SAFETY DATA SHEET
Grazoprevir / Elbasvir Formulation

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Grazoprevir / Elbasvir Formulation
Manufacturer or supplier’s details
Company name of supplier: MSD
Address: Avenida 16 de Septiembre No. 301
Xaltocan - Xochimilco Mexico 16090
Telephone: 52 55 57284444
Telefax: 908-735-1496
Emergency telephone: 1-908-423-6000
E-mail address: EHSDATATESTeward@msd.com
Recommended use of the chemical and restrictions on use
Recommended use: Pharmaceutical

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification
Carcinogenicity (Inhalation): Category 2
Specific target organ systemic 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/ face protection.
Response:
P308 + P313 IF exposed or concerned: Get medical advice/ attention.
Storage:
P405 Store locked up.
Disposal:
P501 Dispose of contents/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

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium chloride</td>
<td>CAS-No. 7647-14-5, Concentration &gt;= 5 - &lt; 10</td>
</tr>
<tr>
<td>Cellulose</td>
<td>CAS-No. 9004-34-6, Concentration &gt;= 5 - &lt; 10</td>
</tr>
<tr>
<td>Grazoprevir</td>
<td>CAS-No. 1350462-55-3, Concentration &gt;= 5 - &lt; 10</td>
</tr>
<tr>
<td>Elbasvir</td>
<td>CAS-No. 1370468-36-2, Concentration &gt;= 1 - &lt; 5</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>CAS-No. 557-04-0, Concentration &gt;= 1 - &lt; 5</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>CAS-No. 13463-67-7, Concentration &gt;= 0.1 - &lt; 1</td>
</tr>
</tbody>
</table>

### 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.

**Notes to physician**
Treat symptomatically and supportively.

### SECTION 5. FIRE-FIGHTING MEASURES

**Suitable extinguishing media**
Water spray
Alcohol-resistant foam
Carbon dioxide (CO2)
## SECTION 6. ACCIDENTAL RELEASE MEASURES

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

**Environmental precautions**: Discharge into the environment must be avoided. Prevent further leakage or spillage if safe to do so. Retain and dispose of contaminated wash water. Local authorities should be advised if significant 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.

Hygiene measures:
- Ensure that eye flushing systems and safety showers are located close to the working place.
- When using do not eat, drink or smoke.
- Wash contaminated clothing before re-use.
- The effective operation of a facility should include review of engineering controls, proper personal protective equipment, appropriate degowning and decontamination procedures, industrial hygiene monitoring, medical surveillance and the use of administrative controls.

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>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>VLE-PPT</td>
<td>10 mg/m³</td>
<td>NOM-010-STPS-2014</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Grazoprevir</td>
<td>1350462-55-3</td>
<td>TWA</td>
<td>25 µg/m³ (OEB 3)</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wipe limit</td>
<td>250 µg/100 cm²</td>
<td>Internal</td>
</tr>
<tr>
<td>Elbasvir</td>
<td>1370468-36-2</td>
<td>TWA</td>
<td>100 µg/m³ (OEB 2)</td>
<td>Internal</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>557-04-0</td>
<td>VLE-PPT</td>
<td>10 mg/m³</td>
<td>NOM-010-STPS-2014</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(Inhalable fraction)</td>
<td>10 mg/m³</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(Respirable fraction)</td>
<td>3 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</td>
<td>VLE-PPT</td>
<td>10 mg/m³</td>
<td>NOM-010-STPS-2014</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
</tbody>
</table>
Engineering measures:
All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment. Containment technologies suitable for controlling compounds are required to control at source and to prevent migration of the compound to uncontrolled areas (e.g., open-face containment devices). Minimize open handling.

Personal protective equipment

Respiratory protection:
Use respiratory protection unless adequate local exhaust ventilation is provided or exposure assessment demonstrates that exposures are within recommended exposure guidelines.

Filter type:
Particulates type

Hand protection:
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.

