1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Grazoprevir / Elbasvir Formulation

Manufacturer or supplier's details
Company name of supplier: MSD
Address: Kumagaya, Saitama Prefecture, Xicheng 810 MSD Co., Ltd. Menuma factory
Telephone: 048-588-8411
E-mail address: EHSDATASTEWARD@msd.com
Emergency telephone number: 1-908-423-6000

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

2. HAZARDS IDENTIFICATION

GHS Classification
Short-term (acute) aquatic hazard: Category 3
Long-term (chronic) aquatic hazard: Category 1

GHS label elements
Hazard pictograms:
Signal word: Warning
Hazard statements: H402 Harmful to aquatic life. H410 Very toxic to aquatic life with long lasting effects.
Precautionary statements:
Prevention: P273 Avoid release to the environment.
Response: P391 Collect spillage.
Disposal: P501 Dispose of contents/container to an approved waste disposal plant.
Other hazards which do not result in classification

Important symptoms and outlines of the emergency assumed:
- 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.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture: Mixture

<table>
<thead>
<tr>
<th>Components</th>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
<th>ENCS No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium n-dodecyl sulfate</td>
<td>151-21-3</td>
<td>&gt;= 0.25 - &lt; 1</td>
<td>2-1679</td>
<td></td>
</tr>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>&gt;= 1 - &lt; 10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grazoprevir</td>
<td>1350462-55-3</td>
<td>&gt;= 2.5 - &lt; 10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elbasvir</td>
<td>1370468-36-2</td>
<td>&gt;= 2.5 - &lt; 10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>557-04-0</td>
<td>&gt;= 1 - &lt; 10</td>
<td>2-611</td>
<td></td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</td>
<td>&gt;= 0.1 - &lt; 1</td>
<td>1-558, 5-5225</td>
<td></td>
</tr>
<tr>
<td>2,6-Di-tert-butyl-p-cresol</td>
<td>128-37-0</td>
<td>&gt;= 0.0025 - &lt; 0.025</td>
<td>3-540, 9-1805</td>
<td></td>
</tr>
</tbody>
</table>

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.

5. FIREFIGHTING MEASURES

Suitable extinguishing media:
- Water spray
- Alcohol-resistant foam
**SAFETY DATA SHEET**

**Grazoprevir / Elbasvir Formulation**

<table>
<thead>
<tr>
<th>Version</th>
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<th>Date of last issue:</th>
<th>Date of first issue:</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.1</td>
<td>04/24/2019</td>
<td>76213-00014</td>
<td>2018/10/16</td>
<td>2015/03/17</td>
</tr>
</tbody>
</table>

**Usable 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.

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**6. ACCIDENTAL RELEASE MEASURES**

**Personal precautions, protective equipment and emergency procedures**

: Use personal protective equipment.  
Follow safe handling advice and personal protective equipment recommendations.

**Environmental precautions**

: Discharge into the environment must be avoided.  
Prevent further leakage or spillage if safe to do so.  
Retain and dispose of contaminated wash water.  
Local authorities should be advised if significant spills cannot be contained.

**Methods and materials for containment and cleaning up**

: Sweep up or vacuum up spillage and collect in suitable container for disposal.  
Avoid dispersal of dust in the air (i.e., clearing dust surfaces with compressed air).  
Dust deposits should not be allowed to accumulate on surfaces, as these may form an explosive mixture if they are released into the atmosphere in sufficient concentration.  
Local or national regulations may apply to releases and disposal of this material, as well as those materials and items employed in the cleanup of releases. You will need to determine which regulations are applicable.  
Sections 13 and 15 of this SDS provide information regarding certain local or national requirements.

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**7. HANDLING AND STORAGE**

**Handling**

**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.

Avoidance of contact: Oxidizing agents
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.

