SAFETY DATA SHEET

Doravirine / Lamivudine / Tenofovir Disoproxil Fumarate Bilayer Formulation

SECTION 1. IDENTIFICATION

Product name: Doravirine / Lamivudine / Tenofovir Disoproxil Fumarate Bilayer Formulation
Other means of identification: No data available

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 Hazardous Products Regulations
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: 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**
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>Common Name/Synonym</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>No data available</td>
<td>9004-34-6</td>
<td>21</td>
</tr>
<tr>
<td>Lamivudine</td>
<td>No data available</td>
<td>134678-17-4</td>
<td>19.2</td>
</tr>
<tr>
<td>Tenofovir</td>
<td>No data available</td>
<td>202138-50-9</td>
<td>19.2</td>
</tr>
<tr>
<td>Doravirine</td>
<td>3-Chloro-5-(((4-((5-oxo-4,5-dihydro-1H-1,2,4-triazol-3-yl)methyl)-2-oxo-4-(trifluoromethyl)-1,2-dihydropyridin-3-yl)oxy)benz</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.
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

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

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>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of)</th>
<th>Control parameters / Permissible</th>
<th>Basis</th>
</tr>
</thead>
</table>
SAFETY DATA SHEET

Doravirine / Lamivudine / Tenofovir Disoproxil Fumarate Bilayer Formulation

**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.

- **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

<table>
<thead>
<tr>
<th>Substance</th>
<th>TWA (Total dust)</th>
<th>TWA (respirable dust fraction)</th>
<th>TWAEV (total dust)</th>
<th>TWA ACGIH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>10 mg/m³</td>
<td>CA AB OEL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TWA (Total dust)</td>
<td>10 mg/m³</td>
<td>CA BC OEL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TWA (respirable dust fraction)</td>
<td>3 mg/m³</td>
<td>CA BC OEL</td>
<td></td>
</tr>
<tr>
<td>Lamivudine</td>
<td>134678-17-4</td>
<td>100 µg/m³ (OEB 2)</td>
<td>Internal</td>
<td></td>
</tr>
<tr>
<td>Tenofovir</td>
<td>202138-50-9</td>
<td>150 µg/m³ (OEB 2)</td>
<td>Internal</td>
<td></td>
</tr>
<tr>
<td>Doravirine</td>
<td>1338225-97-0</td>
<td>500 µg/m³ (OEB2)</td>
<td>Internal</td>
<td></td>
</tr>
</tbody>
</table>
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
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: > 2,000 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
**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>
</thead>
<tbody>
<tr>
<td>5.0</td>
<td>04/04/2023</td>
<td>58619-00027</td>
<td>10/01/2022</td>
<td>02/16/2015</td>
</tr>
</tbody>
</table>

---

**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 sensitization

Skin sensitization
Not classified based on available information.

Respiratory sensitization
Not classified based on available information.

Components:

Lamivudine:

<table>
<thead>
<tr>
<th>Routes of exposure</th>
<th>Dermal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species</td>
<td>Guinea pig</td>
</tr>
<tr>
<td>Result</td>
<td>Not a skin sensitizer.</td>
</tr>
</tbody>
</table>

Tenofovir:

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Maximization Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Routes of exposure</td>
<td>Skin contact</td>
</tr>
<tr>
<td>Species</td>
<td>Guinea pig</td>
</tr>
<tr>
<td>Result</td>
<td>Not a skin sensitizer.</td>
</tr>
</tbody>
</table>

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:

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure time</td>
<td>2 Years</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Mouse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure time</td>
<td>2 Years</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
</tbody>
</table>

Tenofovir:

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>104 weeks</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
</tbody>
</table>

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

Doravirine:

<table>
<thead>
<tr>
<th>Species</th>
<th>Mouse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>6 Months</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
<tr>
<td>Remarks</td>
<td>No significant adverse effects were reported</td>
</tr>
</tbody>
</table>

Reproductive toxicity
Suspected of damaging the unborn child.

Components:

Cellulose:

<table>
<thead>
<tr>
<th>Effects on fertility</th>
<th>Test Type: One-generation reproduction toxicity study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species</td>
<td>Rat</td>
</tr>
<tr>
<td>Application Route</td>
<td>Ingestion</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Effects on fetal development</th>
<th>Test Type: Fertility/early embryonic development</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species</td>
<td>Rat</td>
</tr>
<tr>
<td>Application Route</td>
<td>Ingestion</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
</tbody>
</table>

Lamivudine:

<table>
<thead>
<tr>
<th>Effects on fertility</th>
<th>Test Type: Two-generation reproduction toxicity study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species</td>
<td>Rat</td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Fertility</td>
<td>NOAEL: 900 mg/kg body weight</td>
</tr>
<tr>
<td>Result</td>
<td>No effects on fertility and early embryonic</td>
</tr>
</tbody>
</table>
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
- Application Route: Oral
- Developmental Toxicity: NOAEL: 450 mg/kg body weight
- Result: No adverse effects.

