1. PRODUCT AND COMPANY IDENTIFICATION

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

Manufacturer or supplier’s details
Company: MSD
Address: 199 Wenhai North Road
          HEDA, Hangzhou - Zhejiang Province - CHINA  310018
Telephone: 908-740-4000
Emergency telephone number: 86-571-87268110
E-mail address: EHSDATASTEWARD@msd.com

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

2. HAZARDS IDENTIFICATION

Emergency Overview

<table>
<thead>
<tr>
<th>Appearance</th>
<th>powder</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colour</td>
<td>No data available</td>
</tr>
<tr>
<td>Odour</td>
<td>No data available</td>
</tr>
</tbody>
</table>

May be harmful if swallowed. Causes mild skin irritation. Causes serious eye irritation. Suspected of damaging the unborn child. May cause damage to organs through prolonged or repeated exposure. Harmful to aquatic life.

GHS Classification

<table>
<thead>
<tr>
<th>Acute toxicity (Oral)</th>
<th>Category 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin corrosion/irritation</td>
<td>Category 3</td>
</tr>
<tr>
<td>Serious eye damage/eye irritation</td>
<td>Category 2A</td>
</tr>
<tr>
<td>Reproductive toxicity</td>
<td>Category 2</td>
</tr>
<tr>
<td>Specific target organ toxicity - repeated exposure</td>
<td>Category 2</td>
</tr>
<tr>
<td>Short-term (acute) aquatic hazard</td>
<td>Category 3</td>
</tr>
</tbody>
</table>

GHS label elements
Doravirine / Lamivudine / Tenofovir Disoproxil Fumarate Bilayer Formulation

Hazard pictograms: 
- Warning

Signal word: Warning

Hazard statements: 
- H303 May be harmful if swallowed.
- H316 Causes mild skin irritation.
- H319 Causes serious eye irritation.
- H361d Suspected of damaging the unborn child.
- H373 May cause damage to organs through prolonged or repeated exposure.
- H402 Harmful to aquatic life.

Precautionary statements: 
Prevention: 
- P201 Obtain special instructions before use.
- P202 Do not handle until all safety precautions have been read and understood.
- P260 Do not breathe dust.
- P264 Wash skin thoroughly after handling.
- P273 Avoid release to the environment.
- P280 Wear protective gloves/ protective clothing/ eye protection/ face protection.

Response: 
- P305 + P351 + P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
- P312 Call a POISON CENTER/doctor if you feel unwell.
- P332 + P313 If skin irritation occurs: 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.

Physical and chemical hazards
Not classified based on available information.

Health hazards
May be harmful if swallowed. Causes mild skin irritation. Causes serious eye irritation. Suspected of damaging the unborn child. May cause damage to organs through prolonged or repeated exposure.

Environmental hazards
Harmful to aquatic life.
Other hazards which do not result in classification
May form explosive dust-air mixture during processing, handling or other means.

3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Chemical name</td>
</tr>
<tr>
<td></td>
<td>Cellulose</td>
</tr>
<tr>
<td></td>
<td>Lamivudine</td>
</tr>
<tr>
<td></td>
<td>Tenofovir</td>
</tr>
<tr>
<td></td>
<td>Doravirine</td>
</tr>
</tbody>
</table>

4. FIRST AID MEASURES

General advice : In the case of accident or if you feel unwell, seek medical advice immediately. When symptoms persist or in all cases of doubt seek medical advice.

If inhaled : If inhaled, remove to fresh air. Get medical attention.

In case of skin contact : In case of contact, immediately flush skin with plenty of water. Remove contaminated clothing and shoes. 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 : May be harmful if swallowed. Causes mild skin irritation. Causes serious eye irritation. Suspected of damaging the unborn child. May cause damage to organs through prolonged or repeated exposure.

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

Notes to physician : Treat symptomatically and supportively.

5. FIREFIGHTING MEASURES

Suitable extinguishing media : Water spray Alcohol-resistant foam Carbon dioxide (CO2) Dry chemical
SAFETY DATA SHEET
according to GB/T 16483 and GB/T 17519

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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

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

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

6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures:
Use personal protective equipment.
Follow safe handling advice and personal protective equipment recommendations.

Environmental precautions:
Discharge into the environment must be avoided.
Prevent further leakage or spillage if safe to do so.
Retain and dispose of contaminated wash water.
Local authorities should be advised if significant spillages cannot be contained.