Storage
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
Packaging material: Unsuitable material: None known.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Threshold limit value and permissible exposure limits for each component in the work environment

<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>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>OEL-M</td>
<td>1 mg/m³</td>
<td>JP OEL</td>
</tr>
</tbody>
</table>
Further information: Class 2 Dust

<table>
<thead>
<tr>
<th></th>
<th>(Respirable dust)</th>
<th>(Titanium)</th>
<th>JSOH</th>
</tr>
</thead>
<tbody>
<tr>
<td>OEL-M (Total dust)</td>
<td>4 mg/m³</td>
<td>JSOH</td>
<td></td>
</tr>
<tr>
<td>JP OEL</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Further information: Class 2 Dust

<table>
<thead>
<tr>
<th></th>
<th>TWA</th>
<th>10 mg/m³ (Titanium dioxide)</th>
<th>ACGIH</th>
</tr>
</thead>
<tbody>
<tr>
<td>2,6-Di-tert-butyl-p-cresol</td>
<td>TWA (Inhalable fraction and vapor)</td>
<td>2 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. 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.

9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance: powder
Colour: white
Odour: No data available
Odour Threshold: No data available
pH: No data available
Melting point/freezing point: No data available
Initial boiling point and boiling range: No data available
Flash point: Not applicable
Evaporation rate: Not applicable
Flammability (solid, gas): May form explosive dust-air mixture during processing, handling or other means.
Flammability (liquids): No data available
Upper explosion limit / Upper flammability limit: No data available
Lower explosion limit / Lower flammability limit: No data available
Vapour pressure: Not applicable
Relative vapour density: Not applicable
Relative density: No data available
Density: No data available
Solubility(ies)
Water solubility: No data available
Partition coefficient: n-octanol/water: Not applicable
Auto-ignition temperature: No data available
Decomposition temperature: No data available
Viscosity
Viscosity, kinematic: Not applicable
Explosive properties: Not explosive
Oxidizing properties: The substance or mixture is not classified as oxidizing.
Particle size: No data available

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.
11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure:

Inhalation
Skin contact
Ingestion
Eye contact

Acute toxicity:
Not classified based on available information.

Components:

**Sodium n-dodecyl sulfate:**
Acute oral toxicity: LD50 (Rat): 1,200 mg/kg
Method: OECD Test Guideline 401

Acute dermal toxicity: LD50 (Rat): > 2,000 mg/kg
Method: OECD Test Guideline 402
Remarks: Based on data from similar materials

**Cellulose:**
Acute oral toxicity: LD50 (Rat): > 5,000 mg/kg

Acute inhalation toxicity: LC50 (Rat): > 5.8 mg/l
Exposure time: 4 h
Test atmosphere: dust/mist

Acute dermal toxicity: LD50 (Rabbit): > 2,000 mg/kg

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

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

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

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

**Titanium dioxide:**
SAFETY DATA SHEET

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Version 8.1  Revision Date: 04/24/2019  SDS Number: 76213-00014  Date of last issue: 2018/10/16
Date of first issue: 2015/03/17

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

2,6-Di-tert-butyl-p-cresol:
  Acute oral toxicity: LD50 (Rat): > 6,000 mg/kg
  Method: OECD Test Guideline 401

  Acute dermal toxicity: LD50 (Rat): > 2,000 mg/kg
  Method: OECD Test Guideline 402
  Assessment: The substance or mixture has no acute dermal toxicity

Skin corrosion/irritation
Not classified based on available information.

Components:

Sodium n-dodecyl sulfate:
Species: Rabbit
Result: Skin irritation

Grazoprevir:
Result: No skin irritation

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

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

Titanium dioxide:
Species: Rabbit
Result: No skin irritation

2,6-Di-tert-butyl-p-cresol:
Species: Rabbit
Method: OECD Test Guideline 404
Result: No skin irritation
Remarks: Based on data from similar materials
Serious eye damage/eye irritation
Not classified based on available information.

Components:

Sodium n-dodecyl sulfate:
Species: Rabbit
Result: Irreversible effects on the eye
Method: OECD Test Guideline 405

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

2,6-Di-tert-butyl-p-cresol:
Species: Rabbit
Result: No eye irritation
Method: OECD Test Guideline 405
Remarks: Based on data from similar materials

Respiratory or skin sensitisation

Skin sensitisation
Not classified based on available information.

Respiratory sensitisation
Not classified based on available information.

Components:

Sodium n-dodecyl sulfate:
Test Type: Maximisation Test
Exposure routes: Skin contact
Species: Guinea pig
Result: negative
Remarks: Based on data from similar materials
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

2,6-Di-tert-butyl-p-cresol:  
Test Type: Human repeat insult patch test (HRIPT)  
Exposure routes: Skin contact  
Species: Humans  
Result: negative

Germ cell mutagenicity  
Not classified based on available information.