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.
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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.
  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:**

**Sodium chloride:**
- **Acute oral toxicity**: LD50 (Rat): 3,550 mg/kg
- **Acute inhalation toxicity**: LC50 (Rat): > 42 mg/l
  Exposure time: 1 h
  Test atmosphere: dust/mist
- **Acute dermal toxicity**: LD50 (Rabbit): > 5,000 mg/kg

**Cellulose:**
- **Acute oral toxicity**: LD50 (Rat): > 5,000 mg/kg
- **Acute inhalation toxicity**: LC50 (Rat): > 5.8 mg/l
  Exposure time: 4 h
  Test atmosphere: dust/mist
- **Acute dermal toxicity**: LD50 (Rabbit): > 2,000 mg/kg

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

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

**Magnesium stearate:**
- **Acute oral toxicity**: LD50 (Rat): > 2,000 mg/kg
  Method: OECD Test Guideline 423
  Assessment: The substance or mixture has no acute oral toxicity
  Remarks: Based on data from similar materials
- **Acute dermal toxicity**: LD50 (Rabbit): > 2,000 mg/kg
  Remarks: Based on data from similar materials

**Titanium dioxide:**
- **Acute oral toxicity**: LD50 (Rat): > 5,000 mg/kg
SAFETY DATA SHEET

Grazoprevir / Elbasvir Formulation

Acute inhalation toxicity: LC50 (Rat): > 6.82 mg/l
  Exposure time: 4 h
  Test atmosphere: dust/mist
  Assessment: The substance or mixture has no acute inhalation toxicity

Skin corrosion/irritation
Not classified based on available information.

Components:

Sodium chloride:
Species: Rabbit
Result: No skin irritation

Grazoprevir:
Result: No skin irritation

Elbasvir:
Species: reconstructed human epidermis (RhE)
Result: No skin irritation

Magnesium stearate:
Species: Rabbit
Result: No skin irritation
Remarks: Based on data from similar materials

Titanium dioxide:
Species: Rabbit
Result: No skin irritation

Serious eye damage/eye irritation
Not classified based on available information.

Components:

Sodium chloride:
Species: Rabbit
Result: No eye irritation

Grazoprevir:
Species: Bovine cornea
Result: No eye irritation

Elbasvir:
Species: Bovine cornea
Result: No eye irritation
Magnesium stearate:
Species: Rabbit
Result: No eye irritation
Remarks: Based on data from similar materials

Titanium dioxide:
Species: Rabbit
Result: No eye irritation

Respiratory or skin sensitization
Skin sensitization
Not classified based on available information.
Respiratory sensitization
Not classified based on available information.

Components:
Sodium chloride:
Test Type: Local lymph node assay (LLNA)
Routes of exposure: Skin contact
Species: Mouse
Result: negative

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:

Sodium chloride:
Genotoxicity in vitro:
- Test Type: In vitro mammalian cell gene mutation test
  Result: positive
- Test Type: Bacterial reverse mutation assay (AMES)
  Result: negative
- Test Type: Saccharomyces cerevisiae, gene mutation assay (in vitro)
  Result: positive
- Test Type: DNA damage and repair, unscheduled DNA synthesis in mammalian cells (in vitro)
  Result: positive
- Test Type: Chromosome aberration test in vitro
  Result: positive
- Test Type: Chromosome aberration test in vitro
  Result: negative

Genotoxicity in vivo:
- Test Type: In vivo micronucleus test
  Species: Mouse
  Application Route: Intraperitoneal injection
  Result: negative
- Test Type: Mutagenicity (in vivo mammalian bone-marrow cytogenetic test, chromosomal analysis)
  Species: Rat
  Application Route: Intraperitoneal injection
  Result: positive

Germ cell mutagenicity assessment:
Weight of evidence does not support classification as a germ cell mutagen.

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:
<table>
<thead>
<tr>
<th>Material</th>
<th>Genotoxicity in vitro</th>
<th>Genotoxicity in vivo</th>
<th>Germ cell mutagenicity - Assessment</th>
</tr>
</thead>
</table>
| Grazoprevir / Elbasvir Formulation | Test Type: Bacterial reverse mutation assay (AMES)  
Result: negative  
Test Type: Chromosome aberration test in vitro  
Result: negative | Test Type: In vivo micronucleus test  
Application Route: Oral  
Result: negative | Weight of evidence does not support classification as a germ cell mutagen. |
| Elbasvir            | Test Type: Bacterial reverse mutation assay (AMES)  
Result: negative  
Test Type: Chromosome aberration test in vitro  
Result: negative | Test Type: In vivo micronucleus test  
Species: Rat  
Application Route: Oral  
Result: negative | Weight of evidence does not support classification as a germ cell mutagen. |
| Magnesium stearate  | 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    | Test Type: Bacterial reverse mutation assay (AMES)  
Result: negative | Test Type: In vivo micronucleus test  
Species: Mouse  
Result: negative |  |
| **Carcinogenicity** | Suspected of causing cancer if inhaled. |  |  |
Components:

Sodium chloride:
Species: Rat
Application Route: Ingestion
Exposure time: 2 Years
Result: negative

Cellulose:
Species: Rat
Application Route: Ingestion
Exposure time: 72 weeks
Result: negative

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

Carcinogenicity - Assessment: Limited evidence of carcinogenicity in inhalation studies with animals.

