SECTION 1. IDENTIFICATION

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

Manufacturer or supplier's details
Company name of supplier: Merck & Co., Inc
Address: 126 E. Lincoln Avenue
Rahway, New Jersey U.S.A. 07065
Telephone: 908-740-4000
Emergency telephone: 1-908-423-6000
E-mail address: EHSDATASTEWARD@merck.com

Recommended use of the chemical and restrictions on use
Recommended use: Pharmaceutical
Restrictions on use: Not applicable

SECTION 2. HAZARDS IDENTIFICATION

GHS classification in accordance with the OSHA Hazard Communication Standard (29 CFR 1910.1200)
Combustible dust
Eye irritation: Category 2A
Reproductive toxicity: Category 2
Specific target organ toxicity - repeated exposure (Oral): Category 2 (Blood, Bone, Kidney)

GHS label elements
Hazard pictograms:

Signal Word: Warning

Hazard Statements:
If small particles are generated during further processing, handling or by other means, may form combustible dust concentrations in air.
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.

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.
P280 Wear protective gloves, protective clothing, eye protection and 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 attention.
P337 + P313 IF eye irritation persists: Get medical attention.

Storage:
P405 Store locked up.

Disposal:
P501 Dispose of contents and container to an approved waste disposal plant.

Other hazards
None known.

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>21</td>
</tr>
<tr>
<td>Lamivudine</td>
<td>134678-17-4</td>
<td>19.2</td>
</tr>
<tr>
<td>Tenofovir</td>
<td>202138-50-9</td>
<td>19.2</td>
</tr>
<tr>
<td>Doravirine</td>
<td>1338225-97-0</td>
<td>6.4</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.

In case of skin contact : In case of contact, immediately flush skin with 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.

If swallowed : If swallowed, DO NOT induce vomiting.
**SAFETY DATA SHEET**

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

<table>
<thead>
<tr>
<th>Version</th>
<th>Revision Date:</th>
<th>SDS Number:</th>
<th>Date of last issue:</th>
<th>Date of first issue:</th>
</tr>
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<tr>
<td>12.0</td>
<td>04/04/2023</td>
<td>58636-00028</td>
<td>10/01/2022</td>
<td>02/16/2015</td>
</tr>
</tbody>
</table>

- **Get medical attention.** Rinse mouth thoroughly with water.
- **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.

### SECTION 5. FIRE-FIGHTING MEASURES

<table>
<thead>
<tr>
<th>Suitable extinguishing media</th>
<th>Water spray</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Alcohol-resistant foam</td>
</tr>
<tr>
<td></td>
<td>Carbon dioxide (CO2)</td>
</tr>
<tr>
<td></td>
<td>Dry chemical</td>
</tr>
</tbody>
</table>

- **Unsuitable extinguishing media:** None known.
- **Specific hazards during fire fighting:**
  - 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:**
  - In the event of fire, wear self-contained breathing apparatus.
  - Use personal protective equipment.

### SECTION 6. ACCIDENTAL RELEASE MEASURES

- **Personal precautions, protective equipment and emergency procedures:**
  - Use personal protective equipment.
  - Follow safe handling advice (see section 7) and personal 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 get on skin or clothing. Do not breathe dust. Do not swallow. Do not get in eyes. Wash skin thoroughly after handling. 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 locked up. 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>inert or nuisance dust</th>
<th>50 Million particles per cubic foot</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value type (Form of exposure): TWA (total dust)</td>
<td>Basis: OSHA Z-3</td>
</tr>
<tr>
<td>15 mg/m³</td>
<td>Value type (Form of exposure): TWA (total dust)</td>
</tr>
<tr>
<td>Basis: OSHA Z-3</td>
<td></td>
</tr>
<tr>
<td>5 mg/m³</td>
<td>Value type (Form of exposure): TWA (respirable fraction)</td>
</tr>
<tr>
<td>Basis: OSHA Z-3</td>
<td></td>
</tr>
</tbody>
</table>
15 Million particles per cubic foot
Value type (Form of exposure): TWA (respirable fraction)
Basis: OSHA Z-3

Dust, nuisance dust and particulates
10 mg/m³
Value type (Form of exposure): PEL (Total dust)
Basis: CAL PEL

