SAFETY DATA SHEET

Grazoprevir / Elbasvir Formulation

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:

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SAFETY DATA SHEET
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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:
Contact with dust can cause mechanical irritation or drying of the skin.
Dust contact with the eyes can lead to mechanical irritation.
Suspected of causing cancer if inhaled.
May cause damage to organs through prolonged or repeated exposure if swallowed.

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

Unsuitable extinguishing media:
- None known.

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

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

<table>
<thead>
<tr>
<th>Inert or nuisance dust</th>
<th>50 Million particles per cubic foot</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value type (Form of exposure): TWA (total dust)</td>
<td>Basis: OSHA Z-3</td>
</tr>
<tr>
<td>15 mg/m³</td>
<td>Value type (Form of exposure): TWA (total dust)</td>
</tr>
<tr>
<td>Basis: OSHA Z-3</td>
<td></td>
</tr>
<tr>
<td>5 mg/m³</td>
<td>Value type (Form of exposure): TWA (respirable fraction)</td>
</tr>
<tr>
<td>Basis: OSHA Z-3</td>
<td></td>
</tr>
<tr>
<td>15 Million particles per cubic foot</td>
<td>Value type (Form of exposure): TWA (respirable fraction)</td>
</tr>
<tr>
<td>Basis: OSHA Z-3</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dust, nuisance dust and particulates</th>
<th>10 mg/m³</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value type (Form of exposure): PEL (Total dust)</td>
<td>Basis: CAL PEL</td>
</tr>
<tr>
<td>5 mg/m³</td>
<td>Value type (Form of exposure): PEL (respirable dust fraction)</td>
</tr>
<tr>
<td>Basis: CAL PEL</td>
<td></td>
</tr>
</tbody>
</table>

<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>
</tbody>
</table>
### Grazoprevir / Elbasvir Formulation

<table>
<thead>
<tr>
<th>Chemical</th>
<th>TWA (Respirable)</th>
<th>TWA (Total)</th>
<th>NIOSH REL</th>
<th>OSHA Z-1</th>
<th>ACNIH</th>
<th>ACGIH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grazoprevir</td>
<td>TWA (total dust)</td>
<td>15 mg/m³</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>TWA (respirable fraction)</td>
<td>5 mg/m³</td>
<td>OSHA Z-1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elbasvir</td>
<td>TWA (total dust)</td>
<td>15 mg/m³</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>TWA (respirable fraction)</td>
<td>5 mg/m³</td>
<td>OSHA Z-1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>TWA (Inhalable particulate matter)</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>TWA (Respirable particulate matter)</td>
<td>3 mg/m³</td>
<td>ACGIH</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>TWA (Total dust)</td>
<td>15 mg/m³</td>
<td></td>
<td>OSHA Z-1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>TWA (Respirable particulate matter)</td>
<td>2.5 mg/m³ (Titanium dioxide)</td>
<td>ACGIH</td>
<td></td>
<td></td>
<td></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 flammability limit**: No data available
- **Lower explosion limit / Lower flammability limit**: No data available
- **Vapor pressure**: Not applicable
**Relative vapor density** : Not applicable

**Relative density** : No data available

**Density** : No data available

**Solubility(ies)**

- **Water solubility** : No data available

**Partition coefficient: n-octanol/water** : Not applicable

**Autoignition temperature** : No data available

**Decomposition temperature** : No data available

**Viscosity**

- **Viscosity, kinematic** : Not applicable

**Explosive properties** : Not explosive

**Oxidizing properties** : The substance or mixture is not classified as oxidizing.

**Particle size** : 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.

**Incompatible materials** : Avoid dust formation.

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

### SECTION 11. TOXICOLOGICAL INFORMATION

**Information on likely routes of exposure**

- **Inhalation**
- **Skin contact**
- **Ingestion**
- **Eye contact**

**Acute toxicity**

Not classified based on available information.

