1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Grazoprevir / Elbasvir Formulation

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

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

2. HAZARDS IDENTIFICATION

Emergency Overview
Appearance : powder
Colour : white
Odour : No data available

Harmful to aquatic life. Very toxic to aquatic life with long lasting effects.

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:
Grazoprevir / Elbasvir Formulation

P391 Collect spillage.

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

Physical and chemical hazards
Not classified based on available information.

Health hazards
Not classified based on available information.

Environmental hazards
Harmful to aquatic life. Very toxic to aquatic life with long lasting effects.

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

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Chemical name</td>
</tr>
<tr>
<td></td>
<td>Sodium chloride</td>
</tr>
<tr>
<td></td>
<td>Cellulose</td>
</tr>
<tr>
<td></td>
<td>Grazoprevir</td>
</tr>
<tr>
<td></td>
<td>Elbasvir</td>
</tr>
<tr>
<td></td>
<td>Magnesium stearate</td>
</tr>
<tr>
<td></td>
<td>Titanium dioxide</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

Unsuitable extinguishing media: None known.

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

Hazardous combustion products: Carbon oxides
Metal oxides
Chlorine compounds
Nitrogen oxides (NOx)

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

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

6. ACCIDENTAL RELEASE MEASURES

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

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

Methods and materials for containment and cleaning up: Sweep up or vacuum up spillage and collect in suitable container for disposal.
Avoid dispersal of dust in the air (i.e., clearing dust surfaces with compressed air).
Dust deposits should not be allowed to accumulate on surfaces, as these may form an explosive mixture if they are released into the atmosphere in sufficient concentration.
Local or national regulations may apply to releases and disposal of this material, as well as those materials and items employed in the cleanup of releases. You will need to determine which regulations are applicable.
SAFETY DATA SHEET
according to GB/T 16483 and GB/T 17519

Grazoprevir / Elbasvir Formulation

Version 4.9  Revision Date: 04/24/2019  SDS Number: 76207-00015  Date of last issue: 2018/10/16  Date of first issue: 2015/03/17

Sections 13 and 15 of this SDS provide information regarding certain local or national requirements.

7. HANDLING AND STORAGE

Handling
Technical measures: Static electricity may accumulate and ignite suspended dust causing an explosion. 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 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.

Avoidance of contact: Oxidizing agents

Storage
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

Packaging material: Unsuitable material: None known.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Components with workplace control parameters

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters / Permissible concentration</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>PC-TWA</td>
<td>10 mg/m3</td>
<td>GBZ 2.1-2007</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA</td>
<td>10 mg/m3</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Grazoprevir</td>
<td>1350462-55-3</td>
<td>TWA</td>
<td>25 µg/m3 (OEB 3)</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wipe limit</td>
<td>250 µg/100 cm²</td>
<td>Internal</td>
</tr>
<tr>
<td>Elbasvir</td>
<td>1370468-36-2</td>
<td>TWA</td>
<td>100 µg/m3 (OEB 2)</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>
</tbody>
</table>
Titanium dioxide | 13463-67-7 | PC-TWA (Total dust) | 8 mg/m³ | GBZ 2.1-2007
| | | TWA | 10 mg/m³ | ACGIH

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

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

- **Hand protection**: Chemical-resistant gloves

- **Remarks**: Consider double gloving.

- **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
Grazoprevir / Elbasvir Formulation

10. STABILITY AND REACTIVITY

Reactivity: Not classified as a reactivity hazard.
Chemical stability: Stable under normal conditions.
Possibility of hazardous reac-
## 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>
</tr>
</thead>
<tbody>
<tr>
<td>4.9</td>
<td>04/24/2019</td>
<td>76207-00015</td>
<td>2018/10/16</td>
<td>2015/03/17</td>
</tr>
</tbody>
</table>

- **Conditions to avoid**: Heat, flames and sparks. Avoid dust formation.
- **Incompatible materials**: Oxidizing agents
- **Hazardous decomposition products**: No hazardous decomposition products are known.

