SAFETY DATA SHEET

Doravirine / Lamivudine / Tenofovir Disoproxil Fumarate Bilayer Formulation

Section 1: Identification

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

Manufacturer or supplier's details

Company: MSD
Address: 33 Whakatiki Street - Private Bag 908 Upper Hutt - New Zealand
Telephone: 908-740-4000
Emergency telephone number: 1-908-423-6000
E-mail address: EHSDATASTEWARD@msd.com
Telefax: 908-735-1496

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

Section 2: Hazard identification

GHS Classification

Serious eye damage/eye irritation: 2A
Reproductive toxicity: Repr.2
Specific target organ toxicity - repeated exposure (Oral): STOT RE2 (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 eye protection/ face protection.
P281 Use personal protective equipment as required.

**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**
May form explosive dust-air mixture during processing, handling or other means.

---

**Section 3: Composition/information on ingredients**

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

**Components**

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>&gt;= 10 - &lt; 30</td>
</tr>
<tr>
<td>Lamivudine</td>
<td>134678-17-4</td>
<td>&gt;= 10 - &lt; 30</td>
</tr>
<tr>
<td>Tenofovir</td>
<td>202138-50-9</td>
<td>&gt;= 10 - &lt; 30</td>
</tr>
<tr>
<td>Doravirine</td>
<td>1338225-97-0</td>
<td>&lt;= 10</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.
### Section 5: Fire-fighting measures

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

**Unsuitable extinguishing media**
- None known.

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

**Hazardous combustion products**
- Carbon oxides
- Nitrogen oxides (NOx)
- Halogenated compounds

**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.

### Section 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.

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. 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.

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.

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

Section 8: Exposure controls/personal protection

Components with workplace control parameters

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type</th>
<th>Control parameter</th>
<th>Basis</th>
</tr>
</thead>
</table>

4 / 20
SAFETY DATA SHEET

Doravirine / Lamivudine / Tenofovir Disoproxil Fumarate Bilayer Formulation

Version 3.11  Revision Date: 09/13/2019  SDS Number: 58633-00016  Date of last issue: 13.02.2019

<table>
<thead>
<tr>
<th>Form of exposure</th>
<th>TWA</th>
<th>NZ OEL</th>
<th>ACGIH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose 9004-34-6</td>
<td>10 mg/m3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lamivudine 134678-17-4</td>
<td>150 µg/m3 (OEB 2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tenofovir 202138-50-9</td>
<td>200 ug/m3 (OEB 2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doravirine 1338225-97-0</td>
<td>500 ug/m3 (OEB2)</td>
<td></td>
<td></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.

Section 9: Physical and chemical properties

Appearance: powder

Colour: No data available

Odour: No data available

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

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: No hazardous decomposition products are known.
Section 11: Toxicological information

Exposure routes:
- 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.
**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>
</table>

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

### Doravirine:
- **Remarks**: No data available

### Chronic toxicity

#### 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

**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.

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

**Reproductive toxicity - As:**
Some evidence of adverse effects on development, based on
Doravirine / Lamivudine / Tenofovir Disoproxil Fumarate Bilayer Formulation

SAFETY DATA SHEET

Version 3.11
Revision Date: 09/13/2019
SDS Number: 58633-00016
Date of last issue: 13.02.2019
Date of first issue: 16.02.2015

streamlined 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

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

Test Type: Embryo-foetal 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:
Exposure routes: Ingestion
Target Organs: Blood
Assessment: May cause damage to organs through prolonged or repeated exposure.
SAFETY DATA SHEET

Doravirine / Lamivudine / Tenofovir Disoproxil Fumarate Bilayer Formulation

Version 3.11  Revision Date: 09/13/2019  SDS Number: 58633-00016  Date of last issue: 13.02.2019
Date of first issue: 16.02.2015