**Product:**

**Acute oral toxicity** : Acute toxicity estimate: > 5,000 mg/kg

**Method:** Calculation method
Components:

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

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

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
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### Grazoprevir / Elbasvir Formulation

<table>
<thead>
<tr>
<th>Version</th>
<th>Revision Date</th>
<th>SDS Number</th>
<th>Date of last issue</th>
<th>Date of first issue</th>
</tr>
</thead>
<tbody>
<tr>
<td>13.0</td>
<td>04/04/2023</td>
<td>76219-00025</td>
<td>10/24/2022</td>
<td>03/17/2015</td>
</tr>
</tbody>
</table>

### Test Data

#### Genotoxicity in vitro

- **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 hu-
## Carcinogenicity - Assessment

- **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
  
  - 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.
Grazoprevir / Elbasvir Formulation

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:

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 fetal development
Test Type: Embryo-fetal development
Species: Rat
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 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
### Repeated dose toxicity

**Components:**

#### Cellulose:
- **Species:** Rat
- **NOAEL:** $\geq 9,000$ 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
- **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 y

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  
| Exposition 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  
| Exposition time: 48 h  
| Method: OECD Test Guideline 202  
| Remarks: No toxicity at the limit of solubility.  
| LC50 (Americamysis): 8.9 mg/l  
| Exposition time: 96 h |
| Toxicity to algae/aquatic plants | EC50 (Pseudokirchneriella subcapitata (green algae)): > 10 mg/l  
| Exposition time: 72 hrs  
| Method: OECD Test Guideline 201  
| Remarks: No toxicity at the limit of solubility.  
| NOEC (Pseudokirchneriella subcapitata (green algae)): 10 mg/l  
| Exposition 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  
| Exposition 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  
| Exposition time: 21 d  
| Method: OECD Test Guideline 211 |
| Toxicity to microorganisms | EC50: > 1,000 mg/l  
| Exposition time: 3 h  
| Test Type: Respiration inhibition  
| Method: OECD Test Guideline 209  
| NOEC: 1.3 mg/l  
| Exposition time: 3 h  
| Test Type: Respiration inhibition  
| Method: OECD Test Guideline 209 |

#### Elbasvir:

| Toxicity to fish | LC50 (Lepomis macrochirus (Bluegill sunfish)): > 10 mg/l  
| Exposition time: 96 h  
| Method: OECD Test Guideline 203  
| Remarks: No toxicity at the limit of solubility.  
<p>| LC50 (Menidia beryllina (Silverside)): &gt; 10 mg/l |</p>
<table>
<thead>
<tr>
<th>Toxicity to daphnia and other aquatic invertebrates</th>
<th>Remarks: No toxicity at the limit of solubility.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure time: 96 h</td>
<td></td>
</tr>
<tr>
<td>Remarks: No toxicity at the limit of solubility.</td>
<td></td>
</tr>
<tr>
<td>EC50 (Daphnia magna (Water flea)): &gt; 10 mg/l</td>
<td></td>
</tr>
<tr>
<td>Exposure time: 48 h</td>
<td></td>
</tr>
<tr>
<td>Method: OECD Test Guideline 202</td>
<td></td>
</tr>
<tr>
<td>LC50 (Americamysis): 7.7 mg/l</td>
<td></td>
</tr>
<tr>
<td>Exposure time: 96 h</td>
<td></td>
</tr>
<tr>
<td>Method: US-EPA OPPTS 850.1035</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Toxicity to algae/aquatic plants</th>
<th>Remarks: No toxicity at the limit of solubility.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure time: 96 h</td>
<td></td>
</tr>
<tr>
<td>Remarks: No toxicity at the limit of solubility.</td>
<td></td>
</tr>
<tr>
<td>NOEC (Pseudokirchneriella subcapitata (green algae)): 0.081 mg/l</td>
<td></td>
</tr>
<tr>
<td>Exposure time: 72 h</td>
<td></td>
</tr>
<tr>
<td>Method: OECD Test Guideline 201</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Toxicity to fish (Chronic toxicity)</th>
<th>Remarks: No toxicity at the limit of solubility.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure time: 32 d</td>
<td></td>
</tr>
<tr>
<td>Remarks: No toxicity at the limit of solubility.</td>
<td></td>
</tr>
<tr>
<td>NOEC (Pimephales promelas (fathead minnow)): 0.0023 mg/l</td>
<td></td>
</tr>
<tr>
<td>NOEC (Pimephales promelas (fathead minnow)): 0.0023 mg/l</td>
<td></td>
</tr>
<tr>
<td>Method: OECD Test Guideline 210</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Toxicity to microorganisms</th>
<th>Remarks: No toxicity at the limit of solubility.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure time: 3 h</td>
<td></td>
</tr>
<tr>
<td>Test Type: Respiration inhibition</td>
<td></td>
</tr>
<tr>
<td>NOEC (Leuciscus idus (Golden orfe)): &gt; 100 mg/l</td>
<td></td>
</tr>
<tr>
<td>Exposure time: 3 h</td>
<td></td>
</tr>
<tr>
<td>Test Type: Respiration inhibition</td>
<td></td>
</tr>
<tr>
<td>EC50: &gt; 1,000 mg/l</td>
<td></td>
</tr>
<tr>
<td>Test Type: Respiration inhibition</td>
<td></td>
</tr>
</tbody>
</table>

