SAFETY DATA SHEET
Grazoprevir / Elbasvir Formulation

SECTION 1. IDENTIFICATION

Product name: Grazoprevir / Elbasvir Formulation
Other means of identification: No data available

Manufacturer or supplier's details
Company name of supplier: Merck & Co., Inc
Address: 2000 Galloping Hill Road
Kenilworth - New Jersey - U.S.A. 07033
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 Hazardous Products Regulations
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: 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.
May form explosive dust-air mixture during processing, handling or other means.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture

Components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>Common Name/Synonym</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>No data available</td>
<td>9004-34-6</td>
<td>&gt;= 5 - &lt; 10 *</td>
</tr>
<tr>
<td>Grazoprevir</td>
<td>No data available</td>
<td>1350462-55-3</td>
<td>&gt;= 5 - &lt; 10 *</td>
</tr>
<tr>
<td>Elbasvir</td>
<td>No data available</td>
<td>1370468-36-2</td>
<td>&gt;= 1 - &lt; 5 *</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>Octadecanoic acid, magnesi-um salt (2:1)</td>
<td>557-04-0</td>
<td>&gt;= 1 - &lt; 5 *</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>Titanium anhydride</td>
<td>13463-67-7</td>
<td>&gt;= 0.1 - &lt; 1 *</td>
</tr>
</tbody>
</table>

* Actual concentration or concentration range 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 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 spills 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.

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>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>CA AB OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Total dust)</td>
<td>10 mg/m³</td>
<td>CA BC OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (respirable dust fraction)</td>
<td>3 mg/m³</td>
<td>CA BC OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (total dust)</td>
<td>10 mg/m³</td>
<td>CA QC OEL</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>100 µg/m³ (OEB 2)</td>
<td>Internal</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>557-04-0</td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>CA AB OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>CA BC OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Inhalable)</td>
<td>10 mg/m³</td>
<td>CA BC OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (total dust)</td>
<td>10 mg/m³</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (respirable dust fraction)</td>
<td>3 mg/m³</td>
<td>CA BC OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWAEV (total dust)</td>
<td>10 mg/m³</td>
<td>CA QC OEL</td>
</tr>
</tbody>
</table>
**SAFETY DATA SHEET**

**Grazoprevir / Elbasvir Formulation**

<table>
<thead>
<tr>
<th>Particulate (Respirable particulate matter)</th>
<th>TWA (Respirable particulate matter)</th>
<th>3 mg/m³</th>
<th>ACGIH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Titanium dioxide 13463-67-7</td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>CA AB OEL</td>
</tr>
<tr>
<td></td>
<td>TWA (Total dust)</td>
<td>10 mg/m³</td>
<td>CA BC OEL</td>
</tr>
<tr>
<td></td>
<td>TWA (respirable dust fraction)</td>
<td>3 mg/m³</td>
<td>CA BC OEL</td>
</tr>
<tr>
<td></td>
<td>TWA (Total dust)</td>
<td>10 mg/m³</td>
<td>CA QC OEL</td>
</tr>
<tr>
<td></td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>(Titanium dioxide) 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 Hand protection**: Particulates type

**Material**: Chemical-resistant gloves

**Remarks**: Consider double gloving.

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

**Skin and body protection**: Work uniform or laboratory coat. Additional body garments should be used based upon the task being performed (e.g., sleevelets, apron, gauntlets, disposable suits) to avoid exposed skin surfaces. Use appropriate degowning techniques to remove potentially contaminated clothing.

**Hygiene measures**: 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

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>powder</td>
</tr>
<tr>
<td>Color</td>
<td>white</td>
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<tr>
<td>Odor</td>
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</tr>
<tr>
<td>Odor Threshold</td>
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</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>Vapor pressure</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Relative vapor 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>Autoignition 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>
</tbody>
</table>
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.
- 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
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

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
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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

Genotoxicity in vivo:

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:

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:

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
Titanium dioxide:
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES) Result: negative
Remarks: Based on data from similar materials

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.

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.

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.

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

**Magnesium stearate:**

Effects on fertility

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

Effects on 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
**Grazoprevir / Elbasvir Formulation**

<table>
<thead>
<tr>
<th>Species</th>
<th>Dog</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>15 mg/kg</td>
</tr>
<tr>
<td>LOAEL</td>
<td>100 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>270 Days</td>
</tr>
<tr>
<td>Target Organs</td>
<td>Liver, Blood, Bone marrow, gallbladder, spleen, Testis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Mouse</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>200 mg/kg</td>
</tr>
<tr>
<td>LOAEL</td>
<td>500 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>90 Days</td>
</tr>
<tr>
<td>Target Organs</td>
<td>Liver, Kidney, Blood</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Dog</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>20 mg/kg</td>
</tr>
<tr>
<td>LOAEL</td>
<td>600 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>30 Days</td>
</tr>
<tr>
<td>Target Organs</td>
<td>Blood, Testis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Monkey</th>
</tr>
</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>
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  
  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
**SAFETY DATA SHEET**