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 depression

**Section 12: Ecological information**

**Ecotoxicity**

**Components:**

**Cellulose:**
**Toxicity to fish**

<table>
<thead>
<tr>
<th>Substance</th>
<th>LC50 (Unit)</th>
<th>Exposure time</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doravirine</td>
<td>&gt; 100 mg/l</td>
<td>48 h</td>
<td>LC50 (Oryzias latipes (Japanese medaka)): &gt; 100 mg/l Exposure time: 48 h Remarks: Based on data from similar materials</td>
</tr>
<tr>
<td>Lamivudine</td>
<td>&gt; 97.7 mg/l</td>
<td>96 h</td>
<td>LC50 (Pimephales promelas (fathead minnow)): &gt; 97.7 mg/l Exposure time: 96 h Method: OECD Test Guideline 203</td>
</tr>
<tr>
<td>Tenofovir</td>
<td>&gt; 92 mg/l</td>
<td>96 h</td>
<td>LC50 (Oncorhynchus mykiss (rainbow trout)): &gt; 92 mg/l Exposure time: 96 h Method: OECD Test Guideline 203</td>
</tr>
</tbody>
</table>

**Toxicity to daphnia and other aquatic invertebrates**

<table>
<thead>
<tr>
<th>Substance</th>
<th>EC50 (Unit)</th>
<th>Exposure time</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamivudine</td>
<td>&gt; 100 mg/l</td>
<td>48 h</td>
<td>EC50 (Daphnia magna (Water flea)): &gt; 100 mg/l Exposure time: 48 h Method: OECD Test Guideline 202</td>
</tr>
<tr>
<td>Tenofovir</td>
<td>&gt; 98 mg/l</td>
<td>48 h</td>
<td>EC50 (Daphnia magna (Water flea)): &gt; 98 mg/l Exposure time: 48 h Method: OECD Test Guideline 202</td>
</tr>
</tbody>
</table>

**Toxicity to algae/aquatic plants**

<table>
<thead>
<tr>
<th>Substance</th>
<th>EC50 (Unit)</th>
<th>Exposure time</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamivudine</td>
<td>&gt; 96.9 mg/l</td>
<td>72 h</td>
<td>EC50 (Pseudokirchneriella subcapitata (green algae)): &gt; 96.9 mg/l Exposure time: 72 h Method: OECD Test Guideline 201</td>
</tr>
<tr>
<td>Tenofovir</td>
<td>47 mg/l</td>
<td>72 h</td>
<td>EC50 (Pseudokirchneriella subcapitata (green algae)): 47 mg/l Exposure time: 72 h Method: OECD Test Guideline 201</td>
</tr>
</tbody>
</table>

**NOEC**

<table>
<thead>
<tr>
<th>Substance</th>
<th>NOEC (Unit)</th>
<th>Exposure time</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamivudine</td>
<td>96.9 mg/l</td>
<td>72 h</td>
<td>NOEC (Pseudokirchneriella subcapitata (green algae)): 96.9 mg/l Exposure time: 72 h Method: OECD Test Guideline 201</td>
</tr>
<tr>
<td>Tenofovir</td>
<td>14 mg/l</td>
<td>72 h</td>
<td>NOEC (Pseudokirchneriella subcapitata (green algae)): 14 mg/l Exposure time: 72 h Method: OECD Test Guideline 201</td>
</tr>
</tbody>
</table>

**Toxicity to microorganisms**

<table>
<thead>
<tr>
<th>Test Type</th>
<th>EC50 (Unit)</th>
<th>Exposure time</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test Type: Respiration inhibition</td>
<td>940 mg/l</td>
<td>3 h</td>
<td>EC50: 940 mg/l Exposure time: 3 h</td>
</tr>
</tbody>
</table>

**Test Type**

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiration inhibition</td>
<td></td>
</tr>
</tbody>
</table>

**Other aquatic invertebrates (Chronic toxicity)**

<table>
<thead>
<tr>
<th>Substance</th>
<th>NOEC (Unit)</th>
<th>Exposure time</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamivudine</td>
<td>1.9 mg/l</td>
<td>32 d</td>
<td>NOEC (Pimephales promelas (fathead minnow)): 1.9 mg/l Exposure time: 32 d Method: OECD Test Guideline 210</td>
</tr>
<tr>
<td>Tenofovir</td>
<td>13 mg/l</td>
<td>21 d</td>
<td>NOEC (Daphnia magna (Water flea)): 13 mg/l Exposure time: 21 d Method: OECD Test Guideline 211</td>
</tr>
</tbody>
</table>