5 mg/m³
Value type (Form of exposure): PEL (respirable dust fraction)
Basis: CAL PEL

<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>
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<td></td>
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<td>TWA (Respirable)</td>
<td>5 mg/m³</td>
<td>NIOSH REL</td>
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<tr>
<td></td>
<td></td>
<td>TWA (total)</td>
<td>10 mg/m³</td>
<td>NIOSH REL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (total dust)</td>
<td>15 mg/m³</td>
<td>OSHA Z-1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (respirable fraction)</td>
<td>5 mg/m³</td>
<td>OSHA Z-1</td>
</tr>
<tr>
<td>Lamivudine</td>
<td>134678-17-4</td>
<td>TWA</td>
<td>100 µg/m³ (OEB 2)</td>
<td>Internal</td>
</tr>
<tr>
<td>Tenofovir</td>
<td>202138-50-9</td>
<td>TWA</td>
<td>150 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: 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
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: No data available
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.
Product:
Acute oral toxicity : Acute toxicity estimate: 2,604 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.
  - 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
Doravirine / Lamivudine / Tenofovir Disoproxil Fumarate Bilayer Formulation

Result: Mild skin irritation

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

Remarks: No data available

Respiratory or skin sensitization

Skin sensitization
Not classified based on available information.

Respiratory sensitization
Not classified based on available information.

Components:

Lamivudine:
Routes of exposure: Dermal
Species: Guinea pig
Result: Not a skin sensitizer.

Tenofovir:
Test Type: Maximization Test
Routes of exposure: Skin contact
Species: Guinea pig
Result: Not a skin sensitizer.

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: Rat
- Exposure time: 2 Years
- Result: negative
- Species: Mouse
- Exposure time: 2 Years
- Result: negative

Tenofovir:
- Species: Mouse
- Application Route: Oral
- Exposure time: 104 weeks
- Result: negative
- Species: Rat
- Application Route: Oral
- Exposure time: 104 weeks
- Result: negative

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

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.

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

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 fetal development : Test Type: Embryo-fetal development
Species: Rabbit
Application Route: Oral
Result: Embryotoxic effects and adverse effects on the offspring were detected.

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

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 fetal development:
- Test Type: Embryo-fetal development
  - Species: Rat
  - Application Route: Oral
  - Result: No adverse effects.

  Test Type: Embryo-fetal development
  - Species: Rabbit
  - 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 fetal development**
- Test Type: Embryo-fetal development
  - Species: Rat
  - Developmental Toxicity: NOAEL: 450 mg/kg body weight
  - Result: No adverse effects.

  Test Type: Embryo-fetal development
  - Species: Rabbit
  - Developmental Toxicity: NOAEL: 300 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:**

- Routes of exposure: 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:** $\geq 9,000$ 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, Diarrhea, 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:** $\geq 10$ 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, Diarrhea, Cough

#### Tenofovir:

- **Ingestion**: Symptoms: Nausea, Diarrhea, Vomiting, flatulence, Headache, Rash

#### 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

### Experience with human exposure**

**Components:**

#### Lamivudine:

- **Ingestion**: Symptoms: Headache, Fatigue, Respiratory disorders, Diarrhea, Cough

#### Tenofovir:

- **Ingestion**: Symptoms: Nausea, Diarrhea, Vomiting, flatulence, Headache, Rash

#### Doravirine:

- **Ingestion**: Symptoms: confusion, Headache, Dizziness, Nausea, Rash, abnormal dreams, flushing, Neurological disorders, mental depression
### Toxicity to fish

<table>
<thead>
<tr>
<th>End point</th>
<th>EC50 (Pimephales promelas (fathead minnow))</th>
<th>Exposure time: 96 h</th>
<th>Method: OECD Test Guideline 203</th>
</tr>
</thead>
</table>

### Toxicity to daphnia and other aquatic invertebrates

<table>
<thead>
<tr>
<th>End point</th>
<th>EC50 (Daphnia magna (Water flea))</th>
<th>Exposure time: 48 h</th>
<th>Method: OECD Test Guideline 202</th>
</tr>
</thead>
</table>

