1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Grazoprevir / Elbasvir Formulation

Manufacturer or supplier’s details
Company : MSD
Address : Briahnager - Off Pune Nagar Road
           Wagholi - Pune - India 412 207
Telephone : 908-740-4000
Emergency telephone number : 1-908-423-6000
E-mail address : EHSDATASTEWARD@msd.com
Telefax : 908-735-1496

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

2. HAZARDS IDENTIFICATION

Manufacture, Storage and Import of Hazardous Chemicals Rules 1989
Classification
Not classified as hazardous according to criteria laid down in Part I of Schedule-1.

GHS Classification
Short-term (acute) aquatic hazard : Category 3
Long-term (chronic) aquatic hazard : Category 1

GHS label elements
Hazard pictograms : 
Signal word : Warning
Hazard statements : H402 Harmful to aquatic life.
                  H410 Very toxic to aquatic life with long lasting effects.
Precautionary statements : Prevention:
                           P273 Avoid release to the environment.
                           Response:
P391 Collect spillage.

**Disposal:**
P501 Dispose of contents/ container to an approved waste disposal plant.

**Other hazards which do not result in classification**
Dust contact with the eyes can lead to mechanical irritation.
Contact with dust can cause mechanical irritation or drying of the skin.
May form explosive dust-air mixture during processing, handling or other means.

### 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>Sodium chloride</td>
<td>7647-14-5</td>
<td>&gt;= 5 - &lt; 10</td>
</tr>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>&gt;= 5 - &lt; 10</td>
</tr>
<tr>
<td>Grazoprevir</td>
<td>1350462-55-3</td>
<td>&gt;= 5 - &lt; 10</td>
</tr>
<tr>
<td>Elbasvir</td>
<td>1370468-36-2</td>
<td>&gt;= 2.5 - &lt; 5</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>557-04-0</td>
<td>&gt;= 1 - &lt; 5</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</td>
<td>&gt;= 0.1 - &lt; 1</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:** Wash with water and soap. Get medical attention if symptoms occur.

**In case of eye contact:** If in eyes, rinse well with water. Get medical attention if irritation develops and persists.

**If swallowed:** If swallowed, DO NOT induce vomiting. Get medical attention if symptoms occur. Rinse mouth thoroughly with water.

**Most important symptoms and effects, both acute and delayed:** Contact with dust can cause mechanical irritation or drying of the skin. Dust contact with the eyes can lead to mechanical irritation.

**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.

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

### 5. FIREFIGHTING MEASURES

**Suitable extinguishing media:** Water spray
Alcohol-resistant foam
Carbon dioxide (CO2)
Dry chemical
3. UNSUITABLE EXTINGUISHING MEDIA:

None known.

4. 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.

5. HAZARDOUS COMBUSTION PRODUCTS:

Carbon oxides
Metal oxides
Chlorine compounds
Nitrogen oxides (NOx)

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:

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.
SAFETY DATA SHEET

Grazoprevir / Elbasvir Formulation

Version 4.9  Revision Date: 04/24/2019
SDS Number: 76520-00015  Date of last issue: 16.10.2018
Date of first issue: 17.03.2015

Advice on safe handling:
- Do not breathe dust.
- Do not swallow.
- Avoid contact with eyes.
- Avoid prolonged or repeated contact with skin.
- 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 labelled containers.
- Store in accordance with the particular national regulations.

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

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>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Grazoprevir</td>
<td>1350462-55-3</td>
<td>TWA</td>
<td>25 µg/m³ (OEB 3)</td>
<td>Internal</td>
</tr>
<tr>
<td>Elbasvir</td>
<td>1370468-36-2</td>
<td>TWA</td>
<td>Wipe limit 250 µg/100 cm²</td>
<td>Internal</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>557-04-0</td>
<td>TWA (Inhalable fraction)</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Respirable fraction)</td>
<td>3 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</td>
<td>TWA</td>
<td>10 mg/m³ (Titanium dioxide)</td>
<td>ACGIH</td>
</tr>
</tbody>
</table>

Engineering measures:
- All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment.
- Containment technologies suitable for controlling compounds are required to control at source and to prevent migration of the compound to uncontrolled areas (e.g., open-face containment devices).
- Minimize open handling.

