SAFETY DATA SHEET

Grazoprevir / Elbasvir Formulation

Section 1: Identification

Product name : Grazoprevir / Elbasvir Formulation

Manufacturer or supplier’s details

Company : MSD

Address : 33 Whakatiki Street - Private Bag 908
Upper Hutt - New Zealand

Telephone : 908-740-4000

Emergency telephone number : 1-908-423-6000

E-mail address : EHSDATASTEWARD@msd.com

Telefax : 908-735-1496

Recommended use of the chemical and restrictions on use

Recommended use : Pharmaceutical

Section 2: Hazard identification

GHS Classification
Not a hazardous substance or mixture.

GHS label elements
Not a hazardous substance or mixture.

Other hazards which do not result in classification
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>&lt; 10</td>
</tr>
<tr>
<td>Grazoprevir</td>
<td>1350462-55-3</td>
<td>&lt; 10</td>
</tr>
<tr>
<td>Elbasvir</td>
<td>1370468-36-2</td>
<td>&lt; 10</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>557-04-0</td>
<td>&lt; 10</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</td>
<td>&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: 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 firefighting: 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 firefighters: In the event of fire, wear self-contained breathing apparatus. Use personal protective equipment.

Hazchem Code: 2Z

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.

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 labelled 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

Components 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>WES-TWA</td>
<td>10 mg/m³</td>
<td>NZ OEL</td>
</tr>
<tr>
<td>Grazoprevir</td>
<td>1350462-55-3</td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td></td>
<td></td>
<td></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>WES-TWA</td>
<td>10 mg/m³</td>
<td>NZ OEL</td>
</tr>
<tr>
<td></td>
<td></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>WES-TWA</td>
<td>10 mg/m³</td>
<td>NZ 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: 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

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>powder</td>
</tr>
<tr>
<td>Colour</td>
<td>white</td>
</tr>
<tr>
<td>Odour</td>
<td>No data available</td>
</tr>
<tr>
<td>Odour 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>Vapour pressure</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Relative vapour density</td>
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<tr>
<td>Relative density</td>
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</tr>
<tr>
<td>Density</td>
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<tr>
<td>Solubility(ies)</td>
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</tr>
<tr>
<td>Water solubility</td>
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<tr>
<td>Partition coefficient: n-octanol/water</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Auto-ignition temperature</td>
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</tr>
<tr>
<td>Decomposition temperature</td>
<td>No data available</td>
</tr>
<tr>
<td>Viscosity</td>
<td></td>
</tr>
<tr>
<td>Viscosity, kinematic</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Explosive properties</td>
<td>Not explosive</td>
</tr>
<tr>
<td>Oxidizing properties</td>
<td>The substance or mixture is not classified as oxidizing.</td>
</tr>
</tbody>
</table>
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

Exposure routes:
- 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

Elbasvir:
- 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
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 sensitisation

Skin sensitisation
Not classified based on available information.

Respiratory sensitisation
Not classified based on available information.

Components:

Grazoprevir:
Test Type: Local lymph node assay (LLNA)
Exposure routes: Dermal
Result: Not a skin sensitizer.

Elbasvir:
Test Type: Local lymph node assay (LLNA)
Exposure routes: Dermal
Species: Mouse
Result: negative

Magnesium stearate:
Test Type: Maximisation Test
Exposure routes: 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)
Exposure routes: Skin contact
Species: Mouse
Result: negative

Chronic toxicity

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

- **Grazoprevir**: Mammalian erythrocyte micronucleus test (in vivo cytogenetic assay)  
  - Species: Mouse  
  - Application Route: Ingestion  
  - Result: negative  

- **Elbasvir**: In vivo micronucleus test  
  - Species: Rat  
  - Application Route: Oral  
  - Result: negative  

- **Titanium dioxide**: Bacterial reverse mutation assay (AMES)  
  - Result: negative

### Germ cell mutagenicity - Assessment

- **Grazoprevir**: Weight of evidence does not support classification as a germ cell mutagen.  
- **Elbasvir**: Weight of evidence does not support classification as a germ cell mutagen.  