### Toxicity to algae/aquatic plants

<table>
<thead>
<tr>
<th>End point</th>
<th>EC50 (Pseudokirchneriella subcapitata (green algae))</th>
<th>Exposure time: 72 h</th>
<th>Method: OECD Test Guideline 201</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NOEC (Pseudokirchneriella subcapitata (green algae))</td>
<td>Exposure time: 72 h</td>
<td>Method: OECD Test Guideline 201</td>
</tr>
</tbody>
</table>

#### Tenofovir:

### Toxicity to algae/aquatic plants

<table>
<thead>
<tr>
<th>End point</th>
<th>EC50 (Raphidocelis subcapitata (freshwater green alga))</th>
<th>Exposure time: 72 h</th>
<th>Method: OECD Test Guideline 201</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NOEC (Raphidocelis subcapitata (freshwater green alga))</td>
<td>Exposure time: 72 h</td>
<td>Method: OECD Test Guideline 201</td>
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</table>

### Toxicity to fish (Chronic toxicity)

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<thead>
<tr>
<th>End point</th>
<th>NOEC (Pimephales promelas (fathead minnow))</th>
<th>Exposure time: 32 d</th>
<th>Method: OECD Test Guideline 210</th>
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</table>

### Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity)

<table>
<thead>
<tr>
<th>End point</th>
<th>NOEC (Daphnia magna (Water flea))</th>
<th>Exposure time: 21 d</th>
<th>Method: OECD Test Guideline 211</th>
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</table>

### Toxicity to microorganisms

<table>
<thead>
<tr>
<th>End point</th>
<th>EC50: &gt; 1,000 mg/l</th>
<th>Exposure time: 3 h</th>
<th>Test Type: Respiration inhibition</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>NOEC: &gt; 1,000 mg/l</td>
<td>Exposure time: 3 h</td>
<td>Method: OECD Test Guideline 209</td>
</tr>
</tbody>
</table>

#### Doravirine:

### Toxicity to daphnia and other aquatic invertebrates

<table>
<thead>
<tr>
<th>End point</th>
<th>EC50 (Daphnia magna (Water flea))</th>
<th>Exposure time: 48 h</th>
<th>Method: OECD Test Guideline 202</th>
</tr>
</thead>
</table>
### 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 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.
  - Biodegradation: **3.66 %**
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: 1.06  
  pH: 7

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: 3.33  
  Method: OECD Test Guideline 106

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.  
  Do not dispose of waste into sewer.
- 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.

Domestic regulation

49 CFR
Not regulated as a dangerous good

Special precautions for user
Not applicable

SECTION 15. REGULATORY INFORMATION

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
- Combustible dust
- Reproductive toxicity
- Specific target organ toxicity (single or repeated exposure)
- Serious eye damage or eye irritation

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

- Cellulose, 2-hydroxypropyl methyl ether, acetate hydrogen butanedioate: 71138-97-1
- Cellulose: 9004-34-6
- Lamivudine: 134678-17-4
- Tenofovir: 202138-50-9
- Doravirine: 1338225-97-0
- Croscarmellose sodium: 74811-65-7
California Permissible Exposure Limits for Chemical Contaminants
Cellulose 9004-34-6

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

**NFPA 704:**

Flammability

Health

Health

Instability

Special hazard

**HMIS® IV:**

HEALTH

FLAMMABILITY

PHYSICAL HAZARD

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

ACGIH: USA. ACGIH Threshold Limit Values (TLV)
CAL PEL: California permissible exposure limits for chemical contaminants (Title 8, Article 107)
NIOSH REL: USA. NIOSH Recommended Exposure Limits
OSHA Z-1: USA. Occupational Exposure Limits (OSHA) - Table Z-1 Limits for Air Contaminants
OSHA Z-3: USA. Occupational Exposure Limits (OSHA) - Table Z-3 Mineral Dusts
ACGIH / TWA: 8-hour, time-weighted average
CAL PEL / PEL: Permissible exposure limit
NIOSH REL / TWA: Time-weighted average concentration for up to a 10-hour workday during a 40-hour workweek
OSHA Z-1 / TWA: 8-hour time weighted average
OSHA Z-3 / TWA: 8-hour time weighted average
SAFETY DATA SHEET

Doravirine / Lamivudine / Tenofovir Disoproxil Fumarate Bilayer Formulation

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Date of first issue:  02/16/2015


Revision Date:  04/04/2023

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.

US / Z8