Personal protective equipment

Respiratory protection:
- Use respiratory protection unless adequate local exhaust ventilation is provided or exposure assessment demonstrates that exposures are within recommended exposure guidelines.

Filter type: Particulates type

Hand protection: Particulates type
Material: Chemical-resistant gloves

Remarks: Consider double gloving.

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. Additional body garments should be used based upon the task being performed (e.g., sleevelets, apron, gauntlets, disposable suits) to avoid exposed skin surfaces. Use appropriate degowning techniques to remove potentially contaminated clothing.

Hygiene measures: Ensure that eye flushing systems and safety showers are located 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: white
Odour: No data available
Odour Threshold: No data available
pH: No data available
Melting point/freezing point: No data available
Initial boiling point and boiling range: No data available
Flash point: Not applicable
Evaporation rate: Not applicable
Flammability (solid, gas): May form explosive dust-air mixture during processing, handling or other means.
Flammability (liquids): No data available
Upper explosion limit / Upper flammability limit: No data available
Lower explosion limit / Lower flammability limit: No data available
Vapour pressure: Not applicable
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

- **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: > 5,000 mg/kg
  Method: Calculation method
## Components:

### Sodium chloride:
- **Acute oral toxicity**: LD50 (Rat): 3,550 mg/kg
- **Acute inhalation toxicity**: LC50 (Rat): > 42 mg/l
  - Exposure time: 1 h
  - Test atmosphere: dust/mist
- **Acute dermal toxicity**: LD50 (Rabbit): > 5,000 mg/kg

### 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

### Grazoprevir:
- **Acute oral toxicity**: LD50 (Rat): > 2,000 mg/kg
- **LD50 (Mouse)**: > 1,000 mg/kg

### Elbasvir:
- **Acute oral toxicity**: LD50 (Rat): > 2,000 mg/kg

### Magnesium stearate:
- **Acute oral toxicity**: LD50 (Rat): > 2,000 mg/kg
  - Method: OECD Test Guideline 423
  - Assessment: The substance or mixture has no acute oral toxicity
  - Remarks: Based on data from similar materials
- **Acute dermal toxicity**: LD50 (Rabbit): > 2,000 mg/kg
  - Remarks: Based on data from similar materials

### Titanium dioxide:
- **Acute oral toxicity**: LD50 (Rat): > 5,000 mg/kg
- **Acute inhalation toxicity**: LC50 (Rat): > 6.82 mg/l
  - Exposure time: 4 h
  - Test atmosphere: dust/mist
  - Assessment: The substance or mixture has no acute inhalation toxicity

### Skin corrosion/irritation
Not classified based on available information.
Components:

Sodium chloride:
Species: Rabbit
Result: No skin irritation

Grazoprevir:
Result: No skin irritation

Elbasvir:
Species: reconstructed human epidermis (RhE)
Result: No skin irritation

Magnesium stearate:
Species: Rabbit
Result: No skin irritation
Remarks: Based on data from similar materials

Titanium dioxide:
Species: Rabbit
Result: No skin irritation

Serious eye damage/eye irritation
Not classified based on available information.

Components:

Sodium chloride:
Species: Rabbit
Result: No eye irritation

Grazoprevir:
Species: Bovine cornea
Result: No eye irritation

Elbasvir:
Species: Bovine cornea
Result: No eye irritation

Magnesium stearate:
Species: Rabbit
Result: No eye irritation
Remarks: Based on data from similar materials

Titanium dioxide:
Species: Rabbit
Result: No eye irritation
Respiratory or skin sensitisation

Skin sensitisation
Not classified based on available information.

Respiratory sensitisation
Not classified based on available information.

Components:

Sodium chloride:
Test Type : Local lymph node assay (LLNA)
Exposure routes : Skin contact
Species : Mouse
Result : negative

Grazoprevir:
Test Type : Local lymph node assay (LLNA)
Exposure routes : Dermal
Result : Not a skin sensitizer.