### 11. TOXICOLOGICAL INFORMATION

**Exposure routes**
- Inhalation
- Skin contact
- Ingestion
- Eye contact

**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

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

**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 - Assessment:**
Weight of evidence does not support classification as a germ cell mutagen.
### Grazoprevir / Elbasvir Formulation

<table>
<thead>
<tr>
<th>Cellulose:</th>
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</thead>
<tbody>
<tr>
<td>Genotoxicity in vitro</td>
<td>Test Type: Bacterial reverse mutation assay (AMES)</td>
<td>Result: negative</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Test Type: In vitro mammalian cell gene mutation test</td>
<td>Result: negative</td>
<td></td>
</tr>
<tr>
<td>Genotoxicity in vivo</td>
<td>Test Type: Mammalian erythrocyte micronucleus test (in vivo cytogenetic assay)</td>
<td>Species: Mouse</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Application Route: Ingestion</td>
<td>Result: negative</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Grazoprevir:</th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Genotoxicity in vitro</td>
<td>Test Type: Bacterial reverse mutation assay (AMES)</td>
<td>Result: negative</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Test Type: Chromosome aberration test in vitro</td>
<td>Result: negative</td>
<td></td>
</tr>
<tr>
<td>Genotoxicity in vivo</td>
<td>Test Type: In vivo micronucleus test</td>
<td>Application Route: Oral</td>
<td></td>
</tr>
<tr>
<td>Germ cell mutagenicity - Assessment</td>
<td>Weight of evidence does not support classification as a germ cell mutagen.</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Elbasvir:</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Genotoxicity in vitro</td>
<td>Test Type: Bacterial reverse mutation assay (AMES)</td>
<td>Result: negative</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Test Type: Chromosome aberration test in vitro</td>
<td>Result: negative</td>
<td></td>
</tr>
<tr>
<td>Genotoxicity in vivo</td>
<td>Test Type: In vivo micronucleus test</td>
<td>Species: Rat</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Application Route: Oral</td>
<td>Result: negative</td>
<td></td>
</tr>
<tr>
<td>Germ cell mutagenicity - Assessment</td>
<td>Weight of evidence does not support classification as a germ cell mutagen.</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Magnesium stearate:</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotoxicity in vitro</td>
<td>Test Type: In vitro mammalian cell gene mutation test</td>
<td>Result: negative</td>
<td></td>
</tr>
<tr>
<td>Remarks: Based on data from similar materials</td>
<td>Test Type: Chromosome aberration test in vitro</td>
<td>Method: OECD Test Guideline 473</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Result: negative</td>
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<td></td>
</tr>
</tbody>
</table>
Grazoprevir / Elbasvir Formulation

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
Application Route : Ingestion
Exposure time : 72 weeks
Result : negative

Titanium dioxide:
Species : Rat
Application Route : inhalation (dust/mist/fume)
Exposure time : 2 Years
Method : OECD Test Guideline 453
Result : positive
Remarks : The mechanism or mode of action may not be relevant in humans.

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
Grazoprevir / Elbasvir Formulation

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

- **Grazoprevir:**
  - Test Type: Fertility
  - Species: Rat
  - Application Route: Oral
  - Fertility: NOAEL: 400 mg/kg body weight
  - Result: no effects on fertility, no effects on foetal development

- **Grazoprevir:**
  - 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

- **Grazoprevir:**
  - 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

- **Grazoprevir:**
  - 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:
- **Elbasvir:**
  - 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

- **Elbasvir:**
  - 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
**Grazoprevir / Elbasvir Formulation**

<table>
<thead>
<tr>
<th>SAFETY DATA SHEET</th>
<th>GB/T 16483 and GB/T 17519</th>
</tr>
</thead>
<tbody>
<tr>
<td>Version</td>
<td>4.9</td>
</tr>
<tr>
<td>Revision Date</td>
<td>04/24/2019</td>
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</tr>
</tbody>
</table>

**NOAEL**

- **Grazoprevir:**
  - Species: Rat
  - NOAEL: 400 mg/kg
  - Application Route: Oral
  - Exposure time: 30 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

