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 : 2000 Galloping Hill Road
Kenilworth - New Jersey - U.S.A. 07033
Telephone : 908-740-4000
Telefax : 908-735-1496
Emergency telephone : 1-908-423-6000
E-mail address : EHSDATASTeward@merck.com

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

SECTION 2. HAZARDS IDENTIFICATION

GHS classification in accordance with 29 CFR 1910.1200
Combustible dust

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 : 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/ face protection.

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

Date of last issue: 10/16/2018
Date of first issue: 03/17/2015
**SAFETY DATA SHEET**

Grazoprevir / Elbasvir Formulation

**Version** 10.0  
**Revision Date:** 04/24/2019  
**SDS Number:** 76219-00014  
**Date of last issue:** 10/16/2018  
**Date of first issue:** 03/17/2015

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**Storage:**  
P405 Store locked up.

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

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

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**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

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**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.

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**SECTION 5. FIRE-FIGHTING MEASURES**
### 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 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.
SAFETY DATA SHEET

Grazoprevir / Elbasvir Formulation

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.
Keep 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>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Respirable)</td>
<td>5 mg/m³</td>
<td>NIOSH REL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (total)</td>
<td>10 mg/m³</td>
<td>NIOSH REL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (total dust)</td>
<td>15 mg/m³</td>
<td>OSHA Z-1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (respirable fraction)</td>
<td>5 mg/m³</td>
<td>OSHA Z-1</td>
</tr>
<tr>
<td>Grazoprevir</td>
<td>1350462-55-3</td>
<td>TWA</td>
<td>25 µg/m³ (OEB 3)</td>
<td>Internal</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>TWA (Inhalable fraction)</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Respirable fraction)</td>
<td>3 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</td>
<td>TWA (total dust)</td>
<td>15 mg/m³</td>
<td>OSHA Z-1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA</td>
<td>10 mg/m³ (Titanium dioxide)</td>
<td>ACGIH</td>
</tr>
</tbody>
</table>

Engineering measures : All engineering controls should be implemented by facility
design and operated in accordance with GMP principles to protect products, workers, and the environment. Containment technologies suitable for controlling compounds are required to control at source and to prevent migration of the compound to uncontrolled areas (e.g., open-face containment devices). Minimize open handling.

**Personal protective equipment**

**Respiratory protection**: General and local exhaust ventilation is recommended to maintain vapor exposures below recommended limits. Where concentrations are above recommended limits or are unknown, appropriate respiratory protection should be worn. Follow OSHA respirator regulations (29 CFR 1910.134) and use NIOSH/MSHA approved respirators. Protection provided by air purifying respirators against exposure to any hazardous chemical is limited. Use a positive pressure air supplied respirator if there is any potential for uncontrolled release, exposure levels are unknown, or any other circumstance where air purifying respirators may not provide adequate protection.

**Hand protection**

**Material**: Chemical-resistant gloves

**Remarks**: Consider double gloving.

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

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

**Hygiene measures**: 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.

### 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>
</tr>
<tr>
<td>Odor</td>
<td>No data available</td>
</tr>
<tr>
<td>Odor Threshold</td>
<td>No data available</td>
</tr>
</tbody>
</table>
### SECTION 10. STABILITY AND REACTIVITY

<table>
<thead>
<tr>
<th>Property</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Reactivity</strong></td>
<td>Not classified as a reactivity hazard.</td>
</tr>
<tr>
<td><strong>Chemical stability</strong></td>
<td>Stable under normal conditions.</td>
</tr>
<tr>
<td><strong>Possibility of hazardous reactions</strong></td>
<td>May form explosive dust-air mixture during processing, handling or other means.</td>
</tr>
<tr>
<td><strong>Flammability (solid, gas)</strong></td>
<td>May form explosive dust-air mixture during processing, handling or other means.</td>
</tr>
<tr>
<td><strong>Flammability (liquids)</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Upper explosion limit / Upper flammability limit</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Lower explosion limit / Lower flammability limit</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Vapor pressure</strong></td>
<td>Not applicable</td>
</tr>
<tr>
<td><strong>Relative vapor density</strong></td>
<td>Not applicable</td>
</tr>
<tr>
<td><strong>Relative density</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Density</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Solubility(ies)</strong></td>
<td>Water solubility: No data available</td>
</tr>
<tr>
<td><strong>Partition coefficient: n-octanol/water</strong></td>
<td>Not applicable</td>
</tr>
<tr>
<td><strong>Autoignition temperature</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Decomposition temperature</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Viscosity</strong></td>
<td>Viscosity, kinematic: Not applicable</td>
</tr>
<tr>
<td><strong>Explosive properties</strong></td>
<td>Not explosive</td>
</tr>
<tr>
<td><strong>Oxidizing properties</strong></td>
<td>The substance or mixture is not classified as oxidizing.</td>
</tr>
<tr>
<td><strong>Particle size</strong></td>
<td>No data available</td>
</tr>
</tbody>
</table>
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
  LD50 (Mouse): > 1,000 mg/kg

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

**Magnesium stearate:**
- **Acute oral toxicity:** LD50 (Rat): > 2,000 mg/kg
  Method: OECD Test Guideline 423
  Assessment: The substance or mixture has no acute oral toxicity
  Remarks: Based on data from similar materials
- **Acute dermal toxicity:** LD50 (Rabbit): > 2,000 mg/kg
  Remarks: Based on data from similar materials
Titanium dioxide:
Acute oral toxicity: LD50 (Rat): > 5,000 mg/kg
Acute inhalation toxicity: LC50 (Rat): > 6.82 mg/l
  Exposure time: 4 h
  Test atmosphere: dust/mist
  Assessment: The substance or mixture has no acute inhalation toxicity

Skin corrosion/irritation
Not classified based on available information.

