SAFETY DATA SHEET
according to the OSHA Hazard Communication Standard

Grazoprevir / Elbasvir Formulation

Version 13.1
Revision Date: 09/30/2023
SDS Number: 76219-00026
Date of last issue: 04/04/2023
Date of first issue: 03/17/2015

SECTION 1. IDENTIFICATION

Product name: Grazoprevir / Elbasvir Formulation

Manufacturer or supplier’s details
Company name of supplier: Merck & Co., Inc
Address: 126 E. Lincoln Avenue
Rahway, New Jersey U.S.A. 07065
Telephone: 908-740-4000
Emergency telephone: 1-908-423-6000
E-mail address: EHSDATASTEWARD@merck.com

Recommended use of the chemical and restrictions on use
Recommended use: Pharmaceutical
Restrictions on use: Not applicable

SECTION 2. HAZARDS IDENTIFICATION

GHS classification in accordance with the OSHA Hazard Communication Standard (29 CFR 1910.1200)
Combustible dust
Carcinogenicity (Inhalation): Category 2
Specific target organ toxicity - repeated exposure (Oral): Category 2 (Liver, Testis)

GHS label elements
Hazard pictograms:

Signal Word: Warning

Hazard Statements:
If small particles are generated during further processing, handling or by other means, may form combustible dust concentrations in air.

H351 Suspected of causing cancer if inhaled.
H373 May cause damage to organs (Liver, Testis) through prolonged or repeated exposure if swallowed.

Precautionary Statements:
Prevention:
P201 Obtain special instructions before use.
P202 Do not handle until all safety precautions have been read and understood.
P260 Do not breathe dust.
P280 Wear protective gloves, protective clothing, eye protection and face protection.

Response:
P308 + P313 IF exposed or concerned: Get medical attention.

Storage:
P405 Store locked up.

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

Other hazards
Dust contact with the eyes can lead to mechanical irritation.
Contact with dust can cause mechanical irritation or drying of the skin.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture

Components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>&gt;= 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;= 1 - &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>

Actual concentration is withheld as a trade secret

SECTION 4. FIRST AID MEASURES

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

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

In case of skin contact : 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 : Suspected of causing cancer if inhaled.
May cause damage to organs through prolonged or repeated exposure if swallowed.
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 (see section 8).

Notes to physician : Treat symptomatically and supportively.
SECTION 5. FIRE-FIGHTING MEASURES

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

Unsuitable extinguishing media:
None known.

Specific hazards during 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 fire-fighters:
In the event of fire, wear self-contained breathing apparatus. Use personal protective equipment.

SECTION 6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures:
Use personal protective equipment. Follow safe handling advice (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. Sections 13 and 15 of this SDS provide information regarding certain local or national requirements.
SECTION 7. HANDLING AND STORAGE

Technical measures: Static electricity may accumulate and ignite suspended dust causing an explosion. Provide adequate precautions, such as electrical grounding and bonding, or inert atmospheres.

Local/Total ventilation: Use only with adequate ventilation.

Advice on safe handling: Do not 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 labeled containers. Store in accordance with the particular national regulations.

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

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Ingredients with workplace control parameters

inert or nuisance dust
- 50 Million particles per cubic foot
  Value type (Form of exposure): TWA (total dust)
  Basis: OSHA Z-3

- 15 mg/m³
  Value type (Form of exposure): TWA (total dust)
  Basis: OSHA Z-3

- 5 mg/m³
  Value type (Form of exposure): TWA (respirable fraction)
  Basis: OSHA Z-3

- 15 Million particles per cubic foot
  Value type (Form of exposure): TWA (respirable fraction)
  Basis: OSHA Z-3

Dust, nuisance dust and particulates
- 10 mg/m³
  Value type (Form of exposure): PEL (Total dust)
  Basis: CAL PEL

- 5 mg/m³
  Value type (Form of exposure): PEL (respirable dust fraction)
  Basis: CAL PEL
SAFETY DATA SHEET
according to the OSHA Hazard Communication Standard

