SAFETY DATA SHEET

Doravirine / Lamivudine / Tenofovir Disoproxil Fumarate Bilayer Formulation

1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Doravirine / Lamivudine / Tenofovir Disoproxil Fumarate Bilayer Formulation

Manufacturer or supplier’s details
Company name of supplier: MSD
Address: Kumagaya, Saitama Prefecture, Xicheng 810 MSD Co., Ltd. Menuma factory
Telephone: 048-588-8411
E-mail address: EHSDATASTEWARD@msd.com
Emergency telephone number: 1-908-423-6000

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

2. HAZARDS IDENTIFICATION

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

GHS label elements
Hazard pictograms: 
Signal word: Warning
Hazard statements: H319 Causes serious eye irritation.
H361d Suspected of damaging the unborn child.
H373 May cause damage to organs (Blood, Bone, Kidney) 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.
P264 Wash skin thoroughly after handling.
P273 Avoid release to the environment.
P280 Wear protective gloves/ protective clothing/ eye protection/ face protection.

Response:
P305 + P351 + P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P308 + P313 IF exposed or concerned: Get medical advice/ attention.
P337 + P313 If eye irritation persists: 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
Important symptoms and outlines of the emergency assumed: May form explosive dust-air mixture during processing, handling or other means.

3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Mixture</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Components</th>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
<th>ENCS No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>&gt;= 20 - &lt; 30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lamivudine</td>
<td>134678-17-4</td>
<td>&gt;= 10 - &lt; 20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tenofovir</td>
<td>202138-50-9</td>
<td>&gt;= 10 - &lt; 20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doravirine</td>
<td>1338225-97-0</td>
<td>&gt;= 2.5 - &lt; 10</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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 plenty of water. Remove contaminated clothing and shoes.
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Version 5.4  Revision Date: 09/13/2019  SDS Number: 58629-00016
Date of last issue: 2019/02/13  Date of first issue: 2015/02/16

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.

If swallowed: If swallowed, DO NOT induce vomiting.
Get medical attention.

Most important symptoms and effects, both acute and delayed:
Causes serious eye irritation.
Suspected of damaging the unborn child.
May cause damage to organs through prolonged or repeated exposure if swallowed.

Protection of first-aiders: First Aid responders should pay attention to self-protection, and use the recommended personal protective equipment when the potential for exposure exists (see section 8).

Notes to physician: Treat symptomatically and supportively.

5. FIREFIGHTING 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

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

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:
- Use only with adequate ventilation.

Advice on safe handling:
- Do not get on skin or clothing.
- Do not breathe dust.
- Do not swallow.
- Do not get in eyes.
- 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.

Avoidance of contact
Hygiene measures:
- Oxidizing agents
- 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.

Storage
Conditions for safe storage:
- Keep in properly labelled containers.
Store locked up. Store in accordance with the particular national regulations.

Materials to avoid:
- Do not store with the following product types:
  - Strong oxidizing agents

Packaging material:
- Unsuitable material: None known.

### 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

**Threshold limit value and permissible exposure limits for each component in the work environment**

<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>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</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>Tenofovir</td>
<td>202138-50-9</td>
<td>TWA</td>
<td>200 µg/m³ (OEB 2)</td>
<td>Internal</td>
</tr>
<tr>
<td>Doravirine</td>
<td>1338225-97-0</td>
<td>TWA</td>
<td>500 µg/m³ (OEB2)</td>
<td>Internal</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.
  - Filter type: Particulates type

**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.

### 9. PHYSICAL AND CHEMICAL PROPERTIES

**Appearance**
- Powder

**Colour**
- No data available

**Odour**
- No data available
10. STABILITY AND REACTIVITY

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 : 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
Vapour pressure : Not applicable
Relative vapour 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
   Auto-ignition 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
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:
Not classified based on available information.

Product:
Acute oral toxicity: Acute toxicity estimate: > 2,000 mg/kg
Method: Calculation method

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

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

Tenofovir:
Acute oral toxicity: LD50 (Rat): > 1,500 mg/kg
LD50 (Dog): 30 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.

Skin corrosion/irritation
Not classified based on available information.

Components:

Lamivudine:
Species: Rabbit
Result: Mild skin irritation

Tenofovir:
Species: Rabbit
Result: Mild skin irritation

Doravirine:
Remarks: No data available

Serious eye damage/eye irritation
Causes serious eye irritation.

Components:

Lamivudine:
Species: Rabbit
Result: No eye irritation

Tenofovir:
Species: Rabbit
Result: Severe irritation

Doravirine:
Remarks: No data available

Respiratory or skin sensitisation

Skin sensitisation
Not classified based on available information.
Respiratory sensitisation
Not classified based on available information.

Components:

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

Tenofovir:
- Test Type: Maximisation Test
- Exposure routes: Skin contact
- Species: Guinea pig
- Result: Not a skin sensitizer.