Methods and materials for containment and cleaning up:
Sweep up or vacuum up spillage and collect in suitable container for disposal.
Avoid dispersal of dust in the air (i.e., clearing dust surfaces with compressed air).
Dust deposits should not be allowed to accumulate on surfaces, as these may form an explosive mixture if they are released into the atmosphere in sufficient concentration.
Local or national regulations may apply to releases and disposal of this material, as well as those materials and items employed in the cleanup of releases. You will need to determine which regulations are applicable.
Sections 13 and 15 of this SDS provide information regarding certain local or national requirements.

7. HANDLING AND STORAGE

Handling:
Technical measures:
Static electricity may accumulate and ignite suspended dust causing an explosion.
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according to GB/T 16483 and GB/T 17519

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Provide adequate precautions, such as electrical grounding and bonding, or inert atmospheres.

Local/Total ventilation: Use only with adequate ventilation.
Advice on safe handling:
- Do not get on skin or clothing.
- Do not breathe dust.
- Do not swallow.
- Do not get in eyes.
- Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment.
- Minimize dust generation and accumulation.
- Keep container closed when not in use.
- Keep away from heat and sources of ignition.
- Take precautionary measures against static discharges.
- Take care to prevent spills, waste and minimize release to the environment.

Avoidance of contact: Oxidizing agents

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

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

Packaging material: Unsuitable material: None known.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Components with workplace control parameters

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters / Permissible concentration</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>PC-TWA</td>
<td>10 mg/m3</td>
<td>GBZ 2.1-2007</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA</td>
<td>10 mg/m3</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Lamivudine</td>
<td>134678-17-4</td>
<td>TWA</td>
<td>150 µg/m3 (OEB 2)</td>
<td>Internal</td>
</tr>
<tr>
<td>Tenofovir</td>
<td>202138-50-9</td>
<td>TWA</td>
<td>200 µg/m3 (OEB 2)</td>
<td>Internal</td>
</tr>
<tr>
<td>Doravirine</td>
<td>1338225-97-0</td>
<td>TWA</td>
<td>500 µg/m3 (OEB2)</td>
<td>Internal</td>
</tr>
</tbody>
</table>

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

Personal protective equipment
Respiratory protection:
- If adequate local exhaust ventilation is not available or exposure assessment demonstrates exposures outside the rec-
Filter type: Particulates type

Eye/face 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.

Hand protection:
- Chemical-resistant gloves

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.

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
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flammability limit
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

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.

11. TOXICOLOGICAL INFORMATION
Exposure routes : Inhalation
   Skin contact
   Ingestion
   Eye contact
SAFETY DATA SHEET
according to GB/T 16483 and GB/T 17519

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Acute toxicity
May be harmful if swallowed.

Product:
Acute oral toxicity: Acute toxicity estimate: 2,605 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
Causes mild skin irritation.
Components:

Lamivudine:
Species : Rabbit
Result : Mild skin irritation

Tenofovir:
Species : Rabbit
Result : Mild skin irritation

Doravirine:
Remarks : No data available

Serious eye damage/eye irritation
Causes serious eye irritation.

Components:

Lamivudine:
Species : Rabbit
Result : No eye irritation

Tenofovir:
Species : Rabbit
Result : Severe irritation

Doravirine:
Remarks : No data available

Respiratory or skin sensitisation

Skin sensitisation
Not classified based on available information.

Respiratory sensitisation
Not classified based on available information.

Components:

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

Tenofovir:
Test Type : Maximisation Test
Exposure routes : Skin contact
Species : Guinea pig
Result : Not a skin sensitizer.
Doravirine:
Remarks: No data available

Germ cell mutagenicity
Not classified based on available information.

Components:
Cellulose:
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES)
Result: negative
Test Type: In vitro mammalian cell gene mutation test
Result: negative

Genotoxicity in vivo: Test Type: Mammalian erythrocyte micronucleus test (in vivo cytogenetic assay)
Species: Mouse
Application Route: Ingestion
Result: negative

Lamivudine:
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES)
Result: negative
Test Type: Mouse Lymphoma
Result: equivocal

Genotoxicity in vivo: Test Type: Micronucleus test
Species: Rat
Application Route: Oral
Result: negative
Test Type: Unscheduled DNA synthesis (UDS) test with mammalian liver cells in vivo
Species: Rat
Result: negative

Tenofovir:
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES)
Result: equivocal
Test Type: In vitro mammalian cell gene mutation test
Result: positive

Genotoxicity in vivo: Test Type: Mutagenicity (in vivo mammalian bone-marrow cytogenetic test, chromosomal analysis)
Species: Mouse
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---

### 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
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<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>5.9</td>
<td>09/13/2019</td>
<td>58623-00016</td>
<td>2019/02/13</td>
<td>2015/02/16</td>
</tr>
</tbody>
</table>