Grazoprevir / Elbasvir Formulation

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters / Permissible concentration</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Respirable)</td>
<td>5 mg/m³</td>
<td>NIOSH REL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (total)</td>
<td>10 mg/m³</td>
<td>NIOSH REL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (total dust)</td>
<td>15 mg/m³</td>
<td>OSHA Z-1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (respirable fraction)</td>
<td>5 mg/m³</td>
<td>OSHA Z-1</td>
</tr>
<tr>
<td>Grazoprevir</td>
<td>1350462-55-3</td>
<td>TWA</td>
<td>85 µg/m³ (OEB 3)</td>
<td>Internal</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>150 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>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</td>
<td>TWA (total dust)</td>
<td>15 mg/m³</td>
<td>OSHA Z-1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Respirable particulate matter)</td>
<td>2.5 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: General and local exhaust ventilation is recommended to maintain vapor exposures below recommended limits. Where concentrations are above recommended limits or are unknown, appropriate respiratory protection should be worn. Follow OSHA respirator regulations (29 CFR 1910.134) and use NIOSH/MSHA approved respirators. Protection provided by air purifying respirators against exposure to any hazardous chemical is limited. Use a positive pressure air supplied respirator if there is any potential for uncontrolled release, exposure levels are unknown, or any other circumstance where air purifying respirators may not provide adequate protection.

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

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance : powder
Color : white
Odor : No data available
Odor 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 : No data available
SECTION 10. STABILITY AND REACTIVITY

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

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

Incompatible materials : Oxidizing agents

Hazardous decomposition products : No hazardous decomposition products are known.

SECTION 11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure
Inhalation
Skin contact
Grazoprevir / Elbasvir Formulation

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:**

**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:

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:

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 sensitization

Skin sensitization
Not classified based on available information.

Respiratory sensitization
Not classified based on available information.
Components:

Grazoprevir:
Test Type: Local lymph node assay (LLNA)
Routes of exposure: Dermal
Result: Not a skin sensitizer.

Elbasvir:
Test Type: Local lymph node assay (LLNA)
Routes of exposure: Dermal
Species: Mouse
Result: negative

Magnesium stearate:
Test Type: Maximization Test
Routes of exposure: 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)
Routes of exposure: Skin contact
Species: Mouse
Result: negative

Germ cell mutagenicity
Not classified based on available information.

Components:

Cellulose:
Genotoxicity in vitro:
Test Type: Bacterial reverse mutation assay (AMES)
Result: negative
Test Type: In vitro mammalian cell gene mutation test
Result: negative

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

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

- 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

Suspected of causing cancer if inhaled.
Components:

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.

IARC
Group 2B: Possibly carcinogenic to humans
Titanium dioxide 13463-67-7

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

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

Reproductive toxicity
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 fetal 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
### Grazoprevir / Elbasvir Formulation

<table>
<thead>
<tr>
<th>Version</th>
<th>Revision Date</th>
<th>SDS Number</th>
<th>Date of last issue: 04/04/2023</th>
<th>Date of first issue: 03/17/2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>13.1</td>
<td>09/30/2023</td>
<td>76219-00026</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **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 fetal development.

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

- **Test Type:** Embryo-fetal development  
- **Species:** Rabbit  
- **Application Route:** Oral  
- **Embryo-fetal toxicity:** NOAEL: 200 mg/kg body weight  
- **Result:** No effects on fetal development.