Doravirine:
- Remarks: No data available

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

Lamivudine:
- Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES)
  Result: negative
  Test Type: Mouse Lymphoma
  Result: equivocal
- Genotoxicity in vivo: Test Type: Micronucleus test
  Species: Rat
  Application Route: Oral
  Result: negative
  Test Type: Unscheduled DNA synthesis (UDS) test with
mammalian liver cells in vivo  
Species: Rat  
Result: negative

**Tenofovir:**
Genotoxicity in vitro :  
Test Type: Bacterial reverse mutation assay (AMES)  
Result:equivocal
Test Type: In vitro mammalian cell gene mutation test  
Result: positive
Genotoxicity in vivo :  
Test Type: Mutagenicity (in vivo mammalian bone-marrow cytogenetic test, chromosomal analysis)  
Species: Mouse  
Application Route: Intraperitoneal injection  
Result: negative
Germ cell mutagenicity - Assessment :  
Weight of evidence does not support classification as a germ cell mutagen.

**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  
Cell type: Bone marrow  
Application Route: Oral  
Result: negative

**Carcinogenicity**
Not classified based on available information.

**Components:**

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

**Lamivudine:**
Species :  
Exposure time: 2 Years  
Result: negative
Species: Mouse
## Exposure time and Result

<table>
<thead>
<tr>
<th>Drug</th>
<th>Species</th>
<th>Application Route</th>
<th>Exposure Time</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doravirine</td>
<td>Mouse</td>
<td>Oral</td>
<td>6 Months</td>
<td>negative</td>
</tr>
<tr>
<td>Tenofovir</td>
<td>Mouse</td>
<td>Oral</td>
<td>104 weeks</td>
<td>negative</td>
</tr>
<tr>
<td>Tenofovir</td>
<td>Rat</td>
<td>Oral</td>
<td>104 weeks</td>
<td>negative</td>
</tr>
</tbody>
</table>

### Tenofovir:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Species</th>
<th>Application Route</th>
<th>Exposure Time</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tenofovir</td>
<td>Mouse</td>
<td>Oral</td>
<td>104 weeks</td>
<td>negative</td>
</tr>
</tbody>
</table>

### Doravirine:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Species</th>
<th>Application Route</th>
<th>Exposure Time</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doravirine</td>
<td>Mouse</td>
<td>Oral</td>
<td>6 Months</td>
<td>negative</td>
</tr>
</tbody>
</table>

### Reproductive toxicity

Suspected of damaging the unborn child.

### Components:

#### 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

#### 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.
**SAFETY DATA SHEET**

**Doravirine / Lamivudine / Tenofovir Disoproxil Fumarate Bilayer Formulation**

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<th>Date of last issue:</th>
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<tr>
<td>5.4</td>
<td>09/13/2019</td>
<td>58629-00016</td>
<td>2019/02/13</td>
<td>2015/02/16</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Test Type:</th>
<th>Embryo-foetal development</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species:</td>
<td>Rat</td>
</tr>
<tr>
<td>Application Route:</td>
<td>Oral</td>
</tr>
<tr>
<td>Developmental Toxicity: LOAEL:</td>
<td>45 mg/kg body weight</td>
</tr>
<tr>
<td>Symptoms:</td>
<td>Effects on foetal development</td>
</tr>
<tr>
<td>Result:</td>
<td>positive</td>
</tr>
</tbody>
</table>

**Reproductive toxicity - Assessment**: Some evidence of adverse effects on development, based on animal experiments.

**Tenofovir:**

**Effects on fertility**: Test Type: Fertility/early embryonic development  
Species: Rat  
Application Route: Oral  
Result: No effects on fertility

**Effects on foetal development**: Test Type: Embryo-foetal development  
Species: Rat  
Application Route: Oral  
Result: No adverse effects

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

**STOT - single exposure**: Not classified based on available information.

**STOT - repeated exposure**: May cause damage to organs (Blood, Bone, Kidney) 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.

Tenofovir:
Target Organs: Bone, Kidney
Assessment: May cause damage to organs through prolonged or repeated exposure.

Repeated dose toxicity

Components:

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

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

Tenofovir:
Species: Rat
NOAEL: 30 mg/kg
LOAEL: 300 mg/kg
Application Route: Oral
Exposure time: 13 Weeks
Target Organs: Bone

Species: Dog
NOAEL: 3 mg/kg
LOAEL: >= 10 mg/kg
Application Route: Oral
Exposure time: 42 Weeks
Target Organs: Kidney

Species: Monkey
LOAEL: 10 mg/kg
Application Route: Subcutaneous
Exposure time: 10 Months
Target Organs: Bone

**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

Aspiration toxicity
Not classified based on available information.