Reproductive toxicity
Not classified based on available information.

Components:

Cellulose:
Effects on fertility: Test Type: One-generation reproduction toxicity study
Species: Rat
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**

<table>
<thead>
<tr>
<th>Test Type: Embryo-fetal development</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species: Rat</td>
</tr>
<tr>
<td>Application Route: Oral</td>
</tr>
<tr>
<td>Embryo-fetal toxicity.: NOAEL: 200 mg/kg body weight</td>
</tr>
<tr>
<td>Result: No effects on fetal development.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Test Type: Embryo-fetal development</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species: Rabbit</td>
</tr>
<tr>
<td>Application Route: Oral</td>
</tr>
<tr>
<td>Embryo-fetal toxicity.: NOAEL: 200 mg/kg body weight</td>
</tr>
<tr>
<td>Result: No effects on fetal development.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Test Type: Embryo-fetal development</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species: Rabbit</td>
</tr>
<tr>
<td>Application Route: Intravenous</td>
</tr>
<tr>
<td>Embryo-fetal toxicity.: NOAEL: 100 mg/kg body weight</td>
</tr>
<tr>
<td>Result: No effects on fetal development.</td>
</tr>
</tbody>
</table>

**Elbasvir**

**Effects on fertility**

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

**Effects on fetal development**

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

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

**Magnesium stearate**

**Effects on fertility**

<table>
<thead>
<tr>
<th>Test Type: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species: Rat</td>
</tr>
<tr>
<td>Application Route: Ingestion</td>
</tr>
<tr>
<td>Method: OECD Test Guideline 422</td>
</tr>
<tr>
<td>Result: negative</td>
</tr>
<tr>
<td>Remarks: Based on data from similar materials</td>
</tr>
</tbody>
</table>

**Effects on fetal development**

<table>
<thead>
<tr>
<th>Test Type: Embryo-fetal development</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species: Rat</td>
</tr>
<tr>
<td>Application Route: Ingestion</td>
</tr>
<tr>
<td>Result: negative</td>
</tr>
<tr>
<td>Remarks: Based on data from similar materials</td>
</tr>
</tbody>
</table>
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:

Sodium chloride:
Species: Rat
LOAEL: 2,533 mg/kg
Application Route: Ingestion
Exposure time: 2 y

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, Testis, Blood, Bone marrow, gallbladder, spleen

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: Testis, Blood

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:**

**Sodium chloride:**
Toxicity to fish: LC50 (Lepomis macrochirus (Bluegill sunfish)): 5,840 mg/l
Exposure time: 96 h

Toxicity to daphnia and other aquatic invertebrates: EC50 (Daphnia magna (Water flea)): 4,136 mg/l
Exposure time: 48 h

Toxicity to algae/aquatic plants: EC50: > 2,000 mg/l
Exposure time: 96 h

Toxicity to fish (Chronic toxicity): NOEC (Pimephales promelas (fathead minnow)): 252 mg/l
Exposure time: 33 d

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity): NOEC (Daphnia pulex (Water flea)): 314 mg/l
Exposure time: 21 d

Toxicity to microorganisms: EC10: > 1,000 mg/l

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

**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.

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
Exposure time: 32 d
Method: OECD Test Guideline 210

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity):

NOEC (Daphnia magna (Water flea)): 0.84 mg/l
Exposure time: 21 d
Method: OECD Test Guideline 211
Remarks: No toxicity at the limit of solubility.

Toxicity to microorganisms:

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

NOEC: 271.9 mg/l
Exposure time: 3 h
Test Type: Respiration inhibition
Method: OECD Test Guideline 209

Magnesium stearate:

Toxicity to fish:

LC50 (Leuciscus idus (Golden orfe)): > 100 mg/l
Exposure time: 48 h
Method: DIN 38412
Remarks: Based on data from similar materials

Toxicity to daphnia and other aquatic invertebrates:

EL50 (Daphnia magna (Water flea)): > 1 mg/l
Exposure time: 47 h
Test substance: Water Accommodated Fraction
Remarks: Based on data from similar materials
No toxicity at the limit of solubility.