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

### Elbasvir:

<table>
<thead>
<tr>
<th>Effect Type</th>
<th>Fertility/early embryonic development</th>
<th>Species: Rat, male and female</th>
<th>Application Route: Oral</th>
<th>Fertility: NOAEL: 1,000 mg/kg body weight</th>
<th>Result: No effects on fertility.</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Effect Type</th>
<th>Embryo-fetal development</th>
<th>Species: Rat</th>
<th>Application Route: Oral</th>
<th>Developmental Toxicity: NOAEL: 1,000 mg/kg body weight</th>
<th>Result: No effects on early embryonic development.</th>
</tr>
</thead>
</table>

### Magnesium stearate:

| Effect 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  
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Remarks</td>
<td>Based on data from similar materials</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Effects on fetal development
  Test Type: Embryo-fetal 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
May cause damage to organs (Liver, Testis) through prolonged or repeated exposure if swallowed.

Components:

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

Repeated dose toxicity

Components:

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

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
### Grazoprevir / Elbasvir Formulation

<table>
<thead>
<tr>
<th>Application Route</th>
<th>Oral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure time</td>
<td>90 Days</td>
</tr>
<tr>
<td>Target Organs</td>
<td>Liver, Kidney, Blood</td>
</tr>
</tbody>
</table>

**Species**: Dog  
**NOAEL**: 20 mg/kg  
**LOAEL**: 600 mg/kg

**Application Route**: Oral  
**Exposure time**: 30 Days  
**Target Organs**: Blood, Testis

<table>
<thead>
<tr>
<th>Species</th>
<th>Monkey</th>
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</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>10 mg/kg</td>
</tr>
<tr>
<td>Exposure time</td>
<td>8 Days</td>
</tr>
<tr>
<td>Remarks</td>
<td>No significant adverse effects were reported</td>
</tr>
</tbody>
</table>

**Elbasvir**:

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>1,000 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>180 d</td>
</tr>
<tr>
<td>Remarks</td>
<td>No significant adverse effects were reported</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Dog</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>1,000 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>270 d</td>
</tr>
<tr>
<td>Remarks</td>
<td>No significant adverse effects were reported</td>
</tr>
</tbody>
</table>

**Magnesium stearate**:

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>&gt; 100 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Ingestion</td>
</tr>
<tr>
<td>Exposure time</td>
<td>90 Days</td>
</tr>
<tr>
<td>Remarks</td>
<td>Based on data from similar materials</td>
</tr>
</tbody>
</table>

**Titanium dioxide**:

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>24,000 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Ingestion</td>
</tr>
<tr>
<td>Exposure time</td>
<td>28 Days</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>10 mg/m³</td>
</tr>
<tr>
<td>Application Route</td>
<td>inhalation (dust/mist/fume)</td>
</tr>
<tr>
<td>Exposure time</td>
<td>2 y</td>
</tr>
</tbody>
</table>

**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

### SECTION 12. ECOLOGICAL INFORMATION

**Ecotoxicity**

**Components:**

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

**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 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.
## SAFETY DATA SHEET
according to the OSHA Hazard Communication Standard

### 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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<tbody>
<tr>
<td>13.1</td>
<td>09/30/2023</td>
<td>76219-00026</td>
<td>04/04/2023</td>
<td>03/17/2015</td>
</tr>
</tbody>
</table>

### 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

#### 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.

#### 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 (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
### Toxicity to microorganisms

<table>
<thead>
<tr>
<th>Test Substance</th>
<th>EC50</th>
<th>Exposure Time</th>
<th>Test Type</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grazoprevir / Elbasvir</td>
<td>&gt; 1,000 mg/l</td>
<td>3 h</td>
<td>Respiration inhibition</td>
<td>OECD Test Guideline 209</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>&gt; 271.9 mg/l</td>
<td>3 h</td>
<td>Respiration inhibition</td>
<td>OECD Test Guideline 209</td>
</tr>
</tbody>
</table>

**Remarks:** No toxicity at the limit of solubility.

### Toxicity to fish

#### Magnesium stearate:

<table>
<thead>
<tr>
<th>Test Substance</th>
<th>LC50</th>
<th>Exposure Time</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leuciscus idus (Golden orfe)</td>
<td>&gt; 100 mg/l</td>
<td>48 h</td>
<td>DIN 38412</td>
</tr>
</tbody>
</table>