**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>7.5</td>
<td>08/27/2021</td>
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<td>03/17/2015</td>
</tr>
</tbody>
</table>

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  
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.  
LC50 (Menidia beryllina (Silverside)): | > 10 mg/l  
Exposure time: | 96 h  
Remarks: No toxicity at the limit of solubility. |

**Toxicity to daphnia and other aquatic invertebrates:**

| EC50 (Daphnia magna (Water flea)): | > 10 mg/l  
Exposure time: | 48 h  
Method: OECD Test Guideline 202  
Remarks: No toxicity at the limit of solubility.  
LC50 (Americamysis): | 7.7 mg/l  
Exposure time: | 96 h  
Method: US-EPA OPPTS 850.1035  
Remarks: No toxicity at the limit of solubility. |

**Toxicity to algae/aquatic plants:**

| EC50 (Pseudokirchneriella subcapitata (algae)): | > 0.081 mg/l  
Exposure time: | 72 h  
Method: OECD Test Guideline 201  
Remarks: No toxicity at the limit of solubility.  
NOEC (Pseudokirchneriella subcapitata (green algae)): | 0.081 mg/l  
Exposure time: | 72 h  
Method: OECD Test Guideline 201  
Remarks: No toxicity at the limit of solubility. |

**Toxicity to fish (Chronic toxicity):**

| NOEC (Pimephales promelas (fathead minnow)): | 0.0023 mg/l |
### Grazoprevir / Elbasvir Formulation

<table>
<thead>
<tr>
<th>Substance</th>
<th>Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity)</th>
<th>Toxicity to microorganisms</th>
<th>Toxicity to algae/aquatic plants</th>
<th>Toxicity to microorganisms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnesium stearate:</td>
<td>NOEC (Daphnia magna (Water flea)): 0.84 mg/l</td>
<td>EC50: &gt; 1,000 mg/l</td>
<td>EL50 (Pseudokirchneriella subcapitata (green algae)): &gt; 1 mg/l</td>
<td>EC10 (Pseudomonas putida): &gt; 100 mg/l</td>
</tr>
<tr>
<td></td>
<td>Exposure time: 21 d</td>
<td>Exposure time: 3 h</td>
<td>Exposure time: 72 h</td>
<td>Exposure time: 16 h</td>
</tr>
<tr>
<td></td>
<td>Method: OECD Test Guideline 211</td>
<td>Test Type: Respiration inhibition</td>
<td>Method: OECD Test Guideline 201</td>
<td>Test substance: Water Accommodated Fraction</td>
</tr>
<tr>
<td></td>
<td>Remarks: No toxicity at the limit of solubility.</td>
<td>Method: OECD Test Guideline 209</td>
<td>Remarks: Based on data from similar materials</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>NOEC: 271.9 mg/l</td>
<td>No toxicity at the limit of solubility.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Exposure time: 3 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Test Type: Respiration inhibition</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Method: OECD Test Guideline 209</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Titanium dioxide:**

| Substance                  | Toxicity to fish                                                      | |
|----------------------------|-----------------------------------------------------------------------| |
|                           | LC50 (Oncorhynchus mykiss (rainbow trout)): > 100 mg/l                | |
|                           | Exposure time: 96 h                                                   | |
|                           | Test substance: Water Accommodated Fraction                            | |
|                           | Remarks: Based on data from similar materials                          | |

**Exposure time:**
- 32 d
- 30 d
- 21 d
- 21 d
- 3 h
- 72 h
- 72 h
- 72 h
- 16 h
- 96 h
SAFETY DATA SHEET

Grazoprevir / Elbasvir Formulation

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

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:
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Grazoprevir / Elbasvir Formulation

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</tr>
</tbody>
</table>

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.
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.
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**

**TDG**

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

Class : 9  
Packing group : III  
Labels : 9  
ERG Code : 171  
Marine pollutant : yes (Elbasvir)

**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.

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**SECTION 15. REGULATORY INFORMATION**

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

AICS : not determined  
DSL : not determined  
IECSC : not determined

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**SECTION 16. OTHER INFORMATION**

**Full text of other abbreviations**

ACGIH : USA. ACGIH Threshold Limit Values (TLV)  
CA BC OEL : Canada. British Columbia OEL  
CA QC OEL : Québec. Regulation respecting occupational health and safety, Schedule 1, Part 1: Permissible exposure values for airborne contaminants  
ACGIH / TWA : 8-hour, time-weighted average  
CA AB OEL / TWA : 8-hour Occupational exposure limit  
CA BC OEL / TWA : 8-hour time weighted average  
CA QC OEL / TWA EV : Time-weighted average exposure value
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Grazoprevir / Elbasvir Formulation

Version 7.5
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SDS Number: 76204-00020
Date of last issue: 04/09/2021
Date of first issue: 03/17/2015

AIIC - 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 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; 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; WHMIS - Workplace Hazardous Materials Information System


Revision Date: 08/27/2021
Date format: mm/dd/yyyy

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.

CA / Z8