Experience with human exposure

**Components:**

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

**Tenofovir:**
Ingestion: Symptoms: Nausea, Diarrhoea, Vomiting, flatulence, Headache, Rash

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

Lamivudine:
Toxicity to fish: LC50 (Pimephales promelas (fathead minnow)): > 97.7 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)): > 96.9 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201

NOEC (Pseudokirchneriella subcapitata (green algae)): 96.9 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201

Tenofovir:
Toxicity to fish: LC50 (Oncorhynchus mykiss (rainbow trout)): > 92 mg/l
Exposure time: 96 h
Method: OECD Test Guideline 203

Toxicity to daphnia and other aquatic invertebrates: EC50 (Daphnia magna (Water flea)): > 98 mg/l
Exposure time: 48 h
Method: OECD Test Guideline 202

Toxicity to algae/aquatic plants: EC50 (Pseudokirchneriella subcapitata (green algae)): 47 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201

NOEC (Pseudokirchneriella subcapitata (green algae)): 14 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201

Toxicity to fish (Chronic toxicity): NOEC (Pimephales promelas (fathead minnow)): 1.9 mg/l
Exposure time: 32 d
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- **Method**: OECD Test Guideline 210
- **Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity)**: NOEC (Daphnia magna (Water flea)): 13 mg/l
  
  Exposure time: 21 d

  Method: OECD Test Guideline 211

- **Toxicity to algae/aquatic plants**: EC50 (Pseudokirchneriella subcapitata (green algae)): > 5.8 mg/l

  Exposure time: 72 h

  Method: OECD Test Guideline 221

  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 221

  Remarks: No toxicity at the limit of solubility

- **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

---

**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 221

  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 221

  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 toxicity)**: NOEC (Daphnia magna (Water flea)): 6.7 mg/l

  Exposure time: 21 d

  Method: OECD Test Guideline 211

  Remarks: No toxicity at the limit of solubility

- **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

Persistence and degradability

**Components:**

**Cellulose:**
Biodegradability : Result: Readily biodegradable.

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

**Tenofovir:**
Biodegradability : Result: Not readily biodegradable.

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

Bioaccumulative potential

**Components:**

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

**Tenofovir:**
Partition coefficient: n-octanol/water : log Pow: 1.18

**Doravirine:**
Partition coefficient: n-octanol/water : log Pow: 2.08

Mobility in soil

**Components:**

**Lamivudine:**
Distribution among environmental compartments : log Koc: 2.03

**Tenofovir:**
Distribution among environmental compartments : log Koc: 1.3

**Doravirine:**
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 Annex II of MARPOL 73/78 and the IBC Code
Not applicable for product as supplied.

National Regulations
Refer to section 15 for specific national regulation.

15. REGULATORY INFORMATION

Related Regulations
Fire Service Law
Not applicable to dangerous materials / designated flammables.

Chemical Substance Control Law
Not applicable for Specified Chemical Substance, Monitoring Chemical Substance and Priority Assessment Chemical Substance.

Industrial Safety and Health Law

Harmful Substances Prohibited from Manufacture
Not applicable

Harmful Substances Required Permission for Manufacture
Not applicable
Substances Prevented From Impairment of Health
Not applicable

Circular concerning Information on Chemicals having Mutagenicity - Annex 2: Information on Existing Chemicals having Mutagenicity
Not applicable

Circular concerning Information on Chemicals having Mutagenicity - Annex 1: Information on Notified Substances having Mutagenicity
Not applicable

Substances Subject to be Notified Names
Not applicable

Substances Subject to be Indicated Names
Not applicable

Ordinance on Prevention of Hazards Due to Specified Chemical Substances
Not applicable

Ordinance on Prevention of Lead Poisoning
Not applicable

Ordinance on Prevention of Tetraalkyl Lead Poisoning
Not applicable

Ordinance on Prevention of Organic Solvent Poisoning
Not applicable

Enforcement Order of the Industrial Safety and Health Law - Attached table 1 (Dangerous Substances)
Not applicable

Poisonous and Deleterious Substances Control Law
Not applicable

Act on Confirmation, etc. of Release Amounts of Specific Chemical Substances in the Environment and Promotion of Improvements to the Management Thereof
Not applicable

High Pressure Gas Safety Act
Not applicable

Explosive Control Law
Not applicable

Vessel Safety Law
Not regulated as a dangerous good

Aviation Law
Not regulated as a dangerous good

Marine Pollution and Sea Disaster Prevention etc Law
Bulk transportation : Not classified as noxious liquid substance
Pack transportation : Not classified as marine pollutant
Narcotics and Psychotropics Control Act
Narcotic or Psychotropic Raw Material (Export / Import Permission)
Not applicable

Specific Narcotic or Psychotropic Raw Material (Export / Import permission)
Not applicable

Waste Disposal and Public Cleansing Law
Industrial waste

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 : yyyy/mm/dd

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

AICS - Australian Inventory of Chemical Substances; ANTT - National Agency for Transport by Land of Brazil; ASTM - American Society for the Testing of Materials; bw - Body weight; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); 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; ERG - Emergency Response Guide; 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; 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; n.o.s. - Not Otherwise Specified; Nch - Chilean Norm; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NOM - Official Mexican Norm; 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, Bioaccumu-
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**Additional Information:***

- PICCS - Philippines Inventory of Chemicals and Chemical Substances
- (Q)SAR - (Quantitative) Structure Activity Relationship
- SADT - Self-Accelerating Decomposition Temperature
- SDS - Safety Data Sheet
- TCSI - Taiwan Chemical Substance Inventory
- TDG - Transportation of Dangerous Goods
- 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
- WHMIS - Workplace Hazardous Materials Information System

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.