SAFETY DATA SHEET

Doravirine Formulation

SECTION 1. IDENTIFICATION

Product name : Doravirine 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
Short-term (acute) aquatic hazard : Category 3

GHS label elements
Hazard Statements : H402 Harmful to aquatic life.
Precautionary Statements : Prevention:
P273 Avoid release to the environment.
Disposal:
P501 Dispose of contents/ container to an approved waste disposal plant.

Other hazards which do not result in classification
Dust contact with the eyes can lead to mechanical irritation.
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

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>Cellulose</td>
<td>9004-34-6</td>
<td>&gt;= 20 - &lt; 30</td>
</tr>
<tr>
<td>Doravirine</td>
<td>1338225-97-0</td>
<td>&gt;= 10 - &lt; 20</td>
</tr>
<tr>
<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 if symptoms occur.

In case of skin contact: Wash with water and soap. Get medical attention if symptoms occur.

In case of eye contact: If in eyes, rinse well with water. Get medical attention if irritation develops and persists.

If swallowed: If swallowed, DO NOT induce vomiting. Get medical attention if symptoms occur. 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. Dust contact with the eyes can lead to mechanical irritation.

Protection of first-aiders: No special precautions are necessary for first aid responders.

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 firefighting: Avoid generating dust; fine dust dispersed in air in sufficient concentrations, and in the presence of an ignition source is a potential dust explosion hazard. Exposure to combustion products may be a hazard to health.

Hazardous combustion products: Carbon oxides
Nitrogen oxides (NOx)
Halogenated compounds
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: Wear self-contained breathing apparatus for firefighting if necessary. Use personal protective equipment.

SECTION 6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment: Follow safe handling advice (see section 7) and personal protective equipment.
tive equipment and emergency procedures protective equipment recommendations (see section 8).

Environmental precautions

Avoid release to the environment.

Prevent further leakage or spillage if safe to do so.

Retain and dispose of contaminated wash water.

Local authorities should be advised if significant spillages cannot be contained.

Methods and materials for containment and cleaning up:

Sweep up or vacuum up spillage and collect in suitable container for disposal.

Avoid dispersal of dust in the air (i.e., clearing dust surfaces with compressed air).

Dust deposits should not be allowed to accumulate on 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 only with adequate ventilation.

Advice on safe handling:

Do not breathe dust.

Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment.

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 in accordance with the particular national regulations.

Materials to avoid:

Do not store with the following product types:

Strong oxidizing agents

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Ingredients 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>Cellulose</td>
<td>9004-34-6</td>
<td>CMP</td>
<td>10 mg/m³</td>
<td>AR OEL</td>
</tr>
</tbody>
</table>

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## SAFETY DATA SHEET

### Doravirine Formulation

<table>
<thead>
<tr>
<th>Substance</th>
<th>TWA</th>
<th>ACGIH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doravirine</td>
<td>10 mg/m³</td>
<td>Internal</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>10 mg/m³</td>
<td>AR OEL</td>
</tr>
<tr>
<td>Silicon, amorphous</td>
<td>10 mg/m³</td>
<td>AR OEL</td>
</tr>
</tbody>
</table>

### Engineering measures

- Use feasible engineering controls to minimize exposure to compound.
- All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment.

### 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.

#### Hand protection
- Material: Chemical-resistant gloves

#### Eye protection
- Wear safety glasses with side shields or goggles.
- If the work environment or activity involves dusty conditions, mists or aerosols, wear the appropriate goggles.
- Wear a faceshield or other full face protection if there is a potential for direct contact to the face with dusts, mists, or aerosols.

#### Skin and body protection
- Work uniform or laboratory coat.

#### 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.
- The effective operation of a facility should include review of engineering controls, proper personal protective equipment, appropriate degowning and decontamination procedures, industrial hygiene monitoring, medical surveillance and the use of administrative controls.

### SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

- **Appearance**: powder
- **Color**: off-white
- **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 : Not applicable
Evaporation rate : Not applicable
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 : Not applicable
Relative vapor density : Not applicable
Relative density : No data available
Density : No data available
Solubility(ies)
   Water solubility : No data available
Partition coefficient: n-octanol/water : Not applicable
Autoignition temperature : No data available
Decomposition temperature : No data available
Viscosity
   Viscosity, kinematic : Not applicable
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.

Components:

**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

**Doravirine:**
Acute oral toxicity: LD50 (Rat): > 750 mg/kg
Remarks: No mortality observed at this dose.

(Rat): Method: Phototoxicity
Remarks: No evidence of phototoxicity was observed

LD50 (Dog): > 1,000 mg/kg
Remarks: No mortality observed at this dose.

LD50 (Mouse): > 450 mg/kg
Remarks: No mortality observed at this dose.

**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
Silicon, amorphous:
Acute oral toxicity: LD50 (Rat): > 5.000 mg/kg
   Method: OECD Test Guideline 401
   Remarks: Based on data from similar materials

Acute inhalation toxicity: LC50 (Rat): > 2.08 mg/l
   Exposure time: 4 h
   Test atmosphere: dust/mist
   Assessment: The substance or mixture has no acute inhalation toxicity
   Remarks: Based on data from similar materials

Acute dermal toxicity: LD50 (Rabbit): > 5.000 mg/kg
   Remarks: Based on data from similar materials

Skin corrosion/irritation
Not classified based on available information.

Components:

Doravirine:
Remarks: No data available

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

Silicon, amorphous:
Species: Rabbit
Method: OECD Test Guideline 404
Result: No skin irritation
Remarks: Based on data from similar materials

Serious eye damage/eye irritation
Not classified based on available information.

Components:

Doravirine:
Remarks: No data available

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

Silicon, amorphous:
Species: Rabbit
Result: No eye irritation
Method: OECD Test Guideline 405
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:

Doravirine:
Remarks: No data available

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:

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

Doravirine:
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES)
Result: negative
Test Type: Chromosomal aberration
Test system: Chinese hamster ovary cells
Result: negative

Genotoxicity in vivo: Test Type: Micronucleus test
Species: Rat
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

Silicon, amorphous:
Genotoxicity in vitro
  Test Type: Bacterial reverse mutation assay (AMES)
  Method: OECD Test Guideline 471
  Result: negative
  Remarks: Based on data from similar materials

Genotoxicity in vivo
  Test Type: Mutagenicity (in vivo mammalian bone-marrow cytogenetic test, chromosomal analysis)
  Species: Rat
  Application Route: Ingestion
  Result: negative
  Remarks: Based on data from similar materials

Carcinogenicity
Not classified based on available information.

Components:

Cellulose:
Species: Rat
Application Route: Ingestion
Exposure time: 72 weeks
Result: negative

Doravirine:
Species: Mouse
Application Route: Oral
Exposure time: 6 Months
Result: negative
Remarks: No significant adverse effects were reported

Silicon, amorphous:
Species: Rat
Application Route: Ingestion
Exposure time: 103 weeks
Result: negative
Remarks: Based on data from similar materials

Reproductive toxicity
Not classified based on available information.

Components:

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

Doravirine:
Effects on fertility: Test Type: Fertility
Species: Rat, male and female
Fertility: NOAEL: 450 mg/kg body weight
Result: No effects on fertility.

Effects on fetal development: Test Type: Embryo-fetal development
Species: Rat
Application Route: Oral
Developmental Toxicity: NOAEL: 450 mg/kg body weight
Result: No adverse effects.

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
Silicon, amorphous:
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
Not classified based on available information.

STOT-repeated exposure
Not classified based on available information.

