SAFETY DATA SHEET

Doravirine / Lamivudine / Tenofovir Disopropxil Fumarate Bilayer Formulation

SECTION 1. IDENTIFICATION

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

Manufacturer or supplier’s details
Company name of supplier: Merck & Co., Inc
Address: 2000 Galloping Hill Road
Kenilworth - New Jersey - U.S.A. 07033
Telephone: 908-740-4000
Telefax: 908-735-1496
Emergency telephone: 1-908-423-6000
E-mail address: EHSDATASTEWARD@merck.com

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

SECTION 2. HAZARDS IDENTIFICATION

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

GHS label elements
Hazard pictograms:

Signal Word: Warning

Hazard Statements: If small particles are generated during further processing, handling or by other means, may form combustible dust concentrations in air.
H319 Causes serious eye irritation.
H361d Suspected of damaging the unborn child.
H373 May cause damage to organs (Blood, Bone, Kidney) through prolonged or repeated exposure if swallowed.

Precautionary Statements: Prevention:
P201 Obtain special instructions before use.
P202 Do not handle until all safety precautions have been read and understood.
P260 Do not breathe dust.
P264 Wash skin thoroughly after handling.

Date of last issue: 02/13/2019
Date of first issue: 02/16/2015
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.
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
None known.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture: Mixture

Components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>&gt;= 20 - &lt; 30</td>
</tr>
<tr>
<td>Lamivudine</td>
<td>134678-17-4</td>
<td>&gt;= 10 - &lt; 20</td>
</tr>
<tr>
<td>Tenofovir</td>
<td>202138-50-9</td>
<td>&gt;= 10 - &lt; 20</td>
</tr>
<tr>
<td>Doravirine</td>
<td>1338225-97-0</td>
<td>&gt;= 5 - &lt; 10</td>
</tr>
</tbody>
</table>

Actual concentration is withheld as a trade secret

SECTION 4. FIRST AID MEASURES

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

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

In case of skin contact: In case of contact, immediately flush skin with plenty of water. Remove contaminated clothing and shoes. Get medical attention. Wash clothing before reuse. Thoroughly clean shoes before reuse.

In case of eye contact: In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. If easy to do, remove contact lens, if worn. Get medical attention.

If swallowed: If swallowed, DO NOT induce vomiting.
**Most important symptoms and effects, both acute and delayed**: 
- Causes serious eye irritation.
- Suspected of damaging the unborn child.
- May cause damage to organs through prolonged or repeated exposure if swallowed.

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

**Notes to physician**: 
- Treat symptomatically and supportively.

### SECTION 5. FIRE-FIGHTING MEASURES

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

**Unsuitable extinguishing media**: 
- None known.

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

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

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

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

### SECTION 6. ACCIDENTAL RELEASE MEASURES

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

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

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

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Ingredients with workplace control parameters

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters / Permissible concentration</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Respirable)</td>
<td>5 mg/m³</td>
<td>NIOSH REL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (total)</td>
<td>10 mg/m³</td>
<td>NIOSH REL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (total dust)</td>
<td>15 mg/m³</td>
<td>OSHA Z-1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (respirable fraction)</td>
<td>5 mg/m³</td>
<td>OSHA Z-1</td>
</tr>
<tr>
<td>Lamivudine</td>
<td>134678-17-4</td>
<td>TWA</td>
<td>150 µg/m³ (OEB 2)</td>
<td>Internal</td>
</tr>
</tbody>
</table>
SAFETYDATA SHEET

Doravirine / Lamivudine / Tenofovir Disoproxil Fumarate Bilayer Formulation

<table>
<thead>
<tr>
<th>Component</th>
<th>CAS Number</th>
<th>TWA Exposure Limit</th>
<th>TWA Internal Exposure Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tenofovir</td>
<td>202138-50-9</td>
<td>200 ug/m³ (OEB2)</td>
<td>Internal</td>
</tr>
<tr>
<td>Doravirine</td>
<td>1338225-97-0</td>
<td>500 ug/m³ (OEB2)</td>
<td>Internal</td>
</tr>
</tbody>
</table>

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

**Personal protective equipment**

**Respiratory protection:** General and local exhaust ventilation is recommended to maintain vapor exposures below recommended limits. Where concentrations are above recommended limits or are unknown, appropriate respiratory protection should be worn. Follow OSHA respirator regulations (29 CFR 1910.134) and use NIOSH/MSHA approved respirators. Protection provided by air purifying respirators against exposure to any hazardous chemical is limited. Use a positive pressure air supplied respirator if there is any potential for uncontrolled release, exposure levels are unknown, or any other circumstance where air purifying respirators may not provide adequate protection.