Elbasvir:
Test Type : Local lymph node assay (LLNA)
Exposure routes : Dermal
Species : Mouse
Result : negative

Magnesium stearate:
Test Type : Maximisation Test
Exposure routes : Skin contact
Species : Guinea pig
Method : OECD Test Guideline 406
Result : negative
Remarks : Based on data from similar materials

Titanium dioxide:
Test Type : Local lymph node assay (LLNA)
Exposure routes : Skin contact
Species : Mouse
Result : negative

Germ cell mutagenicity
Not classified based on available information.

Components:

Sodium chloride:
Genotoxicity in vitro : Test Type: In vitro mammalian cell gene mutation test
Result: positive

Test Type: Bacterial reverse mutation assay (AMES)
Result: negative
Test Type: Saccharomyces cerevisiae, gene mutation assay (in vitro)
Result: positive

Test Type: DNA damage and repair, unscheduled DNA synthesis in mammalian cells (in vitro)
Result: positive

Test Type: Chromosome aberration test in vitro
Result: positive

Test Type: Chromosome aberration test in vitro
Result: negative

Genotoxicity in vivo:
: Test Type: In vivo micronucleus test
  Species: Mouse
  Application Route: Intraperitoneal injection
  Result: negative

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

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

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

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

  Test Type: Chromosome aberration test in vitro
  Result: negative

Genotoxicity in vivo:
: Test Type: In vivo micronucleus test
  Application Route: Oral
  Result: negative

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

**Genotoxicity in vitro**
- Test Type: Bacterial reverse mutation assay (AMES)
  - Result: negative
- Test Type: Chromosome aberration test in vitro
  - Result: negative

**Genotoxicity in vivo**
- Test Type: In vivo micronucleus test
  - Species: Rat
  - Application Route: Oral
  - Result: negative

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

### Magnesium stearate:

**Genotoxicity in vitro**
- Test Type: In vitro mammalian cell gene mutation test
  - Result: negative
- Remarks: Based on data from similar materials
- Test Type: Chromosome aberration test in vitro
  - Method: OECD Test Guideline 473
  - Result: negative
- Remarks: Based on data from similar materials
- Test Type: Bacterial reverse mutation assay (AMES)
  - Result: negative
- Remarks: Based on data from similar materials

### Titanium dioxide:

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

**Genotoxicity in vivo**
- Test Type: In vivo micronucleus test
  - Species: Mouse
  - Result: negative

### Carcinogenicity
Not classified based on available information.

### Components:

#### Sodium chloride:
- **Species**: Rat
- **Application Route**: Ingestion
- **Exposure time**: 2 Years
- **Result**: negative

#### Cellulose:
- **Species**: Rat
### Grazoprevir / Elbasvir Formulation

<table>
<thead>
<tr>
<th>Application Route</th>
<th>Ingestion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure time</td>
<td>72 weeks</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
</tbody>
</table>

#### Titanium dioxide:

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>inhalation (dust/mist/fume)</td>
</tr>
<tr>
<td>Exposure time</td>
<td>2 Years</td>
</tr>
<tr>
<td>Method</td>
<td>OECD Test Guideline 453</td>
</tr>
<tr>
<td>Result</td>
<td>positive</td>
</tr>
<tr>
<td>Remarks</td>
<td>The mechanism or mode of action may not be relevant in humans.</td>
</tr>
</tbody>
</table>

#### Carcinogenicity - Assessment

- Limited evidence of carcinogenicity in inhalation studies with animals.

#### Reproductive toxicity

Not classified based on available information.

### Components:

#### Cellulose:

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

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

#### Grazoprevir:

- Effects on fertility: Test Type: Fertility  
  - Species: Rat  
  - Application Route: Oral  
  - Fertility: NOAEL: 400 mg/kg body weight  
  - Result: negative  
  - Test Type: Multi-generation study  
  - Species: Rat  
  - Application Route: Oral  
  - Fertility: NOAEL: 400 mg/kg body weight  
  - Result: No effects on fertility, No effects on foetal development