Repeated dose toxicity

Components:

Cellulose:
Species: Rat
NOAEL: >= 9,000 mg/kg
Application Route: Ingestion
Exposure time: 90 Days

Doravirine:
Species: Rat
NOAEL: 450 mg/kg
Application Route: Oral
Exposure time: 6 Months
Remarks: No significant adverse effects were reported

Species: Mouse
NOAEL: > 450 mg/kg
Application Route: Oral
Exposure time: 3 Months
Remarks: No significant adverse effects were reported

Species: Dog
NOAEL: > 1,000 mg/kg
Application Route: Oral
Exposure time: 9 Months
Remarks: No significant adverse effects were reported

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

Silicon, amorphous:
Species: Rat
NOAEL: 1,3 mg/l
Application Route: inhalation (dust/mist/fume)
Exposure time: 13 Weeks
Remarks: Based on data from similar materials

Aspiration toxicity
Not classified based on available information.

Experience with human exposure

Components:

Doravirine:
Ingestion: Symptoms: confusion, Headache, Dizziness, Nausea, Rash, abnormal dreams, flushing, Neurological disorders, mental depression

SECTION 12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:

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

Doravirine:
Toxicity to daphnia and other aquatic invertebrates: EC50 (Daphnia magna (Water flea)): > 39 mg/l
Exposure time: 48 h
Method: OECD Test Guideline 202
Remarks: No toxicity at the limit of solubility.

EC50 (Americamysis): 9,1 mg/l
Exposure time: 96 h

Toxicity to algae/aquatic plants: EC50 (Pseudokirchneriella subcapitata (green algae)): > 5,8 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201
Remarks: No toxicity at the limit of solubility.

NOEC (Pseudokirchneriella subcapitata (green algae)): 5,8 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201
Remarks: No toxicity at the limit of solubility.

Toxicity to fish (Chronic toxicity): NOEC (Pimephales promelas (fathead minnow)): 1 mg/l
Exposure time: 32 d
Method: OECD Test Guideline 210
Remarks: No toxicity at the limit of solubility.

Toxicity to daphnia and other aquatic invertebrates (Chronic): NOEC (Daphnia magna (Water flea)): 6,7 mg/l
Exposure time: 21 d
ic toxicity)

Remarks: No toxicity at the limit of solubility.

Toxicity to microorganisms:

Method: OECD Test Guideline 211
Exposure time: 3 h
Test Type: Respiration inhibition

NOEC: 1.000 mg/l
Exposure time: 3 h
Test Type: Respiration inhibition
Method: OECD Test Guideline 209

Magnesium stearate:

Toxicity to fish:

Remarks: Based on data from similar materials

Toxicity to daphnia and other aquatic invertebrates:

Test substance: Water Accommodated Fraction
Remarks: Based on data from similar materials

No toxicity at the limit of solubility.

Toxicity to algae/aquatic plants:

Test substance: Water Accommodated Fraction
Method: OECD Test Guideline 201
Remarks: Based on data from similar materials

No toxicity at the limit of solubility.

Silicon, amorphous:

Toxicity to fish:

Remarks: Based on data from similar materials

Toxicity to daphnia and other aquatic invertebrates:

Remarks: Based on data from similar materials
Toxicity to algae/aquatic plants:
EC50 (Desmodesmus subspicatus (green algae)): > 10.000 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 202
Remarks: Based on data from similar materials

NOEC (Desmodesmus subspicatus (green algae)): 10.000 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201
Remarks: Based on data from similar materials

Persistence and degradability

Components:

Cellulose:
Biodegradability: Result: Readily biodegradable.

Doravirine:
Biodegradability: Result: Not readily biodegradable.
Biodegradation: 2 %
Exposure time: 28 d

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

Bioaccumulative potential

Components:

Doravirine:
Partition coefficient: n-octanol/water: log Pow: 2,08

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

Mobility in soil

Components:

Doravirine:
Distribution among environmental compartments: log Koc: 2,86

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

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

SECTION 16. OTHER INFORMATION

Further information
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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