SAFETY DATA SHEET
according to GB/T 16483 and GB/T 17519

Grazoprevir / Elbasvir Formulation

Version 4.13  Revision Date: 2020/12/08  SDS Number: 76207-00019  Date of last issue: 2020/10/02
   Date of first issue: 2015/03/17

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: +1-908-740-4000
Emergency telephone number: 86-571-87268110
E-mail address: EHSDATASTEWARD@msd.com

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

2. HAZARDS IDENTIFICATION

Emergency Overview

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

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:
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>Chemical name</td>
<td>CAS-No.</td>
</tr>
<tr>
<td>Sodium chloride</td>
<td>7647-14-5</td>
</tr>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
</tr>
<tr>
<td>Grazoprevir</td>
<td>1350462-55-3</td>
</tr>
<tr>
<td>Elbasvir</td>
<td>1370468-36-2</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>557-04-0</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</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,
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 (see section 7) and personal protective equipment recommendations (see section 8).

**Environmental precautions:** Avoid release to the environment. 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.
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>CN OEL</td>
</tr>
<tr>
<td>Grazoprevir</td>
<td>1350462-55-3</td>
<td>TWA</td>
<td>85 µg/m³ (OEB 3)</td>
<td>ACGIH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wipe limit</td>
<td>850 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 particulate matter)</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Respirable particulate matter)</td>
<td>3 mg/m³</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: If adequate local exhaust ventilation is not available or exposure assessment demonstrates exposures outside the recommended guidelines, use respiratory protection.

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

Material: Chemical-resistant gloves

Hygiene measures: Consider double gloving.

9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance: powder
Grazoprevir / Elbasvir Formulation

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colour</td>
<td>white</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>Flammability (liquids)</td>
<td>No data available</td>
</tr>
<tr>
<td>Upper explosion limit / Upper flammability limit</td>
<td>No data available</td>
</tr>
<tr>
<td>Lower explosion limit / Lower flammability limit</td>
<td>No data available</td>
</tr>
<tr>
<td>Vapour pressure</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Relative vapour density</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Relative density</td>
<td>No data available</td>
</tr>
<tr>
<td>Density</td>
<td>No data available</td>
</tr>
<tr>
<td>Solubility(ies)</td>
<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>
<tr>
<td>Particle size</td>
<td>No data available</td>
</tr>
</tbody>
</table>
10. STABILITY AND REACTIVITY

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

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

Incompatible materials:
- Oxidizing agents

Hazardous decomposition products:
- No hazardous decomposition products are known.

11. TOXICOLOGICAL INFORMATION

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

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
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**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
### 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>4.13</td>
<td>2020/12/08</td>
<td>76207-00019</td>
<td>2020/10/02</td>
<td>2015/03/17</td>
</tr>
</tbody>
</table>

**Germ cell mutagenicity - Assessment**: 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 - Assessment**: 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
Grazoprevir / Elbasvir Formulation

<table>
<thead>
<tr>
<th>Component</th>
<th>Genotoxicity in vitro</th>
<th>Genotoxicity in vivo</th>
<th>Carcinogenicity</th>
<th>Reproductive toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium chloride</td>
<td>Test Type: Bacterial reverse mutation assay (AMES) Result: negative</td>
<td>Test Type: In vivo micronucleus test Species: Mouse Result: negative</td>
<td>Not classified based on available information.</td>
<td>Not classified based on available information.</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>Test Type: Chromosome aberration test in vitro Result: negative</td>
<td>Test Type: Bacterial reverse mutation assay (AMES) Result: negative</td>
<td>Carcinogenicity - Assessment Result: Limited evidence of carcinogenicity in inhalation studies with animals.</td>
<td></td>
</tr>
</tbody>
</table>

Carcinogenicity
Not classified based on available information.

Components:

<table>
<thead>
<tr>
<th>Component</th>
<th>Species</th>
<th>Application Route</th>
<th>Exposure time</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium chloride</td>
<td>Rat</td>
<td>Ingestion</td>
<td>2 Years</td>
<td>negative</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>Rat</td>
<td>Inhalation (dust/mist/fume)</td>
<td>2 Years</td>
<td>positive</td>
</tr>
</tbody>
</table>

Remarks:
The mechanism or mode of action may not be relevant in humans.
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
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**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  
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
### Grazoprevir / Elbasvir Formulation

<table>
<thead>
<tr>
<th>Exposure time: 90 Days</th>
</tr>
</thead>
</table>

**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, Blood, Bone marrow, gallbladder, spleen, Testis

- **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:** Blood, Testis

- **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 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

---

**Cellulose:**

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

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**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

- **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 fish (Chronic toxicity)**
  - NOEC (Pimephales promelas (fathead minnow)): 0.98 mg/l
  - Exposure time: 32 d
  - Method: OECD Test Guideline 210
  - Remarks: No toxicity at the limit of solubility

- **Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity)**
  - NOEC (Daphnia magna (Water flea)): 5 mg/l
  - Exposure time: 21 d
  - Method: OECD Test Guideline 211

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

  - NOEC: 1.3 mg/l
  - Exposure time: 3 h
Elbasvir:

**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
- 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)**
- 10

**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
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 (Onchorhynchus 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
- 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:**
Grazoprevir / Elbasvir Formulation

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
SAFETY DATA SHEET
according to GB/T 16483 and GB/T 17519

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GB 6944/12268
UN number : UN 3077
Proper shipping name : ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Elbasvir)
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 : USA. ACGIH Threshold Limit Values (TLV)
CN OEL : Occupational exposure limits for hazardous agents in the workplace - Chemical hazardous agents.
ACGIH / TWA : 8-hour, time-weighted average
CN OEL / PC-TWA : Permissible concentration - time weighted average

AICL - Australian Inventory of Industrial Chemicals; ANTT - National Agency for Transport by Land of Brazil; ASTM - American Society for the Testing of Materials; bw - Body weight; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; ELx - Loading rate associated with x% response; EmS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with
Grazoprevir / Elbasvir Formulation

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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; 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