**Remarks:** Based on data from similar materials.

### Toxicity to daphnia and other aquatic invertebrates

<table>
<thead>
<tr>
<th>Test Substance</th>
<th>EC50</th>
<th>Exposure Time</th>
<th>Method</th>
</tr>
</thead>
</table>

**Remarks:** Based on data from similar materials;
No toxicity at the limit of solubility.

### Toxicity to algae/aquatic plants

<table>
<thead>
<tr>
<th>Test Substance</th>
<th>EL50</th>
<th>Exposure Time</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudokirchneriella subcapitata (green algae)</td>
<td>&gt; 1 mg/l</td>
<td>72 h</td>
<td>OECD Test Guideline 201</td>
</tr>
</tbody>
</table>

**Remarks:** Based on data from similar materials;
No toxicity at the limit of solubility.

### Toxicity to microorganisms

<table>
<thead>
<tr>
<th>Test Substance</th>
<th>EC10</th>
<th>Exposure Time</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudomonas putida</td>
<td>&gt; 100 mg/l</td>
<td>16 h</td>
<td>Water Accommodated Fraction</td>
</tr>
</tbody>
</table>

**Remarks:** Based on data from similar materials.

### Titanium dioxide:

#### Toxicity to fish

<table>
<thead>
<tr>
<th>Test Substance</th>
<th>LC50</th>
<th>Exposure Time</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oncorhynchus mykiss (rainbow trout)</td>
<td>&gt; 100 mg/l</td>
<td>96 h</td>
<td>OECD Test Guideline 203</td>
</tr>
</tbody>
</table>

### Toxicity to daphnia and other aquatic invertebrates

<table>
<thead>
<tr>
<th>Test Substance</th>
<th>EC50</th>
<th>Exposure Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daphnia magna (Water flea)</td>
<td>&gt; 100 mg/l</td>
<td>48 h</td>
</tr>
</tbody>
</table>
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
Grazoprevir / Elbasvir Formulation

Mobility in soil

Components:

Grazoprevir:
Distribution among environmental compartments: \( \log K_{oc} \): 4.01

Elbasvir:
Distribution among environmental compartments: \( \log K_{oc} \): 5.24

Other adverse effects
No data available

SECTION 13. DISPOSAL CONSIDERATIONS

Disposal methods
Waste from residues: Dispose of in accordance with local regulations. Do not dispose of waste into sewer.
Contaminated packaging: Empty containers should be taken to an approved waste handling site for recycling or disposal. If not otherwise specified: Dispose of as unused product.

SECTION 14. TRANSPORT INFORMATION

International Regulations

UNRTDG
UN number: UN 3077
Proper shipping name: ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Elbasvir)
Class: 9
Packing group: III
Labels: 9
Environmentally hazardous: yes

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.
Grazoprevir / Elbasvir Formulation

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.

Domestic regulation

49 CFR
UN/ID/NA number: UN 3077
Proper shipping name: Environmentally hazardous substance, solid, n.o.s. (Elbasvir)
Class: 9
Packing group: III
Labels: CLASS 9
ERG Code: 171
Marine pollutant: yes (Elbasvir)
Remarks: Above applies only to containers over 119 gallons or 450 liters.
Shipment by ground under DOT is non-regulated; however it may be shipped per the applicable hazard classification to facilitate multi-modal transport involving ICAO (IATA) or IMO.

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.

SECTION 15. REGULATORY INFORMATION

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

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

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

SARA 311/312 Hazards: Combustible dust
Carcinogenicity
Specific target organ toxicity (single or repeated exposure)

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

US State Regulations
Pennsylvania Right To Know
D-mannitol
Hydroxypropyl methylcellulose
Croskemelllose sodium
Sodium chloride
Polyvinylpyrolylone / Vinyl Acetate Copolymer
Cellulose
D-Glucose, 4-O-β-D-galactopyranosyl-, monohydrate
Grazoprevir
Elbasvir

California Prop. 65
WARNING: This product can expose you to chemicals including Titanium dioxide, which is/are known to the State of California to cause cancer. For more information go to www.P65Warnings.ca.gov.