Components:  
Sodium n-dodecyl sulfate:  
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES)  
Method: OECD Test Guideline 471  
Result: negative  
Test Type: In vitro mammalian cell gene mutation test  
Result: negative  
Genotoxicity in vivo: Test Type: Rodent dominant lethal test (germ cell) (in vivo)  
Species: Mouse  
Application Route: Ingestion  
Result: negative

Cellulose:  
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES)
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<thead>
<tr>
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</tr>
</tbody>
</table>

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

2,6-Di-tert-butyl-p-cresol:
Genotoxicity in vitro : Test Type: Bacterial reverse mutation assay (AMES)
                        Result: negative

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

                        Test Type: Chromosome aberration test in vitro
                        Result: negative

Genotoxicity in vivo : Test Type: Mutagenicity (in vivo mammalian bone-marrow
                      cytogenetic test, chromosomal analysis)
                      Species: Rat
                      Application Route: Ingestion
                      Result: negative

Carcinogenicity
Not classified based on available information.

Components:

Sodium n-dodecyl sulfate:
Species : Rat
Application Route : Ingestion
Exposure time : 2 Years
Method : OECD Test Guideline 453
Result : negative
Remarks : Based on data from similar materials

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.

2,6-Di-tert-butyl-p-cresol:
Species: Rat
Application Route: Ingestion
Exposure time: 22 Months
Result: negative

Reproductive toxicity
Not classified based on available information.

Components:

Sodium n-dodecyl sulfate:
Effects on fertility: Test Type: Two-generation reproduction toxicity study
Species: Rat
Application Route: Ingestion
Method: OECD Test Guideline 416
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

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
Application Route: Oral
Fertility: NOAEL: 400 mg/kg body weight
Result: No effects on fertility, No effects on foetal development
Effects on foetal development:

Grazoprevir:

- **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

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
  - **Developmental Toxicity**: NOAEL: 1,000 mg/kg body weight
  - **Result**: No effects on early embryonic development

  - **Test Type**: Embryo-foetal 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 foetal development**:
  - **Test Type**: Embryo-foetal development
  - **Species**: Rat
  - **Application Route**: Ingestion
  - **Result**: negative
  - **Remarks**: Based on data from similar materials
SAFETY DATA SHEET
Grazoprevir / Elbasvir Formulation

2,6-Di-tert-butyl-p-cresol:
Effects on fertility : Test Type: Two-generation reproduction toxicity study
Species: Rat
Application Route: Ingestion
Result: negative

Effects on foetal development : Test Type: Embryo-foetal development
Species: Rat
Application Route: Ingestion
Result: negative

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.

2,6-Di-tert-butyl-p-cresol:
Assessment : No significant health effects observed in animals at concentrations of 100 mg/kg bw or less.

Repeated dose toxicity

Components:

Sodium n-dodecyl sulfate:
Species : Rat
NOAEL : 488 mg/kg
Application Route : Ingestion
Exposure time : 90 Days
Remarks : Based on data from similar materials

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
### Grazoprevir / Elbasvir Formulation

<table>
<thead>
<tr>
<th>Species</th>
<th>NOAEL</th>
<th>Application Route</th>
<th>Exposure time</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat</td>
<td>400 mg/kg</td>
<td>Oral</td>
<td>180 Days</td>
<td>No significant adverse effects were reported</td>
</tr>
<tr>
<td>Dog</td>
<td>15 mg/kg</td>
<td>Oral</td>
<td>270 Days</td>
<td>No significant adverse effects were reported</td>
</tr>
<tr>
<td>Mouse</td>
<td>200 mg/kg</td>
<td>Oral</td>
<td>90 Days</td>
<td>Liver, Testis, Blood, Bone marrow, gallbladder, spleen</td>
</tr>
<tr>
<td>Dog</td>
<td>20 mg/kg</td>
<td>Oral</td>
<td>30 Days</td>
<td>Liver, Testis, Blood</td>
</tr>
<tr>
<td>Monkey</td>
<td>10 mg/kg</td>
<td>Oral</td>
<td>8 Days</td>
<td>No significant adverse effects were reported</td>
</tr>
</tbody>
</table>