- Test Type: Embryo-fetal development
- Species: Rabbit
- Application Route: Oral
- 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: >= 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:**
- 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:**
- Species: Mouse
- NOAEL: 500 mg/kg
- Application Route: Oral
- Exposure time: 1 Months
- Target Organs: Blood
### Tenofovir:

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>30 mg/kg</td>
</tr>
<tr>
<td>LOAEL</td>
<td>300 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>13 Weeks</td>
</tr>
<tr>
<td>Target Organs</td>
<td>Bone</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Dog</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>3 mg/kg</td>
</tr>
<tr>
<td>LOAEL</td>
<td>&gt;= 10 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>42 Weeks</td>
</tr>
<tr>
<td>Target Organs</td>
<td>Kidney</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Monkey</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOAEL</td>
<td>10 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Subcutaneous</td>
</tr>
<tr>
<td>Exposure time</td>
<td>10 Months</td>
</tr>
<tr>
<td>Target Organs</td>
<td>Bone</td>
</tr>
</tbody>
</table>

### Doravirine:

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>450 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>6 Months</td>
</tr>
<tr>
<td>Remarks</td>
<td>No significant adverse effects were reported</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Mouse</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>&gt; 450 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>3 Months</td>
</tr>
<tr>
<td>Remarks</td>
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</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Dog</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>&gt; 1,000 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>9 Months</td>
</tr>
<tr>
<td>Remarks</td>
<td>No significant adverse effects were reported</td>
</tr>
</tbody>
</table>

### Aspiration toxicity

Not classified based on available information.

### Experience with human exposure

### Components:

#### Lamivudine:

| Ingestion | Symptoms: Headache, Fatigue, Respiratory disorders, Diarrhea, Cough |

#### Tenofovir:
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

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 algae/aquatic plants: EC50 (Raphidocelis subcapitata (freshwater green alga)): 69 mg/l
End point: Growth
Exposure time: 72 h
Method: OECD Test Guideline 201

NOEC (Raphidocelis subcapitata (freshwater green alga)): 18 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201

Toxicity to fish (Chronic toxicity): NOEC (Pimephales promelas (fathead minnow)): 9 mg/l
Exposure time: 32 d
### Toxicity Data

#### Method: OECD Test Guideline 210

**Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity)**
- NOEC (Daphnia magna (Water flea)): 12 mg/l
- Exposure time: 21 d
- Method: OECD Test Guideline 211

**Exposure time:** 21 d

**Test Type:** Respiration inhibition

**Method:** OECD Test Guideline 209

**Remarks:** No toxicity at the limit of solubility.

**EC50 (Daphnia magna):** > 12 mg/l

**Exposure time:** 21 d

**Remarks:** No toxicity at the limit of solubility.

**NOEC:** > 12 mg/l

**Exposure time:** 21 d

**Remarks:** No toxicity at the limit of solubility.

**EC50 (Americamysis):** 9.1 mg/l

**Exposure time:** 96 h

**Remarks:** No toxicity at the limit of solubility.

**NOEC (Pseudokirchneriella subcapitata):** 5.8 mg/l

**Exposure time:** 72 h

**Remarks:** No toxicity at the limit of solubility.

**EC50 (Pimephales promelas (fathead minnow)):** 1 mg/l

**Exposure time:** 32 d

**Remarks:** No toxicity at the limit of solubility.

**NOEC (Daphnia magna):** 6.7 mg/l

**Exposure time:** 21 d

**Remarks:** No toxicity at the limit of solubility.

**EC50:** > 1,000 mg/l

**Exposure time:** 3 h

**Test Type:** Respiration inhibition

**Method:** OECD Test Guideline 209

**Remarks:** No toxicity at the limit of solubility.

**NOEC:** 1,000 mg/l
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 % |
| Exposure time    | 28 d |
| Method: OECD Test Guideline 314 |

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 |
SAFETY DATA SHEET

Doravirine / Lamivudine / Tenofovir Disoproxil Fumarate Bilayer Formulation

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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
- TDG
  Not regulated as a dangerous good
- Special precautions for user
  Not applicable

SECTION 15. REGULATORY INFORMATION

The ingredients of this product are reported in the following inventories:
- AICS: not determined
- DSL: not determined
- IECSC: not determined
SECTION 16. OTHER INFORMATION

Full text of other abbreviations

ACGIH : USA. ACGIH Threshold Limit Values (TLV)
CA BC OEL : Canada. British Columbia OEL
CA QC OEL : Québec. Regulation respecting occupational health and safety, Schedule 1, Part 1: Permissible exposure values for airborne contaminants
ACGIH / TWA : 8-hour, time-weighted average
CA AB OEL / TWA : 8-hour Occupational exposure limit
CA BC OEL / TWA : 8-hour time weighted average
CA QC OEL / TWAEV : Time-weighted average exposure value

AIIC - Australian Inventory of Industrial Chemicals; 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, Bioaccumulative and Toxic substance; PICCS - Philippines Inventory of Chemicals and Chemical Substances; (Q)SAR - (Quantitative) Structure Activity Relationship; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; SADT - Self-Accelerating Decomposition Temperature; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance Inventory; TDG - Transportation of Dangerous Goods; TECI - Thailand Existing Chemicals Inventory; TSCA - Toxic Substances Control Act (United States); UN - United Nations; UNRTDG - United Nations Recommendations on the Transport of Dangerous Goods; vPvB - Very Persistent and Very Bioaccumulative; WHMIS - Workplace Hazardous Materials Information System

SAFETY DATA SHEET

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Revision Date: 04/04/2023
Date format: mm/dd/yyyy

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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