California Permissible Exposure Limits for Chemical Contaminants
Cellulose
Magnesium stearate

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

SECTION 16. OTHER INFORMATION

Further information

NFPA 704:

HMIS® IV:

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

Full text of other abbreviations

ACGIH : USA. ACGIH Threshold Limit Values (TLV)
## SAFETY DATA SHEET
according to the OSHA Hazard Communication Standard

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<tr>
<th>Source</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>CAL PEL</td>
<td>California permissible exposure limits for chemical contaminants (Title 8, Article 107)</td>
</tr>
<tr>
<td>NIOSH REL</td>
<td>USA. NIOSH Recommended Exposure Limits</td>
</tr>
<tr>
<td>OSHA Z-1</td>
<td>USA. Occupational Exposure Limits (OSHA) - Table Z-1 Limits for Air Contaminants</td>
</tr>
<tr>
<td>OSHA Z-3</td>
<td>USA. Occupational Exposure Limits (OSHA) - Table Z-3 Mineral Dusts</td>
</tr>
<tr>
<td>ACGIH / TWA</td>
<td>8-hour, time-weighted average</td>
</tr>
<tr>
<td>CAL PEL / PEL</td>
<td>Permissible exposure limit</td>
</tr>
<tr>
<td>NIOSH REL / TWA</td>
<td>Time-weighted average concentration for up to a 10-hour workday during a 40-hour workweek</td>
</tr>
<tr>
<td>OSHA Z-1 / TWA</td>
<td>8-hour time weighted average</td>
</tr>
<tr>
<td>OSHA Z-3 / TWA</td>
<td>8-hour time weighted average</td>
</tr>
</tbody>
</table>

AIIC - Australian Inventory of Industrial Chemicals; ASTM - American Society for the Testing of Materials; bw - Body weight; CERCLA - Comprehensive Environmental Response, Compensation, and Liability Act; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DOT - Department of Transportation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; EHS - Extremely Hazardous Substance; ELx - Loading rate associated with x% response; EmS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; ERG - Emergency Response Guide; GHS - Globally Harmonized System; GLP - Good Laboratory Practice; HMIS - Hazardous Materials Identification System; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; IBC - International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk; IC50 - Half maximal inhibitory concentration; ICAO - International Civil Aviation Organization; IECSC - Inventory of Existing Chemical Substances in China; IMDG - International Maritime Dangerous Goods; IMO - International Maritime Organization; ISHL - Industrial Safety and Health Law (Japan); ISO - International Organisation for Standardization; KECI - Korea Existing Chemicals Inventory; LC50 - Lethal Concentration to 50% of a test population; LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose); MARPOL - International Convention for the Prevention of Pollution from Ships; MSHA - Mine Safety and Health Administration; n.o.s. - Not Otherwise Specified; NFPA - National Fire Protection Association; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NTP - National Toxicology Program; NZIoC - New Zealand Inventory of 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; RCRA - Resource Conservation and Recovery Act; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; RO - Reportable Quantity; SADT - Self-Accelerating Decomposition Temperature; SARA - Superfund Amendments and Reauthorization Act; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance Inventory; TECI - Thailand Existing Chemicals Inventory; 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


Revision Date: 09/30/2023
The information provided in this Safety Data Sheet is correct to the best of our knowledge, information and belief at the date of its publication. The information is designed only as a guidance for safe handling, use, processing, storage, transportation, disposal and release and shall not be considered a warranty or quality specification of any type. The information provided relates only to the specific material identified at the top of this SDS and may not be valid when the SDS material is used in combination with any other materials or in any process, unless specified in the text. Material users should review the information and recommendations in the specific context of their intended manner of handling, use, processing and storage, including an assessment of the appropriateness of the SDS material in the user’s end product, if applicable.

US / Z8