### Elbasvir:

<table>
<thead>
<tr>
<th>Species</th>
<th>NOAEL</th>
<th>Application Route</th>
<th>Exposure time</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat</td>
<td>1,000 mg/kg</td>
<td>Oral</td>
<td>180 d</td>
<td>No significant adverse effects were reported</td>
</tr>
<tr>
<td>Dog</td>
<td>1,000 mg/kg</td>
<td>Oral</td>
<td>270 d</td>
<td>No significant adverse effects were reported</td>
</tr>
</tbody>
</table>

### Magnesium stearate:

<table>
<thead>
<tr>
<th>Species</th>
<th>NOAEL</th>
<th>Application Route</th>
<th>Exposure time</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat</td>
<td>&gt; 100 mg/kg</td>
<td>Ingestion</td>
<td>90 Days</td>
<td>Based on data from similar materials</td>
</tr>
</tbody>
</table>

### Titanium dioxide:

---

**Species**: Rat  
**NOAEL**: > 100 mg/kg  
**Application Route**: Ingestion  
**Exposure time**: 90 Days  
**Remarks**: Based on data from similar materials
Grazoprevir / Elbasvir Formulation

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

2,6-Di-tert-butyl-p-cresol:
Species: Rat
NOAEL: 25 mg/kg
Application Route: Ingestion
Exposure time: 22 Months

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

12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:
Sodium n-dodecyl sulfate:
Toxicity to fish: LC50 (Pimephales promelas (fathead minnow)): 29 mg/l
Exposure time: 96 h

Toxicity to daphnia and other aquatic invertebrates: EC50 (Ceriodaphnia dubia (water flea)): 5.55 mg/l
Exposure time: 48 h

Toxicity to algae/aquatic plants: ErC50 (Desmodesmus subspicatus (green algae)): > 120 mg/l
Exposure time: 72 h

NOEC (Desmodesmus subspicatus (green algae)): 30 mg/l
Exposure time: 72 h

Toxicity to fish (Chronic toxicity): NOEC (Pimephales promelas (fathead minnow)): >= 1.357 mg/l
Exposure time: 42 d
Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity):
NOEC (Ceriodaphnia dubia (water flea)): 0.88 mg/l
Exposure time: 7 d

Toxicity to microorganisms:
EC50: 135 mg/l
Exposure time: 3 h

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

M-Factor (Chronic aquatic toxicity): 10

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 (Oncorhynchus mykiss (rainbow trout)): > 100 mg/l
Exposure time: 96 h
Method: OECD Test Guideline 203

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

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

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

2,6-Di-tert-butyl-p-cresol:
Toxicity to fish: LC50 (Danio rerio (zebra fish)): > 0.57 mg/l
Exposure time: 96 h
Toxicity to daphnia and other aquatic invertebrates: EC50 (Daphnia magna (Water flea)): 0.48 mg/l
Exposure time: 48 h
Method: OECD Test Guideline 202

Toxicity to algae/aquatic plants: ErC50 (Pseudokirchneriella subcapitata (green algae)): > 0.24 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201

NOEC (Pseudokirchneriella subcapitata (green algae)): 0.24 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201

M-Factor (Acute aquatic toxicity): 1

Toxicity to fish (Chronic toxicity): NOEC (Oryzias latipes (Japanese medaka)): 0.053 mg/l
Exposure time: 30 d
Method: OECD Test Guideline 210

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity): NOEC (Daphnia magna (Water flea)): 0.316 mg/l
Exposure time: 21 d

M-Factor (Chronic aquatic toxicity): 1

Toxicity to microorganisms: EC50: > 10,000 mg/l
Exposure time: 3 h
Method: OECD Test Guideline 209

Persistence and degradability

Components:

Sodium n-dodecyl sulfate:
Biodegradability: Result: Readily biodegradable.
Biodegradation: 95 %
Exposure time: 28 d
Method: OECD Test Guideline 301B

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

2,6-Di-tert-butyl-p-cresol:
Biodegradability: Result: Not readily biodegradable.
Biodegradation: 4.5%
Exposure time: 28 d
Method: OECD Test Guideline 301C