**Hand protection:** Chemical-resistant gloves

**Eye protection:** Wear safety glasses with side shields or goggles. If the work environment or activity involves dusty conditions, mists or aerosols, wear the appropriate goggles. Wear a faceshield or other full face protection if there is a potential for direct contact to the face with dusts, mists, or aerosols.

**Skin and body protection:** Work uniform or laboratory coat.

**Hygiene measures:** If exposure to chemical is likely during typical use, provide eye flushing systems and safety showers close to the working place. When using do not eat, drink or smoke. Wash contaminated clothing before re-use. The effective operation of a facility should include review of engineering controls, proper personal protective equipment, appropriate degowning and decontamination procedures, industrial hygiene monitoring, medical surveillance and the use of administrative controls.

**SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES**

**Appearance:** powder

**Color:** No data available

**Odor:** No data available
<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odor Threshold</td>
<td>No data available</td>
</tr>
<tr>
<td>pH</td>
<td>No data available</td>
</tr>
<tr>
<td>Melting point/freezing point</td>
<td>No data available</td>
</tr>
<tr>
<td>Initial boiling point and boiling range</td>
<td>No data available</td>
</tr>
<tr>
<td>Flash point</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Evaporation rate</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Flammability (solid, gas)</td>
<td>May form explosive dust-air mixture during processing, handling or other means.</td>
</tr>
<tr>
<td>Flammability (liquids)</td>
<td>No data available</td>
</tr>
<tr>
<td>Upper explosion limit / Upper flammability limit</td>
<td>No data available</td>
</tr>
<tr>
<td>Lower explosion limit / Lower flammability limit</td>
<td>No data available</td>
</tr>
<tr>
<td>Vapor pressure</td>
<td>Not applicable</td>
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<tr>
<td>Relative vapor density</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Relative density</td>
<td>No data available</td>
</tr>
<tr>
<td>Density</td>
<td>No data available</td>
</tr>
<tr>
<td>Solubility(ies)</td>
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</tr>
<tr>
<td>Water solubility</td>
<td>No data available</td>
</tr>
<tr>
<td>Partition coefficient: n-octanol/water</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Autoignition temperature</td>
<td>No data available</td>
</tr>
<tr>
<td>Decomposition temperature</td>
<td>No data available</td>
</tr>
<tr>
<td>Viscosity</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Viscosity, kinematic</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Explosive properties</td>
<td>Not explosive</td>
</tr>
<tr>
<td>Oxidizing properties</td>
<td>The substance or mixture is not classified as oxidizing.</td>
</tr>
<tr>
<td>Molecular weight</td>
<td>No data available</td>
</tr>
<tr>
<td>Particle size</td>
<td>No data available</td>
</tr>
</tbody>
</table>
SECTION 10. STABILITY AND REACTIVITY

Reactivity : Not classified as a reactivity hazard.
Chemical stability : Stable under normal conditions.
Possibility of hazardous reactions :
May form explosive dust-air mixture during processing, handling or other means.
Can react with strong oxidizing agents.

Conditions to avoid :
Heat, flames and sparks.
Avoid dust formation.

Incompatible materials :
Oxidizing agents

Hazardous decomposition products :
No hazardous decomposition products are known.

SECTION 11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure
Inhalation
Skin contact
Ingestion
Eye contact

Acute toxicity
Not classified based on available information.