- Effects on foetal development: Test Type: Embryo-foetal development  
  - Species: Rat  
  - Application Route: Oral  
  - Embryo-foetal toxicity: NOAEL: 200 mg/kg body weight  
  - Result: No effects on foetal development  
  - Test Type: Embryo-foetal development
Species: Rabbit  
Application Route: Oral  
Embryo-foetal toxicity: NOAEL: 200 mg/kg body weight  
Result: No effects on foetal development

Test Type: Embryo-foetal development  
Species: Rabbit  
Application Route: Intravenous  
Embryo-foetal toxicity: NOAEL: 100 mg/kg body weight  
Result: No effects on foetal development

Elbasvir:
Effects on fertility:  
Test Type: Fertility/early embryonic development  
Species: Rat, male and female  
Application Route: Oral  
Fertility: NOAEL: 1,000 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: 1,000 mg/kg body weight  
Result: No effects on early embryonic development

Test Type: Embryo-foetal development  
Species: Rabbit  
Application Route: Oral  
Developmental Toxicity: NOAEL: 1,000 mg/kg body weight  
Result: No effects on early embryonic development

Magnesium stearate:
Effects on fertility:  
Test Type: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test  
Species: Rat  
Application Route: Ingestion  
Method: OECD Test Guideline 422  
Result: negative  
Remarks: Based on data from similar materials

Effects on foetal development:  
Test Type: Embryo-foetal development  
Species: Rat  
Application Route: Ingestion  
Result: negative  
Remarks: Based on data from similar materials

**STOT - single exposure**
Not classified based on available information.

**STOT - repeated exposure**
Not classified based on available information.
Components:

Grazoprevir:
- Target Organs: Liver, Testis
- Assessment: May cause damage to organs through prolonged or repeated exposure.

Repeated dose toxicity

Components:

Sodium chloride:
- Species: Rat
- LOAEL: 2,533 mg/kg
- Application Route: Ingestion
- Exposure time: 2 yr

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

Grazoprevir:
- Species: Rat
- NOAEL: 400 mg/kg
- Application Route: Oral
- Exposure time: 30 Days
- Remarks: No significant adverse effects were reported

Species: Rat
- NOAEL: 400 mg/kg
- Application Route: Oral
- Exposure time: 180 Days
- Remarks: No significant adverse effects were reported

Species: Dog
- NOAEL: 15 mg/kg
- LOAEL: 100 mg/kg
- Application Route: Oral
- Exposure time: 270 Days
- Target Organs: Liver, Testis, Blood, Bone marrow, gallbladder, spleen

Species: Mouse
- NOAEL: 200 mg/kg
- LOAEL: 500 mg/kg
- Application Route: Oral
- Exposure time: 90 Days
- Target Organs: Liver, Kidney, Blood

Species: Dog
- NOAEL: 20 mg/kg
- LOAEL: 600 mg/kg
Application Route: Oral
Exposure time: 30 Days
Target Organs: Testis, Blood

Species: Monkey
NOAEL: 10 mg/kg
Exposure time: 8 Days
Remarks: No significant adverse effects were reported

Elbasvir:
Species: Rat
NOAEL: 1,000 mg/kg
Application Route: Oral
Exposure time: 180 d
Remarks: No significant adverse effects were reported

Species: Dog
NOAEL: 1,000 mg/kg
Application Route: Oral
Exposure time: 270 d
Remarks: No significant adverse effects were reported

Magnesium stearate:
Species: Rat
NOAEL: > 100 mg/kg
Application Route: Ingestion
Exposure time: 90 Days
Remarks: Based on data from similar materials

Titanium dioxide:
Species: Rat
NOAEL: 24,000 mg/kg
Application Route: Ingestion
Exposure time: 28 Days

Species: Rat
NOAEL: 10 mg/m3
Application Route: Inhalation (dust/mist/fume)
Exposure time: 2 yr

Aspiration toxicity
Not classified based on available information.