- **Magnesium stearate:**
  - Species: Rat
  - NOAEL: > 100 mg/kg

**Species:** Rat

**Application Route:** Oral

**Exposure time:** 30 Days

**Remarks:** No significant adverse effects were reported

**Species:** Dog

**NOAEL:** 15 mg/kg

**LOAEL:** 100 mg/kg

**Application Route:** Oral

**Exposure time:** 180 Days

**Remarks:** No significant adverse effects were reported

**Species:** Mouse

**NOAEL:** 200 mg/kg

**LOAEL:** 500 mg/kg

**Application Route:** Oral

**Exposure time:** 90 Days

**Target Organs:** Liver, Testis, Blood, Bone marrow, gallbladder, spleen

**Species:** Dog

**NOAEL:** 20 mg/kg

**LOAEL:** 600 mg/kg

**Application Route:** Oral

**Exposure time:** 30 Days

**Target Organs:** Liver, Kidney, Blood

**Species:** Monkey

**NOAEL:** 10 mg/kg

**Exposure time:** 8 Days

**Remarks:** No significant adverse effects were reported
Grazoprevir / Elbasvir Formulation

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 irritation, rhinitis, Drowsiness, nasal congestion

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 fish (Chronic toxicity): NOEC (Pimephales promelas (fathead minnow)): 252 mg/l
Exposure time: 33 d
Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity): NOEC (Daphnia pulex (Water flea)): 314 mg/l
Exposure time: 21 d
Toxicity to microorganisms: EC10: > 1,000 mg/l
### Grazoprevir / Elbasvir Formulation