Product:
Acute oral toxicity : Acute toxicity estimate: 2,604 mg/kg
Method: Calculation method

Components:
Cellulose:
Acute oral toxicity : LD50 (Rat): > 5,000 mg/kg
Acute inhalation toxicity : LC50 (Rat): > 5.8 mg/l
Exposure time: 4 h
Test atmosphere: dust/mist
Acute dermal toxicity : LD50 (Rabbit): > 2,000 mg/kg

Lamivudine:
Acute oral toxicity : LD50 (Rat): > 2,000 mg/kg
LD50 (Mouse): 4,000 mg/kg
Remarks: No mortality observed at this dose.
Acute toxicity (other routes of administration) : LD50 (Rat): > 2,000 mg/kg
Application Route: Intravenous

Tenofovir:
Acute oral toxicity : LD50 (Rat): > 1,500 mg/kg
LD50 (Dog): 30 mg/kg

**Doravirine:**

Acute oral toxicity: LD50 (Rat): > 750 mg/kg
Remarks: No mortality observed at this dose.
(Rat): Method: Phototoxicity
Remarks: No evidence of phototoxicity was observed

LD50 (Dog): > 1,000 mg/kg
Remarks: No mortality observed at this dose.

LD50 (Mouse): > 450 mg/kg
Remarks: No mortality observed at this dose.

**Skin corrosion/irritation**
Not classified based on available information.

**Components:**

**Lamivudine:**
Species: Rabbit
Result: Mild skin irritation

**Tenofovir:**
Species: Rabbit
Result: Mild skin irritation

**Doravirine:**
Remarks: No data available

**Serious eye damage/eye irritation**
Causes serious eye irritation.

**Components:**

**Lamivudine:**
Species: Rabbit
Result: No eye irritation

**Tenofovir:**
Species: Rabbit
Result: Severe irritation

**Doravirine:**
Remarks: No data available
Respiratory or skin sensitization

Skin sensitization
Not classified based on available information.

Respiratory sensitization
Not classified based on available information.

Components:

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

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

Doravirine:
Remarks : No data available

Germ cell mutagenicity
Not classified based on available information.

Components:

Cellulose:
Genotoxicity in vitro : Test Type: Bacterial reverse mutation assay (AMES)
Result: negative

Test Type: In vitro mammalian cell gene mutation test
Result: negative

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

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

Test Type: Mouse Lymphoma
Result: equivocal

Genotoxicity in vivo : Test Type: Micronucleus test
Species: Rat
Application Route: Oral
Result: negative

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

**Tenofovir:**

Genotoxicity in vitro : Test Type: Bacterial reverse mutation assay (AMES)
Result: equivocal

Test Type: In vitro mammalian cell gene mutation test
Result: positive

Genotoxicity in vivo : Test Type: Mutagenicity (in vivo mammalian bone-marrow cytogenetic test, chromosomal analysis)
Species: Mouse
Application Route: Intraperitoneal injection
Result: negative

Germ cell mutagenicity - Assessment : Weight of evidence does not support classification as a germ cell mutagen.

**Doravirine:**

Genotoxicity in vitro : Test Type: Bacterial reverse mutation assay (AMES)
Result: negative

Test Type: Chromosomal aberration
Test system: Chinese hamster ovary cells
Result: negative

Genotoxicity in vivo : Test Type: Micronucleus test
Species: Rat
Cell type: Bone marrow
Application Route: Oral
Result: negative

**Carcinogenicity:**
Not classified based on available information.

**Components:**

**Cellulose:**
Species : Rat
Application Route : Ingestion
Exposure time : 72 weeks
Result : negative

**Lamivudine:**
Species : Rat
Exposure time: 2 Years  
Species: Mouse  
Result: negative

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

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

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

IARC: No ingredient of this product present at levels greater than or equal to 0.1% is identified as probable, possible or confirmed human carcinogen by IARC.

OSHA: No component of this product present at levels greater than or equal to 0.1% is on OSHA’s list of regulated carcinogens.

NTP: No ingredient of this product present at levels greater than or equal to 0.1% is identified as a known or anticipated carcinogen by NTP.

Reproductive toxicity
Suspected of damaging the unborn child.

Components:  
Cellulose:  
Effects on fertility: Test Type: One-generation reproduction toxicity study  
Species: Rat  
Application Route: Ingestion  
Result: negative

Effects on fetal development: Test Type: Fertility/early embryonic development  
Species: Rat  
Application Route: Ingestion  
Result: negative

Lamivudine:
Effects on fertility:
- Test Type: Two-generation reproduction toxicity study
- Species: Rat
- Application Route: Oral
- Fertility: NOAEL: 900 mg/kg body weight
- Result: No effects on fertility and early embryonic development were detected.