Experience with human exposure

Components:

Grazoprevir:
Ingestion: Symptoms: Headache, Gastrointestinal disturbance

Elbasvir:
Ingestion: Symptoms: Headache, Abdominal pain, constipation, Nausea, Fatigue, muscle pain, joint pain, Dizziness, Cough, Skin irrita-
12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:

Sodium chloride:
- Toxicity to fish: LC50 (Lepomis macrochirus (Bluegill sunfish)): 5,840 mg/l Exposure time: 96 h
- Toxicity to daphnia and other aquatic invertebrates: EC50 (Daphnia magna (Water flea)): 4,136 mg/l Exposure time: 48 h
- Toxicity to algae/aquatic plants: EC50: > 2,000 mg/l Exposure time: 96 h
- Toxicity to microorganisms: EC10: > 1,000 mg/l
- Toxicity to fish (Chronic toxicity): NOEC: 252 mg/l Exposure time: 33 d Species: Pimephales promelas (fathead minnow)
- Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity): NOEC: 314 mg/l Exposure time: 21 d Species: Daphnia pulex (Water flea)

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

Grazoprevir:
- Toxicity to fish: LC50 (Cyprinodon variegatus (sheepshead minnow)): > 10 mg/l Exposure time: 96 h Remarks: No toxicity at the limit of solubility
- Toxicity to daphnia and other aquatic invertebrates: EC50 (Daphnia magna (Water flea)): > 10 mg/l Exposure time: 48 h Method: OECD Test Guideline 202 Remarks: No toxicity at the limit of solubility.
- LC50 (Americamysis): 8.9 mg/l Exposure time: 96 h
- Toxicity to algae/aquatic plants: EC50 (Pseudokirchneriella subcapitata (green algae)): > 10 mg/l Exposure time: 72 hrs Method: OECD Test Guideline 201 Remarks: No toxicity at the limit of solubility.
### NOEC

**Pseudokirchneriella subcapitata (green algae):** 10 mg/l  
*Exposure time: 72 hrs*  
*Method: OECD Test Guideline 201*  
*Remarks: No toxicity at the limit of solubility*

### Toxicity to microorganisms

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Concentration</th>
<th>Exposure Time</th>
<th>Method</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOEC</td>
<td>1.3 mg/l</td>
<td>3 h</td>
<td>OECD Test Guideline 209</td>
<td>No toxicity at the limit of solubility</td>
</tr>
</tbody>
</table>

### Toxicity to microorganisms

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Concentration</th>
<th>Exposure Time</th>
<th>Method</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOEC</td>
<td>&gt; 1,000 mg/l</td>
<td>3 h</td>
<td>OECD Test Guideline 209</td>
<td></td>
</tr>
</tbody>
</table>

### Toxicity to fish (Chronic toxicity)

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Concentration</th>
<th>Exposure Time</th>
<th>Species</th>
<th>Method</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOEC</td>
<td>0.98 mg/l</td>
<td>32 d</td>
<td>Pimephales promelas (fathead minnow)</td>
<td>OECD Test Guideline 210</td>
<td>No toxicity at the limit of solubility</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Concentration</th>
<th>Exposure Time</th>
<th>Species</th>
<th>Method</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOEC</td>
<td>5 mg/l</td>
<td>21 d</td>
<td>Daphnia magna (Water flea)</td>
<td>OECD Test Guideline 211</td>
<td></td>
</tr>
</tbody>
</table>

### Elbasvir:

#### Toxicity to fish

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Concentration</th>
<th>Exposure Time</th>
<th>Species</th>
<th>Method</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>LC50</td>
<td>&gt; 10 mg/l</td>
<td>96 h</td>
<td>Lepomis macrochirus (Bluegill sunfish)</td>
<td>OECD Test Guideline 203</td>
<td>No toxicity at the limit of solubility</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Concentration</th>
<th>Exposure Time</th>
<th>Species</th>
<th>Method</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>LC50</td>
<td>&gt; 10 mg/l</td>
<td>96 h</td>
<td>Menidia beryllina (Silverside)</td>
<td>OECD Test Guideline 203</td>
<td>No toxicity at the limit of solubility</td>
</tr>
</tbody>
</table>

### Toxicity to daphnia and other aquatic invertebrates

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Concentration</th>
<th>Exposure Time</th>
<th>Species</th>
<th>Method</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>EC50</td>
<td>&gt; 10 mg/l</td>
<td>48 h</td>
<td>Daphnia magna (Water flea)</td>
<td>OECD Test Guideline 202</td>
<td>No toxicity at the limit of solubility</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Concentration</th>
<th>Exposure Time</th>
<th>Species</th>
<th>Method</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>LC50</td>
<td>7.7 mg/l</td>
<td>96 h</td>
<td>Americamysis</td>
<td>US-EPA OPPTS 850.1035</td>
<td>No toxicity at the limit of solubility</td>
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</table>

