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
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 the Hazardous Products Regulations
Not a hazardous substance or mixture.

GHS label elements
Not a hazardous substance or mixture.

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>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 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.
SAFETY DATA SHEET

Grazoprevir / Elbasvir Formulation

Get medical attention if symptoms occur.

In case of eye contact:
If in eyes, rinse well with water.
Get medical attention if irritation develops and persists.

If swallowed:
If swallowed, DO NOT induce vomiting.
Get medical attention if symptoms occur.
Rinse mouth thoroughly with water.

Most important symptoms and effects, both acute and delayed:
Contact with dust can cause mechanical irritation or drying of the skin.
Dust contact with the eyes can lead to mechanical irritation.

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)
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 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 causing an explosion.
Provide adequate precautions, such as electrical grounding and bonding, or inert atmospheres.

Local/Total ventilation: Use only with adequate ventilation.

Advice on safe handling: 
- Do not breathe dust.
- Do not swallow.
- Avoid contact with eyes.
- Avoid prolonged or repeated contact with skin.
- Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment
- Minimize dust generation and accumulation.
- Keep container closed when not in use.
- Keep away from heat and sources of ignition.
- Take precautionary measures against static discharges.
- Take care to prevent spills, waste and minimize release to the environment.

Conditions for safe storage: Keep in properly labeled containers.
Store in accordance with the particular national regulations.

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

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Ingredients with workplace control parameters

<table>
<thead>
<tr>
<th>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>TWAEV (total dust)</td>
<td>10 mg/m³</td>
<td>CA QC OEL</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

Material: Chemical-resistant gloves

#### Eye protection

- **Remarks**: Consider double gloving.
- **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>
<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>Water solubility</td>
</tr>
<tr>
<td></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>
</tbody>
</table>
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.

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

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

Elbasvir:
   Acute oral toxicity: LD50 (Rat): > 2,000 mg/kg
SAFETY DATA SHEET

Grazoprevir / Elbasvir Formulation

LD50 (Mouse): > 1,000 mg/kg

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

Acute dermal toxicity: LD50 (Rabbit): > 2,000 mg/kg
   Remarks: Based on data from similar materials

Titanium dioxide:
Acute oral toxicity: LD50 (Rat): > 5,000 mg/kg

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

Skin corrosion/irritation
   Not classified based on available information.

Components:

Grazoprevir:
Result: No skin irritation

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

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

Titanium dioxide:
Species: Rabbit
Result: No skin irritation

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

Components:

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

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

Titanium dioxide:
Species : Rabbit
Result : No eye irritation

Respiratory or skin sensitization

Skin sensitization
Not classified based on available information.

Respiratory sensitization
Not classified based on available information.

Components:

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

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

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

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

Germ cell mutagenicity
Not classified based on available information.
Components:

Cellulose:
- Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES) \( \text{Result: negative} \)
  Test Type: In vitro mammalian cell gene mutation test \( \text{Result: negative} \)
- Genotoxicity in vivo: Test Type: Mammalian erythrocyte micronucleus test (in vivo cytogenetic assay) \( \text{Species: Mouse} \)
  Application Route: Ingestion \( \text{Result: negative} \)

Grazoprevir:
- Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES) \( \text{Result: negative} \)
  Test Type: Chromosome aberration test in vitro \( \text{Result: negative} \)
- Genotoxicity in vivo: Test Type: In vivo micronucleus test \( \text{Application Route: Oral} \)
  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) \( \text{Result: negative} \)
  Test Type: Chromosome aberration test in vitro \( \text{Result: negative} \)
- Genotoxicity in vivo: Test Type: In vivo micronucleus test \( \text{Species: Rat} \)
  Application Route: Oral \( \text{Result: negative} \)
- 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 \( \text{Result: negative} \)
  Remarks: Based on data from similar materials
  Test Type: Chromosome aberration test in vitro \( \text{Method: OECD Test Guideline 473} \)
  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
- Not classified based on available information.

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
SAFETY DATA SHEET

Grazoprevir / Elbasvir Formulation

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**
- Not classified based on available information.

**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  
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 (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
Remarks: Based on data from similar materials

Toxicity to microorganisms: EC10 (Pseudomonas putida): > 100 mg/l
Exposure time: 16 h
Test substance: Water Accommodated Fraction
Remarks: Based on data from similar materials

**Titanium dioxide:**

Toxicity to fish: LC50 (Onchorhynchus 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
plants

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

Persistence and degradability

Components:

Cellulose:
- Biodegradability: Result: Readily biodegradable.

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

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

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

Bioaccumulative potential

Components:

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

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

Magnesium stearate:
- Partition coefficient: n-octanol/water
  - log Pow: > 4
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. (Elbasvir)
Class: 9
Packing group: III
19 / 20
SAFETY DATA SHEET

Grazoprevir / Elbasvir Formulation

Version 6.0  Revision Date: 04/24/2019  SDS Number: 76204-00014  Date of last issue: 10/16/2018  Date of first issue: 03/17/2015

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; 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: 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 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