### Genotoxicity in vitro

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

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

- **Titanium dioxide**:  
  - Bacterial reverse mutation assay (AMES)  
  - Result: negative

### Remarks

- Based on data from similar materials  
  - Chromosome aberration test in vitro  
  - Method: OECD Test Guideline 473  
  - Result: negative  
  - Remarks: Based on data from similar materials  
  - Bacterial reverse mutation assay (AMES)  
  - Result: negative  
  - Remarks: Based on data from similar materials
Genotoxicity in vivo: Test Type: In vivo micronucleus test  
Species: Mouse  
Result: negative

Carcinogenicity  
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 foetal 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
Effects on foetal 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 foetal development**:
  - Test Type: Embryo-foetal development
  - Species: Rat
  - Application Route: Oral
  - Embryo-foetal toxicity: NOAEL: 200 mg/kg body weight
  - Result: No effects on foetal development

  Test Type: Embryo-foetal development
  - Species: Rabbit
  - Application Route: Oral
  - Embryo-foetal toxicity: NOAEL: 200 mg/kg body weight
  - Result: No effects on foetal development

  Test Type: Embryo-foetal development
  - Species: Rabbit
  - Application Route: Intravenous
  - Embryo-foetal toxicity: NOAEL: 100 mg/kg body weight
  - Result: No effects on foetal 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 foetal development**:
  - Test Type: Embryo-foetal 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:** \( \geq 9,000 \) mg/kg
- **Application Route:** Ingestion
- **Exposure time:** 90 Days

**Grazoprevir:**
- **Species:** Rat
- **NOAEL:** 400 mg/kg
- **Application Route:** Oral
- **Exposure time:** 30 Days
- **Remarks:** No significant adverse effects were reported

**Species:** Rat
- **NOAEL:** 400 mg/kg
- **Application Route:** Oral
- **Exposure time:** 180 Days
- **Remarks:** No significant adverse effects were reported

**Species:** Dog
- **NOAEL:** 15 mg/kg
- **LOAEL:** 100 mg/kg
- **Application Route:** Oral
- **Exposure time:** 270 Days
- **Target Organs:** Liver, Testis, Blood, Bone marrow, gallbladder, spleen

**Species:** Mouse
- **NOAEL:** 200 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 yr

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

Toxicity to daphnia and other aquatic invertebrates:
\( \text{EL50 (Daphnia magna (Water flea))}: > 1 \text{ mg/l} \)
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:
\( \text{EL50 (Pseudokirchneriella subcapitata (green algae))}: > 1 \text{ mg/l} \)
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)):
\( \text{EC50} \)
Exposure time: 72 h
Test substance: Water Accommodated Fraction
Method: OECD Test Guideline 201
Remarks: Based on data from similar materials

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

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

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

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

Toxicity to microorganisms:
\( \text{EC50}: > 1,000 \text{ mg/l} \)
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
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.

National Regulations

NZS 5433
UN number : UN 3077
Proper shipping name : ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Elbasvir)
Class : 9
### SAFETY DATA SHEET

**Grazoprevir / Elbasvir Formulation**

<table>
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<th>Version</th>
<th>Revision Date:</th>
<th>SDS Number:</th>
<th>Date of last issue:</th>
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- **Packing group**: III
- **Labels**: 9
- **Hazchem Code**: 2Z

**Special precautions for user**

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

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### Section 15: Regulatory information

**Safety, health and environmental regulations/legislation specific for the substance or mixture**

**HSNO Approval Number**

HSR100425 Pharmaceutical Active Ingredients Group Standard 2017

**HSW Controls**

Certified handler certificate not required.

HSW tracking not required.

Refer to WORKSAFE user guide to the HSW regulations for further information.

**The components of this product are reported in the following inventories:**

- **AICS**: not determined
- **DSL**: not determined
- **IECSC**: not determined

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### Section 16: Other information

**Further information**


Date format: dd.mm.yyyy

**Full text of other abbreviations**

- **ACGIH**: USA. ACGIH Threshold Limit Values (TLV)
- **NZ OEL**: New Zealand. Workplace Exposure Standards for Atmospheric Contaminants
- **ACGIH / TWA**: 8-hour, time-weighted average
- **NZ OEL / WES-TWA**: Workplace Exposure Standard - Time Weighted average

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% re-
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.

NZ / EN