### Toxicity to algae/aquatic plants

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Concentration</th>
<th>Exposure Time</th>
<th>Species</th>
<th>Method</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>EC50</td>
<td>&gt; 0.081 mg/l</td>
<td>72 h</td>
<td>Pseudokirchneriella subcapitata (algae)</td>
<td>OECD Test Guideline 201</td>
<td>No toxicity at the limit of solubility</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Concentration</th>
<th>Exposure Time</th>
<th>Species</th>
<th>Method</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOEC</td>
<td>0.081 mg/l</td>
<td></td>
<td>Pseudokirchneriella subcapitata (green algae)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**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: 271.9 mg/l  
**Exposure time:** 3 h  
**Test Type:** Respiration inhibition  
**Method:** OECD Test Guideline 209

**Toxicity to fish (Chronic toxicity)**  
NOEC: 0.0023 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: 0.84 mg/l  
**Exposure time:** 21 d  
**Species:** Daphnia magna (Water flea)  
**Method:** OECD Test Guideline 211  
**Remarks:** No toxicity at the limit of solubility

**M-Factor (Chronic aquatic toxicity):**  
10

**Magnesium stearate:**

**Toxicity to fish**  
LC50 (Leuciscus idus (Golden orfe)): > 100 mg/l  
**Exposure time:** 48 h  
**Method:** DIN 38412  
**Remarks:** Based on data from similar materials

**Toxicity to daphnia and other aquatic invertebrates**  
EL50 (Daphnia magna (Water flea)): > 1 mg/l  
**Exposure time:** 47 h  
**Test substance:** Water Accommodated Fraction  
**Remarks:** Based on data from similar materials  
No toxicity at the limit of solubility

**Toxicity to algae/aquatic plants**  
EL50 (Pseudokirchneriella subcapitata (green algae)): > 1 mg/l  
**Exposure time:** 72 h  
**Test substance:** Water Accommodated Fraction  
**Method:** OECD Test Guideline 201  
**Remarks:** Based on data from similar materials  
No toxicity at the limit of solubility  
NOELR (Pseudokirchneriella subcapitata (green algae)): > 1 mg/l  
**Exposure time:** 72 h  
**Test substance:** Water Accommodated Fraction  
**Method:** OECD Test Guideline 201
Remarks: Based on data from similar materials

Toxicity to microorganisms: EC10 (Pseudomonas putida): > 100 mg/l
Exposure time: 16 h
Test substance: Water Accommodated Fraction
Remarks: Based on data from similar materials

Titanium dioxide:
Toxicity to fish: LC50 (Oncorhynchus mykiss (rainbow trout)): > 100 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

Toxicity to algae/aquatic plants: EC50 (Skeletonema costatum (marine diatom)): > 10,000 mg/l
Exposure time: 72 h

Toxicity to microorganisms: EC50: > 1,000 mg/l
Exposure time: 3 h
Method: OECD Test Guideline 209

Persistence and degradability

Components:

Cellulose:
Biodegradability: Result: Readily biodegradable.

Grazoprevir:
Biodegradability: Result: Not readily biodegradable.
Biodegradation: 66 %
Exposure time: 28 d

Elbasvir:
Biodegradability: Result: Not readily biodegradable.
Biodegradation: 37 %
Exposure time: 28 d

Magnesium stearate:
Biodegradability: Result: Not biodegradable
Remarks: Based on data from similar materials

Bioaccumulative potential

Components:

Grazoprevir:
Bioaccumulation: Species: Lepomis macrochirus (Bluegill sunfish)
Bioconcentration factor (BCF): 7.62
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Grazoprevir / Elbasvir Formulation

Partition coefficient: n-octanol/water : log Pow: 3.72

**Elbasvir:**
Bioaccumulation : Species: Lepomis macrochirus (Bluegill sunfish)
Bioconcentration factor (BCF): 82
Method: OECD Test Guideline 305