Toxicity to algae/aquatic plants:

EL50 (Pseudokirchneriella subcapitata (green algae)): > 1 mg/l
Exposure time: 72 h
Test substance: Water Accommodated Fraction
Method: OECD Test Guideline 201
Remarks: Based on data from similar materials
No toxicity at the limit of solubility.

NOELR (Pseudokirchneriella subcapitata (green algae)): > 1 mg/l
Exposure time: 72 h
Test substance: Water Accommodated Fraction
Method: OECD Test Guideline 201
Toxicity to microorganisms:
EC10 (Pseudomonas putida): > 100 mg/l
Exposure time: 16 h
Test substance: Water Accommodated Fraction
Remarks: Based on data from similar materials

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

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

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

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

Persistence and degradability

Components:

Cellulose:
Biodegradability:
Result: Readily biodegradable.

Grazoprevir:
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
**Grazoprevir / Elbasvir Formulation**

- **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

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**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
SAFETY DATA SHEET

Grazoprevir / Elbasvir Formulation

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

NOM-002-SCT
UN number: UN 3077
Proper shipping name: ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Elbasvir)
Class: 9
Packing group: III
Labels: 9

Special precautions for user
The transport classification(s) provided herein are for informational purposes only, and solely based upon the properties of the unpackaged material as it is described within this Safety Data Sheet. Transportation classifications may vary by mode of transportation, package sizes, and variations in regional or country regulations.

SECTION 15. REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture
Federal Law for the control of chemical precursors, essential chemical products and machinery for producing capsules, tablets and pills: Not applicable

The ingredients of this product are reported in the following inventories:
AICS: not determined
DSL: not determined
IECSC: not determined
### SECTION 16. OTHER INFORMATION

**Full text of other abbreviations**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACGIH</td>
<td>USA. ACGIH Threshold Limit Values (TLV)</td>
</tr>
<tr>
<td>NOM-010-STPS-2014</td>
<td>Mexico. Norm NOM-010-STPS-2014 on Chemicals Polluting the Work Environment - Identification, Assessment and Control - Appendix 1 Occupational Exposure Limits</td>
</tr>
<tr>
<td>ACGIH / TWA</td>
<td>8-hour, time-weighted average</td>
</tr>
<tr>
<td>NOM-010-STPS-2014 / VLE-PPT</td>
<td>Time weighted average limit value</td>
</tr>
</tbody>
</table>

AICS - Australian Inventory of Chemical Substances; ANTT - National Agency for Transport by Land of Brazil; ASTM - American Society for the Testing of Materials; bw - Body weight; CMR - Carcinogen, Mutagen or Reproductive Toxicant; CPR - Controlled Products Regulations; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; ELx - Loading rate associated with x% response; EmS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; ERG - Emergency Response Guide; GHS - Globally Harmonized System; GLP - Good Laboratory Practice; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; IBC - International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk; IC50 - Half maximal inhibitory concentration; ICAO - International Civil Aviation Organization; IECSCL - Inventory of Existing Chemical Substances in China; IMDG - International Maritime Dangerous Goods; IMO - International Maritime Organization; ISH - Industrial Safety and Health Law (Japan); ISO - International Organisation for Standardization; KECI - Korea Existing Chemicals Inventory; LC50 - Lethal Concentration to 50% of a test population; LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose); MARPOL - International Convention for the Prevention of Pollution from Ships; n.o.s. - Not Otherwise Specified; Nch - Chilean Norm; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NOM - Official Mexican Norm; NTP - National Toxicology Program; NZIoC - New Zealand Inventory of Chemicals; OECD - Organization for Economic Co-operation and Development; OPPTS - Office of Chemical Safety and Pollution Prevention; PBT - Persistent, Bioaccumulative and Toxic substance; PICCS - Philippines Inventory of Chemicals and Chemical Substances; (Q)SAR - (Quantitative) Structure Activity Relationship; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; SADT - Self-Accelerating Decomposition Temperature; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance Inventory; TDG - Transportation of Dangerous Goods; TSCA - Toxic Substances Control Act (United States); UN - United Nations; UNRTDG - United Nations Recommendations on the Transport of Dangerous Goods; vPvB - Very Persistent and Very Bioaccumulative; WHMIS - Workplace Hazardous Materials Information System

**Sources of key data used to compile the Material Safety Data Sheet**


**Revision Date**

04/24/2019

The information is considered as correct, but not exhaustive, and will be used only as a guide, which is based in the current knowledge of the substance or mixture, and is applicable to proper safety precautions for the product.