Doravirine / Lamivudine / Tenofovir Disoproxil Fumarate Bilayer Formulation

SECTION 1: Identification of the substance/mixture and of the company/undertaking

1.1 Product identifier
   Trade name: Doravirine / Lamivudine / Tenofovir Disoproxil Fumarate Bilayer Formulation

1.2 Relevant identified uses of the substance or mixture and uses advised against
   Use of the Substance/Mixture: Pharmaceutical

1.3 Details of the supplier of the safety data sheet
   Company: MSD
   Shotton Lane
   NE23 3JU Cramlington NU - Great Britain
   Telephone: 44 1 670 59 30 00
   Telefax: 908-735-1496
   E-mail address of person responsible for the SDS: EHSDATASTEWARD@msd.com

1.4 Emergency telephone number
   1-908-423-6000

SECTION 2: Hazards identification

2.1 Classification of the substance or mixture
   Classification (REGULATION (EC) No 1272/2008)
   Eye irritation, Category 2: H319: Causes serious eye irritation.
   Reproductive toxicity, Category 2: H361d: Suspected of damaging the unborn child.
   Specific target organ toxicity - repeated exposure, Category 2: H373: May cause damage to organs through prolonged or repeated exposure.

2.2 Label elements
   Labelling (REGULATION (EC) No 1272/2008)
   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 through prolonged or repeated exposure.
Precautionary statements:

**Prevention:**
- P201 Obtain special instructions before use.
- P260 Do not breathe dust.
- P264 Wash skin thoroughly after handling.
- P280 Wear protective gloves/protective clothing/ eye protection/ face protection.

**Response:**
- P308 + P313 IF exposed or concerned: Get medical advice/attention.
- P337 + P313 IF eye irritation persists: Get medical advice/attention.

SECTION 3: Composition/information on ingredients

3.2 Mixtures

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Classification</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chemical name</strong></td>
<td><strong>EC-No.</strong></td>
<td><strong>Index-No.</strong></td>
<td><strong>Registration number</strong></td>
</tr>
<tr>
<td>Lamivudine</td>
<td>134678-17-4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tenofovir</td>
<td>202138-50-9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doravirine</td>
<td>1338225-97-0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

For explanation of abbreviations see section 16.
and use the recommended personal protective equipment when the potential for exposure exists (see section 8).

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.

4.2 Most important symptoms and effects, both acute and delayed

Risks
- Causes serious eye irritation.
- Suspected of damaging the unborn child.
- May cause damage to organs through prolonged or repeated exposure.

4.3 Indication of any immediate medical attention and special treatment needed

Treatment
- Treat symptomatically and supportively.

SECTION 5: Firefighting measures

5.1 Extinguishing media

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

Unsuitable extinguishing media
- None known.

5.2 Special hazards arising from the substance or mixture

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)
5.3 Advice for firefighters

Special protective equipment for firefighters

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

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.

SECTION 6: Accidental release measures

6.1 Personal precautions, protective equipment and emergency procedures

Personal precautions

- Use personal protective equipment.
- Follow safe handling advice and personal protective equipment recommendations.

6.2 Environmental precautions

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.

6.3 Methods and material for containment and cleaning up

Methods for 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.

6.4 Reference to other sections

See sections: 7, 8, 11, 12 and 13.

SECTION 7: Handling and storage

7.1 Precautions for safe handling
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.

7.2 Conditions for safe storage, including any incompatibilities

Requirements for storage areas and containers:
- Keep in properly labelled containers. Store locked up. Store in accordance with the particular national regulations.

Advice on common storage:
- Do not store with the following product types:
  - Strong oxidizing agents

7.3 Specific end use(s)

Specific use(s):
- No data available

SECTION 8: Exposure controls/personal protection

8.1 Control parameters

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>TWA (inhalable dust)</td>
<td>10 mg/m3</td>
<td>GB EH40</td>
</tr>
</tbody>
</table>

Further information: For the purposes of these limits, respirable dust and inhalable dust are those fractions of airborne dust which will be collected when sampling is undertaken in accordance with the methods described in
MDHS14/4 General methods for sampling and gravimetric analysis or respirable, thoracic and inhalable aerosols. The COSHH definition of a substance hazardous to health includes dust of any kind when present at a concentration in air equal to or greater than 10 mg.m\(^{-3}\) 8-hour TWA of inhalable dust or 4 mg.m\(^{-3}\) 8-hour TWA of respirable dust. This means that any dust will be subject to COSHH if people are exposed to dust above these levels. Some dusts have been assigned specific WELs and exposure to these must comply with the appropriate limits. Most industrial dusts contain particles of a wide range of sizes. The behaviour, deposition and fate of any particular particle after entry into the human respiratory system, and the body response that it elicits, depend on the nature and size of the particle. HSE distinguishes two size fractions for limit-setting purposes termed ‘inhalable’ and ‘respirable’. Inhalable dust approximates to the fraction of airborne material that enters the nose and mouth during breathing and is therefore available for deposition in the respiratory tract. Respirable dust approximates to the fraction that penetrates to the gas exchange region of the lung. Fuller definitions and explanatory material are given in MDHS14/4. Where dusts contain components that have their own assigned WEL, all the relevant limits should be complied with.