Components:
Grazoprevir:
Result: No skin irritation

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

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

Titanium dioxide:
Species: Rabbit
Result: No skin irritation

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

Components:
Grazoprevir:
Species: Bovine cornea
Result: No eye irritation

Elbasvir:
Species: Bovine cornea
Result: No eye irritation

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

Titanium dioxide:
Species: Rabbit
Result : No eye irritation

Respiratory or skin sensitization

Skin sensitization
Not classified based on available information.

Respiratory sensitization
Not classified based on available information.

Components:

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

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

Magnesium stearate:
Test Type : Maximization Test
Routes of exposure : Skin contact
Species : Guinea pig
Method : OECD Test Guideline 406
Result : negative
Remarks : Based on data from similar materials

Titanium dioxide:
Test Type : Local lymph node assay (LLNA)
Routes of exposure : Skin contact
Species : Mouse
Result : negative

Germ cell mutagenicity
Not classified based on available information.

Components:

Cellulose:
Genotoxicity in vitro : Test Type: Bacterial reverse mutation assay (AMES)
Result: negative

Test Type: In vitro mammalian cell gene mutation test
Result: negative

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

**Grazoprevir:**
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES) Result: negative
Test Type: Chromosome aberration test in vitro
Result: negative

Genotoxicity in vivo: Test Type: In vivo micronucleus test
Application Route: Oral
Result: negative

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

**Elbasvir:**
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES) Result: negative
Test Type: Chromosome aberration test in vitro
Result: negative

Genotoxicity in vivo: Test Type: In vivo micronucleus test
Species: Rat
Application Route: Oral
Result: negative

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

**Magnesium stearate:**
Genotoxicity in vitro: Test Type: In vitro mammalian cell gene mutation test
Result: negative
Remarks: Based on data from similar materials

Test Type: Chromosome aberration test in vitro
Method: OECD Test Guideline 473
Result: negative
Remarks: Based on data from similar materials

Test Type: Bacterial reverse mutation assay (AMES)
Result: negative
Remarks: Based on data from similar materials

**Titanium dioxide:**
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES) Result: negative

Genotoxicity in vivo: Test Type: In vivo micronucleus test
Species: Mouse
Result: negative
Carcinogenicity

Suspected of causing cancer if inhaled.

| Components: |

<table>
<thead>
<tr>
<th>Cellulose:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species</td>
</tr>
<tr>
<td>Application Route</td>
</tr>
<tr>
<td>Exposure time</td>
</tr>
<tr>
<td>Result</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Titanium dioxide:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species</td>
</tr>
<tr>
<td>Application Route</td>
</tr>
<tr>
<td>Exposure time</td>
</tr>
<tr>
<td>Method</td>
</tr>
<tr>
<td>Result</td>
</tr>
<tr>
<td>Remarks</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>IARC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 2B: Possibly carcinogenic to humans</td>
</tr>
<tr>
<td>Titanium dioxide</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>OSHA</th>
</tr>
</thead>
<tbody>
<tr>
<td>No component of this product present at levels greater than or equal to 0.1% is on OSHA’s list of regulated carcinogens.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>NTP</th>
</tr>
</thead>
<tbody>
<tr>
<td>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.</td>
</tr>
</tbody>
</table>

Reproductive toxicity

Not classified based on available information.

| Components: |

<table>
<thead>
<tr>
<th>Cellulose:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effects on fertility</td>
</tr>
<tr>
<td>Species: Rat</td>
</tr>
<tr>
<td>Application Route: Ingestion</td>
</tr>
<tr>
<td>Result: negative</td>
</tr>
</tbody>
</table>

| Effects on fetal development | Test Type: Fertility/early embryonic development |
| Species: Rat |
| Application Route: Ingestion |
| Result: negative |

<table>
<thead>
<tr>
<th>Grazoprevir:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effects on fertility</td>
</tr>
<tr>
<td>Species: Rat</td>
</tr>
<tr>
<td>Application Route: Oral</td>
</tr>
</tbody>
</table>
**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

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
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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:**