Effects on fetal development:
- Test Type: Embryo-fetal development
- Species: Rabbit
- Application Route: Oral
- Symptoms: Preimplantation loss, Skeletal malformations.
- Result: Embryotoxic effects and adverse effects on the offspring were detected.

Reproductive toxicity - Assessment:
- Some evidence of adverse effects on development, based on animal experiments.

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

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

Doravirine:
Effects on fertility:
- Test Type: Fertility
- Species: Rat, male and female
- Fertility: NOAEL: 450 mg/kg body weight
- Result: No effects on fertility.

Effects on fetal development:
- Test Type: Embryo-fetal development
- Species: Rat
- Application Route: Oral
- Developmental Toxicity: NOAEL: 450 mg/kg body weight
- Result: No adverse effects.
STOT-single exposure
Not classified based on available information.

STOT-repeated exposure
May cause damage to organs (Blood, Bone, Kidney) through prolonged or repeated exposure if swallowed.

Components:

Lamivudine:
Routes of exposure: Ingestion
Target Organs: Blood
Assessment: May cause damage to organs through prolonged or repeated exposure.

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

Repeated dose toxicity

Components:

Cellulose:
Species: Rat
NOAEL: >= 9,000 mg/kg
Application Route: Ingestion
Exposure time: 90 Days

Lamivudine:
Species: Rat
NOAEL: 425 mg/kg
Application Route: Oral
Exposure time: 6 Months
Target Organs: Blood
Symptoms: Gastrointestinal discomfort, Breathing difficulties, Fatality
Remarks: Significant toxicity observed in testing

Species: Dog
LOAEL: 90 mg/kg
Application Route: Oral
Exposure time: 12 Months
Target Organs: Blood, spleen, Liver
Symptoms: Salivation, Diarrhea, Changes in the blood count, Liver disorders, Gastrointestinal disturbance
## SAFETY DATA SHEET

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

<table>
<thead>
<tr>
<th>Version</th>
<th>Revision Date:</th>
<th>SDS Number:</th>
<th>Date of last issue:</th>
<th>Date of first issue:</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.1</td>
<td>09/13/2019</td>
<td>58636-00017</td>
<td>02/13/2019</td>
<td>02/16/2015</td>
</tr>
</tbody>
</table>

### Species: Mouse
- **NOAEL**: 500 mg/kg
- **Application Route**: Oral
- **Exposure time**: 1 Months
- **Target Organs**: Blood

### 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

### Species: Rat
- **NOAEL**: 450 mg/kg
- **Application Route**: Oral
- **Exposure time**: 6 Months
- **Remarks**: No significant adverse effects were reported

### Species: Mouse
- **NOAEL**: > 450 mg/kg
- **Application Route**: Oral
- **Exposure time**: 3 Months
- **Remarks**: No significant adverse effects were reported

### Species: Dog
- **NOAEL**: > 1,000 mg/kg
- **Application Route**: Oral
- **Exposure time**: 9 Months
- **Remarks**: No significant adverse effects were reported

### Aspiration toxicity
Not classified based on available information.
Experience with human exposure

Components:

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

Tenofovir:
Ingestion: Symptoms: Nausea, Diarrhea, Vomiting, flatulence, Headache, Rash

Doravirine:
Ingestion: Symptoms: confusion, Headache, Dizziness, Nausea, Rash, abnormal dreams, flushing, Neurological disorders, mental depression

SECTION 12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:

Cellulose:
Toxicity to fish: LC50 (Oryzias latipes (Japanese medaka)): > 100 mg/l
Exposure time: 48 h
Remarks: Based on data from similar materials

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: EC50 (Daphnia magna (Water flea)): > 98 mg/l
aquatic invertebrates

Toxicity to algae/aquatic plants

EC50 (Pseudokirchneriella subcapitata (green algae)): 47 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 202

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

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

- NOEC (Daphnia magna (Water flea)): 6.7 mg/l
- Exposure time: 21 d

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 211

Remarks: No toxicity at the limit of solubility.