<table>
<thead>
<tr>
<th></th>
<th>TWA (Respirable dust)</th>
<th>STEL (inhalable dust)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamivudine</td>
<td>150 µg/m³ (OEB 2)</td>
<td>Internal</td>
</tr>
<tr>
<td>Tenofovir</td>
<td>150 µg/m³ (OEB 2)</td>
<td>Internal</td>
</tr>
<tr>
<td>Doravirine</td>
<td>500 µg/m³ (OEB2)</td>
<td>Internal</td>
</tr>
</tbody>
</table>

8.2 Exposure controls

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

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.

Hand protection

Material: Chemical-resistant gloves

Skin and body protection

Work uniform or laboratory coat.

Respiratory protection

If adequate local exhaust ventilation is not available or exposure assessment demonstrates exposures outside the recommended guidelines, use respiratory protection.

Equipment should conform to BS EN 143

Filter type

Particulates type (P)
## SECTION 9: Physical and chemical properties

### 9.1 Information on basic physical and chemical properties

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>powder</td>
</tr>
<tr>
<td>Colour</td>
<td>No data available</td>
</tr>
<tr>
<td>Odour</td>
<td>No data available</td>
</tr>
<tr>
<td>Odour 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>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>Vapour pressure</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Relative vapour density</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Relative density</td>
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</tr>
<tr>
<td>Density</td>
<td>No data available</td>
</tr>
<tr>
<td>Solubility(ies)</td>
<td></td>
</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>Auto-ignition temperature</td>
<td>No data available</td>
</tr>
<tr>
<td>Decomposition temperature</td>
<td>No data available</td>
</tr>
<tr>
<td>Viscosity</td>
<td></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>
</tbody>
</table>

### 9.2 Other information
SECTION 10: Stability and reactivity

10.1 Reactivity
Not classified as a reactivity hazard.

10.2 Chemical stability
Stable under normal conditions.

10.3 Possibility of hazardous reactions
Hazardous reactions: May form explosive dust-air mixture during processing, handling or other means. Can react with strong oxidizing agents.

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

10.5 Incompatible materials
Materials to avoid: Oxidizing agents

10.6 Hazardous decomposition products
No hazardous decomposition products are known.

SECTION 11: Toxicological information

11.1 Information on toxicological effects
Information on likely routes of exposure: Inhalation, Skin contact, Ingestion, Eye contact

Acute toxicity
Not classified based on available information.

Product:
Acute oral toxicity: Acute toxicity estimate: > 2,000 mg/kg Method: Calculation method

Components:
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
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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:

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:**

**Lamivudine:**

Species
: Rat
Exposure time
: 2 Years
Result
: negative

Species
: Mouse
Exposure time
: 2 Years
Result
: negative

**Tenofovir:**

Species
: Mouse
Doravirine / Lamivudine / Tenofovir Disoproxil Fumarate Bilayer Formulation

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

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

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

Reproductive toxicity
Suspected of damaging the unborn child.

Components:

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

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

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

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

Doravirine:

- 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.
Repeated dose toxicity

**Components:**

**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: >= 10 mg/kg  
Application Route: Oral  
Exposure time: 42 Weeks  
Target Organs: Kidney

Species: Monkey  
LOAEL: 10 mg/kg  
Application Route: Subcutaneous  
Exposure time: 10 Months  
Target Organs: Bone

**Doravirine:**
Species: Rat  
NOAEL: 450 mg/kg
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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

12.1 Toxicity

Components:

Lamivudine:
Toxicity to fish: LC50 (Pimephales promelas (fathead minnow)): > 97.7 mg/l
Exposure time: 96 h
Method: OECD Test Guideline 203

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

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

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

**Tenofovir:**

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

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

Toxicity to 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

Toxicity to fish (Chronic toxicity) : NOEC: 9 mg/l
Exposure time: 32 d
Species: Pimephales promelas (fathead minnow)
Method: OECD Test Guideline 210

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

**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 201  
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 201  
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