<table>
<thead>
<tr>
<th></th>
<th>Cellulose:</th>
<th>Grazoprevir:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Toxicity to fish</strong></td>
<td>( \text{LC50} ) (\text{Oryzias latipes (Japanese medaka)}): ( &gt; 100 \text{ mg/l} )</td>
<td></td>
</tr>
<tr>
<td>Ex. time</td>
<td>48 h</td>
<td>( \text{LC50} ) (\text{Cyprinodon variegatus (sheepshead minnow)}): ( &gt; 10 \text{ mg/l} )</td>
</tr>
<tr>
<td><strong>Remarks</strong></td>
<td>Based on data from similar materials</td>
<td>No toxicity at the limit of solubility</td>
</tr>
<tr>
<td><strong>Toxicity to daphnia and other aquatic invertebrates</strong></td>
<td>( \text{EC50} ) (\text{Daphnia magna (Water flea)}): ( &gt; 10 \text{ mg/l} )</td>
<td></td>
</tr>
<tr>
<td>Ex. time</td>
<td>48 h</td>
<td>( \text{EC50} ) (\text{Pseudokirchneriella subcapitata (green algae)}): ( &gt; 10 \text{ mg/l} )</td>
</tr>
<tr>
<td>Method</td>
<td>OECD Test Guideline 202</td>
<td>OECD Test Guideline 201</td>
</tr>
<tr>
<td><strong>Remarks</strong></td>
<td>No toxicity at the limit of solubility</td>
<td>No toxicity at the limit of solubility</td>
</tr>
<tr>
<td><strong>LC50</strong> (\text{Americamysis})</td>
<td>8.9 mg/l</td>
<td></td>
</tr>
<tr>
<td>Ex. time</td>
<td>96 h</td>
<td></td>
</tr>
<tr>
<td><strong>Toxicity to algae/aquatic plants</strong></td>
<td>( \text{EC50} ) (\text{Pseudokirchneriella subcapitata (green algae)}): ( &gt; 10 \text{ mg/l} )</td>
<td></td>
</tr>
<tr>
<td>Ex. time</td>
<td>72 hrs</td>
<td>( \text{NOEC} ) (\text{Pseudokirchneriella subcapitata (green algae)}): ( 10 \text{ mg/l} )</td>
</tr>
<tr>
<td>Method</td>
<td>OECD Test Guideline 201</td>
<td>OECD Test Guideline 201</td>
</tr>
<tr>
<td><strong>Remarks</strong></td>
<td>No toxicity at the limit of solubility</td>
<td>No toxicity at the limit of solubility</td>
</tr>
<tr>
<td><strong>NOEC</strong> (\text{Pseudokirchneriella subcapitata (green algae)})</td>
<td>10 mg/l</td>
<td></td>
</tr>
<tr>
<td>Ex. time</td>
<td>72 hrs</td>
<td></td>
</tr>
<tr>
<td><strong>Toxicity to fish (Chronic toxicity)</strong></td>
<td>( \text{NOEC} ) (\text{Pimephales promelas (fathead minnow)}): ( 0.98 \text{ mg/l} )</td>
<td></td>
</tr>
<tr>
<td>Ex. time</td>
<td>32 d</td>
<td>( \text{NOEC} ) (\text{Daphnia magna (Water flea)}): ( 5 \text{ mg/l} )</td>
</tr>
<tr>
<td>Method</td>
<td>OECD Test Guideline 210</td>
<td>OECD Test Guideline 211</td>
</tr>
<tr>
<td><strong>Remarks</strong></td>
<td>No toxicity at the limit of solubility</td>
<td></td>
</tr>
<tr>
<td><strong>Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity)</strong></td>
<td>( \text{NOEC} ) (\text{Daphnia magna (Water flea)}): ( 5 \text{ mg/l} )</td>
<td></td>
</tr>
<tr>
<td>Ex. time</td>
<td>21 d</td>
<td></td>
</tr>
<tr>
<td>Method</td>
<td>OECD Test Guideline 211</td>
<td></td>
</tr>
<tr>
<td><strong>Toxicity to microorganisms</strong></td>
<td>( \text{EC50} ): ( &gt; 1,000 \text{ mg/l} )</td>
<td>( \text{NOEC} ): ( 1.3 \text{ mg/l} )</td>
</tr>
<tr>
<td>Ex. time</td>
<td>3 h</td>
<td>Exposure time: 3 h</td>
</tr>
<tr>
<td>Test Type</td>
<td>Respiration inhibition</td>
<td>Test Type: Respiration inhibition</td>
</tr>
<tr>
<td>Method</td>
<td>OECD Test Guideline 209</td>
<td>OECD Test Guideline 209</td>
</tr>
<tr>
<td><strong>Remarks</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>NOEC</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ex. time</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test Type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Method</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Elbasvir:**

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**Notes:**

- Method: OECD Test Guideline
- Ex. time: Exposure time
- Test Type: Test Type
- Remarks: Remarks

---

**SDS Number:** 76207-00015

**Date of first issue:** 2015/03/17

**Date of last issue:** 2018/10/16
### 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>
</tr>
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<td>4.9</td>
<td>04/24/2019</td>
<td>76207-00015</td>
<td>2018/10/16</td>
<td>2015/03/17</td>
</tr>
</tbody>
</table>

#### Toxicity to fish
- **LC50** *(Lepomis macrochirus (Bluegill sunfish))*: > 10 mg/l  
  Exposure time: 96 h  
  Method: OECD Test Guideline 203  
  Remarks: No toxicity at the limit of solubility
- **LC50** *(Menidia beryllina (Silverside))*: > 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):* 7.7 mg/l  
  Exposure time: 96 h  
  Method: US-EPA OPPTS 850.1035  
  Remarks: No toxicity at the limit of solubility

#### Toxicity to algae/aquatic plants
- **EC50** *(Pseudokirchneriella subcapitata (algae))*: > 0.081 mg/l  
  Exposure time: 72 h  
  Method: OECD Test Guideline 201  
  Remarks: No toxicity at the limit of solubility
- **NOEC** *(Pseudokirchneriella subcapitata (green algae)):* 0.081 mg/l  
  Exposure time: 72 h  
  Method: OECD Test Guideline 201  
  Remarks: No toxicity at the limit of solubility