**Chronic toxicity**

<table>
<thead>
<tr>
<th>Substance</th>
<th>NOEC (Unit)</th>
<th>Exposure time</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamivudine</td>
<td>1.9 mg/l</td>
<td>32 d</td>
<td>NOEC (Pimephales promelas (fathead minnow)): 1.9 mg/l Exposure time: 32 d Method: OECD Test Guideline 210</td>
</tr>
<tr>
<td>Tenofovir</td>
<td>13 mg/l</td>
<td>21 d</td>
<td>NOEC (Daphnia magna (Water flea)): 13 mg/l Exposure time: 21 d Method: OECD Test Guideline 211</td>
</tr>
</tbody>
</table>
**Method**: OECD Test Guideline 209

**NOEC**: 600 mg/l  
**Exposure time**: 3 h  
**Test Type**: Respiration inhibition  
**Remarks**: No toxicity at the limit of solubility

### Doravirine:

**Toxicity to daphnia and other aquatic invertebrates**

<table>
<thead>
<tr>
<th>Method</th>
<th>NOEC</th>
<th>Exposure time</th>
<th>Test Type</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>OECD Test Guideline 209</td>
<td>600 mg/l</td>
<td>3 h</td>
<td>Respiration inhibition</td>
<td>No toxicity at the limit of solubility</td>
</tr>
</tbody>
</table>

**EC50** *(Daphnia magna (Water flea))*: > 39 mg/l  
**Exposure time**: 48 h  
**Remarks**: No toxicity at the limit of solubility

**EC50** *(Americamysis)*: 9.1 mg/l  
**Exposure time**: 96 h

### Toxicity to algae/aquatic plants

<table>
<thead>
<tr>
<th>Method</th>
<th>NOEC</th>
<th>Exposure time</th>
<th>Test Type</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>OECD Test Guideline 221</td>
<td>5.8 mg/l</td>
<td>72 h</td>
<td></td>
<td>No toxicity at the limit of solubility</td>
</tr>
</tbody>
</table>

**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)

<table>
<thead>
<tr>
<th>Method</th>
<th>NOEC</th>
<th>Exposure time</th>
<th>Test Type</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>OECD Test Guideline 210</td>
<td>1 mg/l</td>
<td>32 d</td>
<td></td>
<td>No toxicity at the limit of solubility</td>
</tr>
</tbody>
</table>

**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)

<table>
<thead>
<tr>
<th>Method</th>
<th>NOEC</th>
<th>Exposure time</th>
<th>Test Type</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>OECD Test Guideline 211</td>
<td>6.7 mg/l</td>
<td>21 d</td>
<td></td>
<td>No toxicity at the limit of solubility</td>
</tr>
</tbody>
</table>

**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

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

**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:
Distribution among environmental compartments: log Koc: 2.86

Other adverse effects
No data available
Section 13: Disposal considerations

Disposal methods
Waste from residues: Dispose of in accordance with local regulations.
Contaminated packaging: Empty containers should be taken to an approved waste handling site for recycling or disposal.
If not otherwise specified: Dispose of as unused product.

Section 14: Transport information

International Regulations
UNRTDG
Not regulated as a dangerous good
IATA-DGR
Not regulated as a dangerous good
IMDG-Code
Not regulated as a dangerous good
Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code
Not applicable for product as supplied.

National Regulations
NZS 5433
Not regulated as a dangerous good

Section 15: Regulatory information

Safety, health and environmental regulations/legislation specific for the substance or mixture

HSNO Approval Number
HSR100425 Pharmaceutical Active Ingredients Group Standard 2017

HSW Controls
Certified handler certificate not required.
Tracking hazardous substance not required.
Refer to the Health and Safety at Work (Hazardous Substances) Regulations 2017, for further information.

The components of this product are reported in the following inventories:
AICS: not determined
DSL: not determined
IECSC: not determined
Section 16: Other information

Further information

Date format: dd.mm.yyyy

Full text of other abbreviations
ACGIH: USA. ACGIH Threshold Limit Values (TLV)
NZ OEL: New Zealand. Workplace Exposure Standards for Atmospheric Contaminants
ACGIH / TWA: 8-hour, time-weighted average
NZ OEL / WES-TWA: Workplace Exposure Standard - 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, 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; 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 mate-
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.

NZ / EN