Partition coefficient: n-octanol/water : log Pow: 6.54

**Magnesium stearate:**
Partition coefficient: n-octanol/water : log Pow: > 4

**Mobility in soil**

**Components:**

**Grazoprevir:**
Distribution among environmental compartments : log Koc: 4.01

**Elbasvir:**
Distribution among environmental compartments : log Koc: 5.24

**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**
UN number : UN 3077
Proper shipping name : ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Elbasvir)

Class : 9
Packing group : III
Labels : 9
SAFETY DATA SHEET

Grazoprevir / Elbasvir Formulation

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<td>Revision Date:</td>
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<tr>
<td>4.9</td>
<td>04/24/2019</td>
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IATA-DGR

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<td>UN 3077</td>
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<tr>
<td>Proper shipping name</td>
<td>Environmentally hazardous substance, solid, n.o.s. (Elbasvir)</td>
</tr>
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<tr>
<td>Packing group</td>
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<td>Labels</td>
<td>Miscellaneous</td>
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IMDG-Code

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<td>UN 3077</td>
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<tr>
<td>Proper shipping name</td>
<td>ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Elbasvir)</td>
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<td>EmS Code</td>
<td>F-A, S-F</td>
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<tr>
<td>Marine pollutant</td>
<td>yes</td>
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Transport in bulk according to IMO instruments

Not applicable for product as supplied.

Special precautions for user

The transport classification(s) provided herein are for informational purposes only, and solely based upon the properties of the unpackaged material as it is described within this Safety Data Sheet. Transportation classifications may vary by mode of transportation, package sizes, and variations in regional or country regulations.

15. REGULATORY INFORMATION

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

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

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<thead>
<tr>
<th>Inventory</th>
<th>Value</th>
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<tbody>
<tr>
<td>AICS</td>
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</tr>
<tr>
<td>DSL</td>
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</tr>
<tr>
<td>IECSC</td>
<td>not determined</td>
</tr>
</tbody>
</table>

16. OTHER INFORMATION

Further information

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Grazoprevir / Elbasvir 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>
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<tr>
<td>4.9</td>
<td>04/24/2019</td>
<td>76520-00015</td>
<td>16.10.2018</td>
<td>17.03.2015</td>
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Date format: dd.mm.yyyy

**Full text of other abbreviations**

ACGIH: USA. ACGIH Threshold Limit Values (TLV)

ACGIH / TWA: 8-hour, 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; CPR - Controlled Products Regulations; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECX - Concentration associated with x% response; ELx - Loading rate associated with x% response; EnS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; ERG - Emergency Response Guide; GHS - Globally Harmonized System; GLP - Good Laboratory Practice; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; IBC - International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk; IC50 - Half maximal inhibitory concentration; ICAO - International Civil Aviation Organization; IECSC - Inventory of Existing Chemical Substances in China; IMDG - International Maritime Dangerous Goods; ISO - International Organisation for Standardization; KECI - Korea Existing Chemicals Inventory; LC50 - Lethal Concentration to 50 % of a test population; LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose); MARPOL - International Convention for the Prevention of Pollution from Ships; n.o.s. - Not Otherwise Specified; Nch - Chilean Norm; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NOM - Official Mexican Norm; NTP - National Toxicology Program; NZIoC - New Zealand Inventory of Chemicals; OECD - Organization for Economic Co-operation and Development; OPPTS - Office of Chemical Safety and Pollution Prevention; PBT - Persistent, Bioaccumulative and Toxic substance; PICCS - Philippines Inventory of Chemicals and Chemical Substances; (Q)SAR - (Quantitative) Structure Activity Relationship; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; SADT - Self-Accelerating Decomposition Temperature; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance Inventory; TDG - Transportation of Dangerous Goods; TSCA - Toxic Substances Control Act (United States); UN - United Nations; UNRTDG - United Nations Recommendations on the Transport of Dangerous Goods; vPvB - Very Persistent and Very Bioaccumulative; WHMIS - Workplace Hazardous Materials Information System

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

IN / EN