#### Toxicity to fish (Chronic toxicity)
- **NOEC** *(Pimephales promelas (fathead minnow)):* 0.0023 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)):* 0.84 mg/l  
  Exposure time: 21 d  
  Method: OECD Test Guideline 211  
  Remarks: No toxicity at the limit of solubility

#### M-Factor (Chronic aquatic toxicity)
- Toxicity to microorganisms: 10

#### Magnesium stearate:
- **Toxicity to fish** *(Leuciscus idus (Golden orfe)):* > 100 mg/l

---

**Remarks:**
- No toxicity at the limit of solubility
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 / Elbasvir Formulation

Biodegradability

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

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

**Magnesium stearate:**
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

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

IATA-DGR
UN/ID No.: UN 3077
Proper shipping name: Environmentally hazardous substance, solid, n.o.s. (Elbasvir)
Class: 9
Packing group: III
Labels: Miscellaneous
Packing instruction (cargo aircraft): 956
Packing instruction (passenger aircraft): 956
Environmentally hazardous: yes

IMDG-Code
UN number: UN 3077
Proper shipping name: ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Elbasvir)
Class: 9
Packing group: III
Labels: 9
EmS Code: F-A, S-F
Marine pollutant: yes

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

National Regulations

GB 6944/12268
UN number: UN 3077
Proper shipping name: ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Elbasvir)
Grazoprevir / Elbasvir Formulation

Version: 4.9  
Revision Date: 04/24/2019  
SDS Number: 76207-00015  
Date of last issue: 2018/10/16  
Date of first issue: 2015/03/17

Class: 9  
Packing group: III  
Labels: 9

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

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

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

16. OTHER INFORMATION

Further information

Date format: yyyy/mm/dd

Full text of other abbreviations
ACGIH / TWA: 8-hour, time-weighted average  
GBZ 2.1-2007 / PC-TWA: Permissible concentration - time weighted average

AICS - Australian Inventory of Chemical Substances; ANTT - National Agency for Transport by Land of Brazil; ASTM - American Society for the Testing of Materials; bw - Body weight; CMR - Carcinogen, Mutagen or Reproductive Toxicant; 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; EmS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; ERG - Emergency Response Guide; GHS - Globally Harmonized System; GLP - Good Laboratory Practice; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; IBC - International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk; IC50 - Half maximal inhibitory concentration; ICAO - International Civil Aviation Organization; IECSC - Inventory of Existing Chemical Substances in China; IMDG - International Maritime Dan-
SAFETY DATA SHEET
according to GB/T 16483 and GB/T 17519

Grazoprevir / Elbasvir Formulation

Version 4.9 Revision Date: 04/24/2019 SDS Number: 76207-00015 Date of last issue: 2018/10/16
Date of first issue: 2015/03/17

Dangerous Goods; IMO - International Maritime Organization; ISHL - Industrial Safety and Health Law (Japan); ISO - International Organisation for Standardization; KECI - Korea Existing Chemicals Inventory; LC50 - Lethal Concentration to 50 % of a test population; LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose); MARPOL - International Convention for the Prevention of Pollution from Ships; n.o.s. - Not Otherwise Specified; Nch - Chilean Norm; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NOM - Official Mexican Norm; NTP - National Toxicology Program; NZIoC - New Zealand Inventory of Chemicals; OECD - Organization for Economic Co-operation and Development; OPPTS - Office of Chemical Safety and Pollution Prevention; PBT - Persistent, Bioaccumulative and Toxic substance; PICCS - Philippines Inventory of Chemicals and Chemical Substances; (Q)SAR - (Quantitative) Structure Activity Relationship; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; SADT - Self-Accelerating Decomposition Temperature; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance Inventory; TDG - Transportation of Dangerous Goods; TSCA - Toxic Substances Control Act (United States); UN - United Nations; UNRTDG - United Nations Recommendations on the Transport of Dangerous Goods; vPvB - Very Persistent and Very Bioaccumulative; WHMIS - Workplace Hazardous Materials Information System

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

CN / EN