**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:** NOEC (Daphnia magna (Water flea)): 5 mg/l
aquatic invertebrates (Chronic toxicity)  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
<table>
<thead>
<tr>
<th>Material</th>
<th>Toxicity to fish Description</th>
<th>Experiments and Methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnesium stearate</td>
<td>LC50 (Leuciscus idus (Golden orfe)): &gt; 100 mg/l</td>
<td>Exposure time: 48h Method: DIN 38412 Remarks: Based on data from similar materials</td>
</tr>
<tr>
<td></td>
<td>EL50 (Pseudokirchneriella subcapitata (green algae)): &gt; 1 mg/l</td>
<td>Exposure time: 72h 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)): &gt; 1 mg/l Exposure time: 72h Test substance: Water Accommodated Fraction Method: OECD Test Guideline 201 Remarks: Based on data from similar materials</td>
</tr>
<tr>
<td></td>
<td>EC10 (Pseudomonas putida): &gt; 100 mg/l</td>
<td>Exposure time: 16h Test substance: Water Accommodated Fraction Remarks: Based on data from similar materials</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>LC50 (Oncorhynchus mykiss (rainbow trout)): &gt; 100 mg/l</td>
<td>Exposure time: 96h Method: OECD Test Guideline 203</td>
</tr>
<tr>
<td></td>
<td>EC50 (Daphnia magna (Water flea)): &gt; 100 mg/l</td>
<td>Exposure time: 48h</td>
</tr>
<tr>
<td></td>
<td>EC50 (Skeletonema costatum (marine diatom)): &gt; 10,000 mg/l</td>
<td>Exposure time: 72h</td>
</tr>
<tr>
<td></td>
<td>EC50: &gt; 1,000 mg/l</td>
<td></td>
</tr>
</tbody>
</table>

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
Persistence and degradability

**Components:**

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

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

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

**Magnesium stearate:**
- Biodegradability: Result: Not biodegradable.
  - Remarks: Based on data from similar materials

Bioaccumulative potential

**Components:**

**Grazoprevir:**
- Bioaccumulation: Species: Lepomis macrochirus (Bluegill sunfish)
  - Bioconcentration factor (BCF): 7.62
  - Partition coefficient: n-octanol/water: log Pow: 3.72

**Elbasvir:**
- Bioaccumulation: Species: Lepomis macrochirus (Bluegill sunfish)
  - Bioconcentration factor (BCF): 82
  - Method: OECD Test Guideline 305
  - Partition coefficient: n-octanol/water: log Pow: 6.54

**Magnesium stearate:**
- Partition coefficient: n-octanol/water: log Pow: > 4

Mobility in soil

**Components:**

**Grazoprevir:**
- Distribution among environment: log Koc: 4.01
mental compartments

**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. (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

EPCRA - Emergency Planning and Community Right-to-Know

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
Croskarmellose sodium 74811-65-7
Sodium chloride 7647-14-5
Polyvinylpyrrolidone / Vinyl Acetate Copolymer 25086-89-9
Cellulose 9004-34-6
D-Glucose, 4-O-.beta.-D-galactopyranosyl-, monohydrate 64044-51-5
Grazoprevir 1350462-55-3
California Prop. 65
WARNING: This product can expose you to chemicals including Titanium dioxide, tert-Butyl-4-methoxyphenol, 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

<table>
<thead>
<tr>
<th>Chemical</th>
<th>Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>557-04-0</td>
</tr>
</tbody>
</table>

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:**

- Flammability: 1
- Health: 0
- Instability: 0

**HMIS® IV:**

- HEALTH: 2
- 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)
- NIOSH REL: USA. NIOSH Recommended Exposure Limits
- OSHA Z-1: USA. Occupational Exposure Limits (OSHA) - Table Z-1 Limits for Air Contaminants
- ACGIH / TWA: 8-hour, time-weighted average
- 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

AICS - Australian Inventory of Chemical Substances; 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 Sub-
SAFETY DATA SHEET

Grazoprevir / Elbasvir Formulation

Stances List (Canada); ECx - Concentration associated with x% response; EHS - Extremely Hazardous Substance; ELx - Loading rate associated with x% response; EmS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; ERG - Emergency Response Guide; GHS - Globally Harmonized System; GLP - Good Laboratory Practice; HMIS - Hazardous Materials Identification System; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; IBC - International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk; IC50 - Half maximal inhibitory concentration; ICAO - International Civil Aviation Organization; IECSC - Inventory of Existing Chemical Substances in China; IMDG - International Maritime Dangerous Goods; IMO - International Maritime Organization; ISHL - Industrial Safety and Health Law (Japan); ISO - International Organisation for Standardization; KECI - Korea Existing Chemicals Inventory; LC50 - Lethal Concentration to 50% of a test population; LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose); MARPOL - International Convention for the Prevention of Pollution from Ships; MSHA - Mine Safety and Health Administration; n.o.s. - Not Otherwise Specified; NFPA - National Fire Protection Association; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NTP - National Toxicology Program; NZIoC - New Zealand Inventory of Chemicals; OECD - Organization for Economic Co-operation and Development; OPPTS - Office of Chemical Safety and Pollution Prevention; PBT - Persistent, Bioaccumulative and Toxic substance; PICCS - Philippines Inventory of Chemicals and Chemical Substances; (Q)SAR - (Quantitative) Structure Activity Relationship; RCRA - Resource Conservation and Recovery Act; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; RO - Reportable Quantity; SADT - Self-Accelerating Decomposition Temperature; SARA - Superfund Amendments and Reauthorization Act; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance Inventory; 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 : 04/24/2019

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