SAFETY DATA SHEET

Elbasvir Formulation

Version 1.11  Revision Date: 09/13/2019  SDS Number: 529969-00012  Date of last issue: 24.04.2019
Date of first issue: 23.02.2016

1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Elbasvir Formulation

Manufacturer or supplier’s details
Company: MSD
Address: 50 Tuas West Drive
Singapore - Singapore 638408
Telephone: 908-740-4000
Emergency telephone number: 65 6697 2111 (24/7/365)
E-mail address: EHSDATASTEWARD@msd.com
Telefax: 908-735-1496

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

2. HAZARDS IDENTIFICATION

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

GHS label elements
Hazard pictograms: 
Signal word: Warning
Hazard statements: 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
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

#### 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;= 10 - &lt; 20</td>
</tr>
<tr>
<td>Elbasvir</td>
<td>1370468-36-2</td>
<td>&gt;= 2.5 - &lt; 10</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</td>
<td>&gt;= 0.1 - &lt; 1</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 (see section 8).

#### Notes to physician:
- Treat symptomatically and supportively.

### 5. FIREFIGHTING 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

#### Specific extinguishing method:
- Use extinguishing measures that are appropriate to local cir-
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.

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 labelled containers. Store in accordance with the particular national regulations.

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

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>PEL (long term)</td>
<td>10 mg/m³</td>
<td>SG OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</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>Titanium dioxide</td>
<td>13463-67-7</td>
<td>PEL (long term)</td>
<td>10 mg/m³</td>
<td>SG OEL</td>
</tr>
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<td>10 mg/m³ (Titanium dioxide)</td>
<td>ACGIH</td>
</tr>
</tbody>
</table>

Engineering measures:  Use feasible engineering controls to minimize exposure to compound.

All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment.

Personal protective equipment

Respiratory protection:  If adequate local exhaust ventilation is not available or exposure assessment demonstrates exposures outside the recommended guidelines, use respiratory protection.

Filter type:  Particulates type

Hand protection

Material:  Chemical-resistant gloves

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 face shield 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

Hygiene measures:  If exposure to chemical is likely during typical use, provide eye flushing systems and safety showers 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.
9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance: powder
Colour: brown
Odour: odourless
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.
10. STABILITY AND REACTIVITY

Reactivity : Not classified as a reactivity hazard.

Chemical stability : Stable under normal conditions.

Possibility of hazardous reac-
tions : May form explosive dust-air mixture during processing, han-
dling 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.

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

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

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

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

**Titanium dioxide:**
Species : Rabbit
Result : No skin irritation

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

**Components:**

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

**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:**

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

**Titanium dioxide:**
Test Type : Local lymph node assay (LLNA)
Exposure routes : Skin contact
Species : Mouse
Result : negative

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

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

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.

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 foetal development: Test Type: Fertility/early embryonic development
Species: Rat
Application Route: Ingestion
Result: negative

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

STOT - single exposure
Not classified based on available information.

STOT - repeated exposure
Not classified based on available information.
Repeated dose toxicity

**Components:**

**Cellulose:**
- Species: Rat
- NOAEL: >= 9,000 mg/kg
- Application Route: Ingestion
- Exposure time: 90 Days

**Elbasvir:**
- Species: Rat
- NOAEL: 1,000 mg/kg
- Application Route: Oral
- Exposure time: 180 d
- Remarks: No significant adverse effects were reported

**Species:**
- Species: Dog
- NOAEL: 1,000 mg/kg
- Application Route: Oral
- Exposure time: 270 d
- Remarks: No significant adverse effects were reported

**Titanium dioxide:**
- Species: Rat
- NOAEL: 24,000 mg/kg
- Application Route: Ingestion
- Exposure time: 28 Days

**Species:**
- 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:**

**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:**

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

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
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Method: OECD Test Guideline 209

**Titanium dioxide:**

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

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

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

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

**Persistence and degradability**

**Components:**

**Cellulose:**

Biodegradability:
- Result: Readily biodegradable.

**Elbasvir:**

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

**Bioaccumulative potential**

**Components:**

**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

**Mobility in soil**

**Components:**

**Elbasvir:**

Distribution among environmental compartments:
- log Koc: 5.24

**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.

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

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

Workplace Safety and Health Act and Workplace Safety and Health (General Provisions) Regulations: This product is subjected to the SDS, labelling, PEL and other requirements in the Act/Regulations.

Environmental Protection and Management Act and Environmental Protection and Management (Hazardous Substances) Regulations: Not applicable

Fire Safety (Petroleum and Flammable Materials) Regulations: Not applicable

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


Date format: dd.mm.yyyy

Full text of other abbreviations

ACGIH: USA, ACGIH Threshold Limit Values (TLV)
SG OEL: Singapore, Workplace Safety and Health Act - First Schedule Permissible Exposure Limits of Toxic Substances

ACGIH / TWA: 8-hour, time-weighted average
SG OEL / PEL (long term): Permissible Exposure Level (PEL) Long Term

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; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; ELx - Loading rate associated with x% response; EmS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; ERG - Emergency Response Guide; GHS - Globally Harmonized System; GLP - Good Laboratory Practice; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; IBC - International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk; IC50 - Half maximal inhibitory concentration; ICAO - International Civil Aviation Organization; IECSC - Inventory of Existing Chemic-
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.