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:
SAFETY DATA SHEET

Doravirine / Lamivudine / Tenofovir Disoproxil Fumarate Bilayer Formulation

Version 9.1 Revision Date: 09/13/2019 SDS Number: 58636-00017 Date of last issue: 02/13/2019 Date of first issue: 02/16/2015

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.

Domestic regulation

49 CFR
Not regulated as a dangerous good
SECTION 15. REGULATORY INFORMATION

EPCRA - Emergency Planning and Community Right-to-Know

CERCLA Reportable Quantity
This material does not contain any components with a CERCLA RQ.

SARA 304 Extremely Hazardous Substances Reportable Quantity
This material does not contain any components with a section 304 EHS RQ.

SARA 302 Extremely Hazardous Substances Threshold Planning Quantity
This material does not contain any components with a section 302 EHS TPQ.

SARA 311/312 Hazards
- Combustible dust
- Serious eye damage or eye irritation
- Reproductive toxicity
- Specific target organ toxicity (single or repeated exposure)

SARA 313
- This material does not contain any chemical components with known CAS numbers that exceed the threshold (De Minimis) reporting levels established by SARA Title III, Section 313.

US State Regulations

Pennsylvania Right To Know
- Cellulose, 2-hydroxypropyl methyl ether, acetate hydrogen butanedioate
- Cellulose
- Lamivudine
- Tenofovir
- Doravirine
- Croscarmellose sodium

California Permissible Exposure Limits for Chemical Contaminants
- Cellulose

The ingredients of this product are reported in the following inventories:

AICS : not determined
DSL : not determined
IECSC : not determined
SECTION 16. OTHER INFORMATION

Further information

NFPA 704:

<table>
<thead>
<tr>
<th>Flammability</th>
<th>Health</th>
<th>Reactivity</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>0</td>
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</table>

Special hazard

HMIS® IV:

<table>
<thead>
<tr>
<th>HEALTH</th>
<th>FLAMMABILITY</th>
<th>PHYSICAL HAZARD</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

HMIS® ratings are based on a 0-4 rating scale, with 0 representing minimal hazards or risks, and 4 representing significant hazards or risks. The "*" represents a chronic hazard, while the "/" represents the absence of a chronic hazard.

Full text of other abbreviations

ACGIH : USA. ACGIH Threshold Limit Values (TLV)
NIOSH REL : USA. NIOSH Recommended Exposure Limits
OSHA Z-1 : USA. Occupational Exposure Limits (OSHA) - Table Z-1 Limits for Air Contaminants
ACGIH / TWA : 8-hour, time-weighted average
NIOSH REL / TWA : Time-weighted average concentration for up to a 10-hour workday during a 40-hour workweek
OSHA Z-1 / TWA : 8-hour time weighted average

AICS - Australian Inventory of Chemical Substances; ASTM - American Society for the Testing of Materials; bw - Body weight; CERCLA - Comprehensive Environmental Response, Compensation, and Liability Act; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DOT - Department of Transportation; DSL - Domestic Substances List (Canada); ECX - Concentration associated with x% response; EHS - Extremely Hazardous Substance; 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; HMIS - Hazardous Materials Identification System; 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; MSHA - Mine Safety and Health Administration; n.o.s. - Not Otherwise Specified; NFPA - National Fire Protection Association; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NTP - National Toxicology Program; NZIoC - New Zealand Inventory of...
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Version 9.1
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SDS Number: 58636-00017
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Sources of key data used to compile the Material Safety Data Sheet:

Revision Date: 09/13/2019

The information provided in this Safety Data Sheet is correct to the best of our knowledge, information and belief at the date of its publication. The information is designed only as a guidance for safe handling, use, processing, storage, transportation, disposal and release and shall not be considered a warranty or quality specification of any type. The information provided relates only to the specific material identified at the top of this SDS and may not be valid when the SDS material is used in combination with any other materials or in any process, unless specified in the text. Material users should review the information and recommendations in the specific context of their intended manner of handling, use, processing and storage, including an assessment of the appropriateness of the SDS material in the user’s end product, if applicable.

US / Z8