available

Relative density : No data available

Solubility(ies)
 Water solubility : No data available

Partition coefficient: n-
 octanol/water : No data available

Autoignition temperature : No data available

Decomposition temperature : No data available

Viscosity
 Viscosity, kinematic : No data available

Explosive properties : Not explosive

Oxidizing properties : The substance or mixture is not classified as oxidizing.

Molecular weight : No data available

Particle size : No data available

SECTION 10. STABILITY AND REACTIVITY

Reactivity : Not classified as a reactivity hazard.

Chemical stability : Stable under normal conditions.

Possibility of hazardous reac- : Dust can form an explosive mixture in air.
 tions : Can react with strong oxidizing agents.

Conditions to avoid : None known.

Incompatible materials : Oxidizing agents

Hazardous decomposition : No hazardous decomposition products are known.
 products

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

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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.

Ingredients:

Raltegravir:

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

IARC

No ingredient of this product present at levels greater than or equal to 0.1% is identified as probable, possible or confirmed human carcinogen by IARC.

OSHA

No component of this product present at levels greater than or equal to 0.1% is on OSHA's list of regulated carcinogens.

NTP

No ingredient of this product present at levels greater than or equal to 0.1% is identified as a known or anticipated carcinogen by NTP.

Reproductive toxicity

Suspected of damaging the unborn child.

Ingredients:

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: \geq 600 mg/kg body weight
Teratogenicity: LOAEL F1: 300 mg/kg body weight
Symptoms: Skeletal malformations.
Result: positive

Species: Rabbit
General Toxicity Maternal: NOAEL: \geq 1,000 mg/kg body weight

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Teratogenicity: NOAEL: \geq 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.

Ingredients:**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**Ingredients:****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.

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Experience with human exposure

Ingredients:

Raltegravir:

Ingestion : Symptoms: Nausea, Diarrhea, Headache, Fever, Rash, Skin irritation

SECTION 12. ECOLOGICAL INFORMATION

Ecotoxicity

Ingredients:

Raltegravir:

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

LC50 (Cyprinodon variegatus (sheepshead minnow)): > 100 mg/l
 Exposure time: 96 h
 Method: OECD Test Guideline 203

Toxicity to daphnia and other aquatic invertebrates : EC50 (Daphnia magna (Water flea)): > 100 mg/l
 Exposure time: 48 h
 Method: OECD Test Guideline 202

Toxicity to algae : 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

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49 CFR

Not regulated as a dangerous good

SECTION 15. REGULATORY INFORMATION

EPCRA - Emergency Planning and Community Right-to-Know

CERCLA Reportable Quantity

This material does not contain any components with a CERCLA RQ.

SARA 304 Extremely Hazardous Substances Reportable Quantity

This material does not contain any components with a section 304 EHS RQ.

SARA 302 Extremely Hazardous Substances Threshold Planning Quantity

This material does not contain any components with a section 302 EHS TPQ.

SARA 311/312 Hazards : Fire Hazard
Acute Health Hazard
Chronic Health Hazard

SARA 313 : This material does not contain any chemical components with known CAS numbers that exceed the threshold (De Minimis) reporting levels established by SARA Title III, Section 313.

US State Regulations

Pennsylvania Right To Know

D-mannitol	69-65-8
Raltegravir	871038-72-1
Polyvinyl pyrrolidone	9003-39-8
1,2-Benzisothiazol-3(2H)-one 1,1-dioxide, sodium salt	128-44-9

California Prop. 65

This product does not contain any chemicals known to the State of California to cause cancer, birth, or any other reproductive defects.

California List of Hazardous Substances

Polyvinyl pyrrolidone	9003-39-8
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The ingredients of this product are reported in the following inventories:

AICS	: not determined
DSL	: not determined
IECSC	: not determined

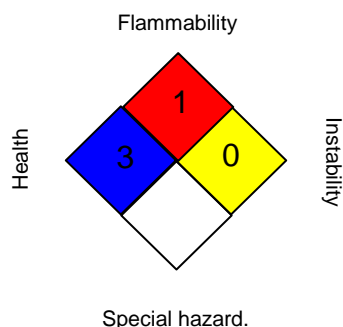
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SECTION 16. OTHER INFORMATION

Further information

NFPA:



HMIS® IV:

HEALTH	*	3
FLAMMABILITY		3
PHYSICAL HAZARD		0

HMIS® ratings are based on a 0-4 rating scale, with 0 representing minimal hazards or risks, and 4 representing significant hazards or risks. The "*" represents a chronic hazard, while the "/" represents the absence of a chronic hazard.

Full text of other abbreviations

AICS - Australian Inventory of Chemical Substances; ASTM - American Society for the Testing of Materials; bw - Body weight; CERCLA - Comprehensive Environmental Response, Compensation, and Liability Act; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DOT - Department of Transportation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; EHS - Extremely Hazardous Substance; 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; HMIS - Hazardous Materials Identification System; 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; MSHA - Mine Safety and Health Administration; n.o.s. - Not Otherwise Specified; NFPA - National Fire Protection Association; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; 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; RCRA - Resource Conservation and Recovery Act; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; RQ - Reportable Quantity; SADT - Self-Accelerating Decomposition Temperature; SARA - Superfund Amendments and Reauthorization Act; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance Inventory; TSCA - Toxic Substances Control Act (United States); UN - United Nations; UNRTDG -

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United Nations Recommendations on the Transport of Dangerous Goods; vPvB - Very Persistent and Very Bioaccumulative

Sources of key data used to compile the Material Safety Data Sheet : Internal technical data, data from raw material SDSs, OECD eChem Portal search results and European Chemicals Agency, <http://echa.europa.eu/>

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Items where changes have been made to the previous version are highlighted in the body of this document by two vertical lines.

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.

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