**Doravirine:**

<table>
<thead>
<tr>
<th>Species</th>
<th>Application Route</th>
<th>Exposure time</th>
<th>Result</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mouse</td>
<td>Oral</td>
<td>6 Months</td>
<td>negative</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: Rat</td>
<td>Application Route: Ingestion</td>
</tr>
<tr>
<td>Result: negative</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Effects on foetal development</th>
<th>Test Type: Fertility/early embryonic development</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species: Rat</td>
<td>Application Route: Ingestion</td>
</tr>
<tr>
<td>Result: negative</td>
<td></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: Rat</td>
<td>Application Route: Oral</td>
</tr>
<tr>
<td>Fertility: NOAEL: 900 mg/kg body weight</td>
<td>Result: No effects on fertility and early embryonic development were detected.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Effects on foetal development</th>
<th>Test Type: Embryo-foetal development</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species: Rabbit</td>
<td>Application Route: Oral</td>
</tr>
<tr>
<td>Symptoms: Preimplantation loss, Skeletal malformations</td>
<td>Result: Embryotoxic effects and adverse effects on the offspring were detected.</td>
</tr>
</tbody>
</table>

Test Type: Embryo-foetal development

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

**Reproductive toxicity - Assessment:**

Some evidence of adverse effects on development, based on animal experiments.

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

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

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 through prolonged or repeated exposure.

Components:

Lamivudine:
- Exposure routes: Ingestion
- Target Organs: Blood
- Assessment: May cause damage to organs through prolonged or repeated exposure.

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

- Species: Monkey
- LOAEL: 10 mg/kg
- Application Route: Subcutaneous
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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

**12. ECOLOGICAL INFORMATION**

**Ecotoxicity**

**Components:**

**Cellulose:**
- **Toxicity to fish:** LC50 (Oryzias latipes (Japanese medaka)): > 100 mg/l
  - **Exposure time:** 48 h
  - **Remarks:** Based on data from similar materials
Lamivudine:
Toxicity to fish: 
LC50 (Pimephales promelas (fathead minnow)): > 97.7 mg/l
Exposure time: 96 h
Method: OECD Test Guideline 203

Toxicity to daphnia and other aquatic invertebrates:
EC50 (Daphnia magna (Water flea)): > 100 mg/l
Exposure time: 48 h
Method: OECD Test Guideline 202

Toxicity to algae/aquatic plants:
EC50 (Pseudokirchneriella subcapitata (green algae)): > 96.9 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201

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

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

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

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

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

Toxicity to fish (Chronic toxicity):
NOEC (Pimephales promelas (fathead minnow)): 1.9 mg/l
Exposure time: 32 d
Method: OECD Test Guideline 210

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity):
NOEC (Daphnia magna (Water flea)): 13 mg/l
Exposure time: 21 d
Method: OECD Test Guideline 211

Toxicity to microorganisms:
EC50: 940 mg/l
Exposure time: 3 h
Test Type: Respiration inhibition
Method: OECD Test Guideline 209
Doravirine / Lamivudine / Tenofovir Disoproxil Fumarate Bilayer Formulation

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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 |
|-------------------------------------------------|-------------------------------------------------|
| 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 |
| 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
13. DISPOSAL CONSIDERATIONS

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

14. TRANSPORT INFORMATION

International Regulations

UNRTDG
Not regulated as a dangerous good

IATA-DGR
Not regulated as a dangerous good

IMDG-Code
Not regulated as a dangerous good

Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code
Not applicable for product as supplied.

National Regulations

GB 6944/12268
Not regulated as a dangerous good

Special precautions for user
Not applicable

15. REGULATORY INFORMATION

National regulatory information
Law on the Prevention and Control of Occupational Diseases

The components of this product are reported in the following inventories:
- AICS: not determined
- DSL: not determined
- IECSC: not determined

16. OTHER INFORMATION

Further information
Sources of key data used to compile the Safety Data:
- Internal technical data, data from raw material SDSs, OECD eChem Portal search results and European Chemicals Agen-
SAFETY DATA SHEET
according to GB/T 16483 and GB/T 17519

Doravirine / Lamivudine / Tenofovir Disoproxil Fumarate Bilayer Formulation


Date format : yyyy/mm/dd

Full text of other abbreviations
ACGIH : USA. ACGIH Threshold Limit Values (TLV)
ACGIH / TWA : 8-hour, time-weighted average
GBZ 2.1-2007 / PC-TWA : Permissible concentration - 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; 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 Civil Aviation Organization; 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 Standardisation; 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

Disclaimer
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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