SAFETY DATA SHEET

Doravirine / Lamivudine / Tenofovir Disoproxil Fumarate Bilayer Formulation

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

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

Manufacturer or supplier’s details

Company: MSD
Address: 26 Talavera Road, Talavera Corp Centre, Macquarie Park New South Wales, 2113 Australia
Telephone: (61)-02-8988-8000
Emergency telephone number: (61)-02-8988-8000
E-mail address: EHSDATASTEWARD@msd.com
Telefax: 908-735-1496

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

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification

Serious eye damage/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 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

Substance / Mixture : Mixture

Components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>&gt;= 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.
If swallowed: Get medical attention.
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. FIREFIGHTING MEASURES

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

Unsuitable extinguishing media:
None known.

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

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

Specific extinguishing methods:
Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.
Use water spray to cool unopened containers.
Remove undamaged containers from fire area if it is safe to do so.
Evacuate area.

Special protective equipment for firefighters:
In the event of fire, wear self-contained breathing apparatus.
Use personal protective equipment.

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>
SAFETY DATA SHEET

Doravirine / Lamivudine / Tenofovir Disoproxil Fumarate Bilayer Formulation

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

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

**Personal protective equipment**

**Respiratory protection**
- If adequate local exhaust ventilation is not available or exposure assessment demonstrates exposures outside the recommended guidelines, use respiratory protection.
  - **Filter type**: Particulates type
  - **Hand protection Material**: Chemical-resistant gloves

**Eye protection**
- Wear safety glasses with side shields or goggles.
- If the work environment or activity involves dusty conditions, mists or aerosols, wear the appropriate goggles. Wear a face shield 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 products: 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
SAFETY DATA SHEET

Doravirine / Lamivudine / Tenofovir Disoproxil Fumarate Bilayer Formulation

Result: Not a skin sensitizer.

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

**Doravirine:**
Remarks: No data available

**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

Genotoxicity in vivo: Test Type: In vitro mammalian cell gene mutation test
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

Tenfovir:
- Species: Mouse
  - Application Route: Oral
**Doravirine / Lamivudine / Tenofovir Disoproxil Fumarate Bilayer Formulation**

<table>
<thead>
<tr>
<th>Component</th>
<th>Effects on fertility</th>
<th>Test Type</th>
<th>Reproduction Toxicity Study</th>
<th>Application Route</th>
<th>NOAEL</th>
<th>Result</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Doravirine:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Species</td>
<td>Mouse</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>No significant adverse effects were reported</td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exposure time</td>
<td>6 Months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Reproductive toxicity**

Suspected of damaging the unborn child.

**Components:**

**Cellulose:**

**Effects on foetal development**

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

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

**Tenofovir:**

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

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

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**

<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:**
- **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 Month
- **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
Doravirine / Lamivudine / Tenofovir Disoproxil Fumarate Bilayer Formulation

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:
<table>
<thead>
<tr>
<th></th>
<th>LC50 (Oryzias latipes (Japanese medaka)): &gt; 100 mg/l</th>
<th>Exposure time: 48 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remarks</td>
<td>Based on data from similar materials</td>
<td></td>
</tr>
</tbody>
</table>

**Lamivudine:**

<table>
<thead>
<tr>
<th></th>
<th>LC50 (Pimephales promelas (fathead minnow)): &gt; 97.7 mg/l</th>
<th>Exposure time: 96 h</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Method: OECD Test Guideline 203</td>
<td></td>
</tr>
</tbody>
</table>

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

|                          | EC50 (Pseudokirchneriella subcapitata (green algae)): > 96.9 mg/l | Exposure time: 72 h |
|--------------------------|==================================================================|---------------------|
|                          | Method: OECD Test Guideline 201                                 |                     |

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

**Tenofovir:**

<table>
<thead>
<tr>
<th></th>
<th>LC50 (Oncorhynchus mykiss (rainbow trout)): &gt; 92 mg/l</th>
<th>Exposure time: 96 h</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Method: OECD Test Guideline 203</td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th></th>
<th>EC50 (Pseudokirchneriella subcapitata (green algae)): 47 mg/l</th>
<th>Exposure time: 72 h</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Method: OECD Test Guideline 201</td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th></th>
<th>NOEC (Pimephales promelas (fathead minnow)): 1.9 mg/l</th>
<th>Exposure time: 32 d</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Method: OECD Test Guideline 210</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>NOEC (Daphnia magna (Water flea)): 13 mg/l</th>
<th>Exposure time: 21 d</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Method: OECD Test Guideline 211</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>EC50: 940 mg/l</th>
<th>Exposure time: 3 h</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Test Type: Respiration inhibition</td>
<td></td>
</tr>
</tbody>
</table>
Method: OECD Test Guideline 209

NOEC: 600 mg/l
Exposure time: 3 h
Test Type: Respiration inhibition
Method: OECD Test Guideline 209

**Doravirine:**

**Toxicity to daphnia and other aquatic invertebrates**

EC50 (Daphnia magna (Water flea)): > 39 mg/l
Exposure time: 48 h
Method: OECD Test Guideline 202
Remarks: No toxicity at the limit of solubility

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

**Toxicity to algae/aquatic plants**

EC50 (Pseudokirchneriella subcapitata (green algae)): > 5.8 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 221
Remarks: No toxicity at the limit of solubility

NOEC (Pseudokirchneriella subcapitata (green algae)): 5.8 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 221
Remarks: No toxicity at the limit of solubility

**Toxicity to fish (Chronic toxicity)**

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

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

NOEC (Daphnia magna (Water flea)): 6.7 mg/l
Exposure time: 21 d
Method: OECD Test Guideline 211
Remarks: No toxicity at the limit of solubility

**Toxicity to microorganisms**

EC50: > 1,000 mg/l
Exposure time: 3 h
Test Type: Respiration inhibition
Method: OECD Test Guideline 209

NOEC: 1,000 mg/l
Exposure time: 3 h
Test Type: Respiration inhibition
Method: OECD Test Guideline 209

**Persistence and degradability**

**Components:**

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

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

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

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

Bioaccumulative potential

**Components:**

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

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

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

Mobility in soil

**Components:**

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

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

**Doravirine:**
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
- ADG: Not regulated as a dangerous good

SECTION 15. REGULATORY INFORMATION

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

Prohibition/Licensing Requirements: There is no applicable prohibition or notification/licensing requirements, including for carcinogens under Commonwealth, State or Territory legislation.

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
SAFETY DATA SHEET

Doravirine / Lamivudine / Tenofovir Disoproxil Fumarate Bilayer Formulation

Revision Date: 09/13/2019
SDS Number: 58616-00016
Date of last issue: 13.02.2019
Date of first issue: 16.02.2015

Revision Date: 09/13/2019
Sources of key data used to compile the Safety Data Sheet:

Date format: dd.mm.yyyy

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

AU / EN