Bioaccumulative potential

Components:

Sodium n-dodecyl sulfate:
Partition coefficient: n-octanol/water: log Pow: 0.83

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

2,6-Di-tert-butyl-p-cresol:
Bioaccumulation: Species: Cyprinus carpio (Carp)
Bioconcentration factor (BCF): 330 - 1,800
Partition coefficient: n-octanol/water: log Pow: 5.1

Mobility in soil

Components:

Grazoprevir:
Distribution among environmental compartments: log Koc: 4.01

Elbasvir:
Distribution among environmental compartments: log Koc: 5.24
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Hazardous to the ozone layer
Not applicable

Other adverse effects
No data available

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.

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
Refer to section 15 for specific national regulation.
SAFETY DATA SHEET

Grazoprevir / Elbasvir Formulation

Version 8.1
Revision Date: 04/24/2019
SDS Number: 76213-00014
Date of last issue: 2018/10/16
Date of first issue: 2015/03/17

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.

15. REGULATORY INFORMATION

Related Regulations

Fire Service Law
Not applicable to dangerous materials / designated flammables.

Chemical Substance Control Law
Priority Assessment Chemical Substance

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium alkyl(C=8-18) sulfate</td>
<td>214</td>
</tr>
<tr>
<td>2,6-Di-tert-butyl-4-methylphenol</td>
<td>64</td>
</tr>
</tbody>
</table>

Industrial Safety and Health Law

Harmful Substances Prohibited from Manufacture
Not applicable

Harmful Substances Required Permission for Manufacture
Not applicable

Substances Prevented From Impairment of Health
Not applicable

Circular concerning Information on Chemicals having Mutagenicity - Annex 2: Information on Existing Chemicals having Mutagenicity
Not applicable

Circular concerning Information on Chemicals having Mutagenicity - Annex 1: Information on Notified Substances having Mutagenicity
Not applicable

Substances Subject to be Notified Names
Article 57-2 (Enforcement Order Table 9)

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>Number</th>
<th>Concentration (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnesium stearate</td>
<td>327</td>
<td>&gt;=1 - &lt;10</td>
</tr>
<tr>
<td>Titanium(IV) oxide</td>
<td>191</td>
<td>&gt;=0.1 - &lt;1</td>
</tr>
</tbody>
</table>

Substances Subject to be Indicated Names
Article 57 (Enforcement Order Article 18)

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnesium stearate</td>
<td>327</td>
</tr>
</tbody>
</table>

Ordinance on Prevention of Hazards Due to Specified Chemical Substances
Not applicable

Ordinance on Prevention of Lead Poisoning
Not applicable

Ordinance on Prevention of Tetraalkyl Lead Poisoning
Not applicable
Ordinance on Prevention of Organic Solvent Poisoning
Not applicable

Enforcement Order of the Industrial Safety and Health Law - Attached table 1 (Dangerous Substances)
Not applicable

Poisonous and Deleterious Substances Control Law
Not applicable

Act on Confirmation, etc. of Release Amounts of Specific Chemical Substances in the Environment and Promotion of Improvements to the Management Thereof
Not applicable

High Pressure Gas Safety Act
Not applicable

Explosive Control Law
Not applicable

Vessel Safety Law
Miscellaneous dangerous substances and articles (Article 2 and 3 of rules on shipping and storage of dangerous goods and its Attached Table 1)

Aviation Law
Miscellaneous dangerous substances and articles (Article 194 of The Enforcement Rules of Aviation Law and its Attached Table 1)

Marine Pollution and Sea Disaster Prevention etc Law
Bulk transportation : Noxious liquid substance (Category Z)
Pack transportation : Classified as marine pollutant

Narcotics and Psychotropics Control Act
Narcotic or Psychotropic Raw Material
Not applicable
Specific Narcotic or Psychotropic Raw Material
Not applicable

Waste Disposal and Public Cleansing Law
Industrial waste

The components of this product are reported in the following inventories:
AICS : not determined
DSL : not determined
IECSC : not determined

16. OTHER INFORMATION

Further information
Sources of key data used to compile the Safety Data : Internal technical data, data from raw material SDSs, OECD eChem Portal search results and European Chemicals Agen-
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.

JP / EN