**Magnesium stearate:**

<table>
<thead>
<tr>
<th>Toxicity to fish</th>
<th>Remarks: Based on data from similar materials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure time: 48 h</td>
<td></td>
</tr>
<tr>
<td>Method: DIN 38412</td>
<td></td>
</tr>
<tr>
<td>LC50 (Leuciscus idus (Golden orfe)): &gt; 100 mg/l</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Toxicity to daphnia and other aquatic invertebrates</th>
<th>Remarks: Based on data from similar materials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure time: 47 h</td>
<td></td>
</tr>
<tr>
<td>EL50 (Daphnia magna (Water flea)): &gt; 1 mg/l</td>
<td></td>
</tr>
</tbody>
</table>
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

**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
  - Method: OECD Test Guideline 201
  - Remarks: Based on data from similar materials

**Titanium dioxide**:

**Toxicity to fish**:
- **LC50** (Oncorhynchus mykiss (rainbow trout)): > 100 mg/l
  - Exposure time: 96 h
  - Method: OECD Test Guideline 203

**Toxicity to daphnia and other aquatic invertebrates**:
- **EC50** (Daphnia magna (Water flea)): > 100 mg/l
  - Exposure time: 48 h

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

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

**Persistence and degradability**

**Components**:

**Cellulose**:
- Biodegradability: Result: Readily biodegradable.

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

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

Magnesium stearate:

<table>
<thead>
<tr>
<th>Biodegradability</th>
<th>Result: Not biodegradable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remarks</td>
<td>Based on data from similar materials</td>
</tr>
</tbody>
</table>

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

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

**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.

**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 69-65-8
Hydroxypropyl methylcellulose 9004-65-3
Croscarmellose sodium 74811-65-7
Sodium chloride 7647-14-5
Polyvinylpyrolidone / Vinyl Acetate Copolymer 25086-89-9
Cellulose 9004-34-6
D-Glucose, 4-O-β-D-galactopyranosyl-, monohydrate 64044-51-5
Grazoprevir 1350462-55-3
Elbasvir 1370468-36-2

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 9004-34-6
Magnesium stearate 557-04-0

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:

<table>
<thead>
<tr>
<th>Health</th>
<th>Flammability</th>
<th>Instability</th>
<th>Special hazard</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

HMIS® IV:

- **HEALTH**: *
- **FLAMMABILITY**: 3
- **PHYSICAL HAZARD**: 0

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

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
SAFETY DATA SHEET

Grazoprevir / Elbasvir Formulation

Version 13.0
Revision Date: 04/04/2023
SDS Number: 76219-00025
Date of last issue: 10/24/2022
Date of first issue: 03/17/2015

Law (Japan); ISO - International Organisation for Standardization; KECl - 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; RQ - 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: 04/04/2023

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

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