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

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity): NOEC: 6.7 mg/l  
Exposure time: 21 d  
Species: Daphnia magna (Water flea)  
Method: OECD Test Guideline 211  
Remarks: No toxicity at the limit of solubility

12.2 Persistence and degradability

**Components:**

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

**Tenofovir:**  
Biodegradability: Result: Not readily biodegradable.  
Biodegradation: 3.66 %  
Exposure time: 28 d  
Method: OECD Test Guideline 314

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

**Components:**

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

**Tenofovir:**
Partition coefficient: n-octanol/water : log Pow: 1.06
pH: 7

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

12.4 Mobility in soil

**Components:**

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

**Tenofovir:**
Distribution among environmental compartments : log Koc: 3.33
Method: OECD Test Guideline 106

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

12.5 Results of PBT and vPvB assessment

Not relevant

12.6 Other adverse effects

No data available

SECTION 13: Disposal considerations

13.1 Waste treatment methods

**Product** : Dispose of in accordance with local regulations. According to the European Waste Catalogue, Waste Codes are not product specific, but application specific. Waste codes should be assigned by the user, preferably in discussion with the waste disposal authorities.

**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

14.1 UN number
Not regulated as a dangerous good

14.2 UN proper shipping name
Not regulated as a dangerous good

14.3 Transport hazard class(es)
Not regulated as a dangerous good

14.4 Packing group
Not regulated as a dangerous good

14.5 Environmental hazards
Not regulated as a dangerous good

14.6 Special precautions for user
Not applicable

14.7 Transport in bulk according to Annex II of Marpol and the IBC Code
Remarks: Not applicable for product as supplied.

SECTION 15: Regulatory information

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

REACH - Restrictions on the manufacture, placing on the market and use of certain dangerous substances, preparations and articles (Annex XVII) : Not applicable
REACH - Candidate List of Substances of Very High Concern for Authorisation (Article 59). : Not applicable
REACH - List of substances subject to authorisation (Annex XIV) : Not applicable
Regulation (EC) No 1005/2009 on substances that deplete the ozone layer : Not applicable
Regulation (EU) 2019/1021 on persistent organic pollutants (recast) : Not applicable
Regulation (EC) No 649/2012 of the European Parliament and the Council concerning the export and import of dangerous chemicals : Not applicable

Other regulations:
Take note of Directive 92/85/EEC regarding maternity protection or stricter national regulations, where applicable.
Take note of Directive 94/33/EC on the protection of young people at work or stricter national regulations, where applicable.

The components of this product are reported in the following inventories:
AICS : not determined
SAFETY DATA SHEET
according to Regulation (EC) No. 1907/2006

Doravirine / Lamivudine / Tenofovir Disoproxil Fumarate Bilayer Formulation

Version 4.9 Revision Date: 11.05.2020 SDS Number: 59640-00021 Date of last issue: 14.04.2020
Date of first issue: 16.02.2015

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15.2 Chemical safety assessment
A Chemical Safety Assessment has not been carried out.

SECTION 16: Other information

Other information: Items where changes have been made to the previous version are highlighted in the body of this document by two vertical lines.

Full text of H-Statements
H302: Harmful if swallowed.
H319: Causes serious eye irritation.
H361d: Suspected of damaging the unborn child.
H373: May cause damage to organs through prolonged or repeated exposure if swallowed.

Full text of other abbreviations
Acute Tox.: Acute toxicity
Eye Irrit.: Eye irritation
Repr.: Reproductive toxicity
STOT RE: Specific target organ toxicity - repeated exposure
GB EH40: UK. EH40 WEL - Workplace Exposure Limits
GB EH40 / TWA: Long-term exposure limit (8-hour TWA reference period)
GB EH40 / STEL: Short-term exposure limit (15-minute reference period)

ADN - European Agreement concerning the International Carriage of Dangerous Goods by Inland Waterways; ADR - European Agreement concerning the International Carriage of Dangerous Goods by Road; AICS - Australian Inventory of Chemical Substances; ASTM - American Society for the Testing of Materials; bw - Body weight; CLP - Classification Labelling Packaging Regulation; Regulation (EC) No 1272/2008; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECHA - European Chemicals Agency; EC-Number - European Community number; 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; 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; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NZIoC - New Zealand Inventory of Chemicals.
Further information

Sources of key data used to compile the Safety Data Sheet:

Classification of the mixture:

<table>
<thead>
<tr>
<th>Substance</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye Irrit. 2</td>
<td>H319 Calculation method</td>
</tr>
<tr>
<td>Repr. 2</td>
<td>H361d Calculation method</td>
</tr>
<tr>
<td>STOT RE 2</td>
<td>H373 Calculation method</td>
</tr>
</tbody>
</table>

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.