SAFETY DATA SHEET

Temozolomide Injection Formulation

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Temozolomide Injection Formulation

Manufacturer or supplier's details

Company : MSD
Address : 26 Talavera Road, Talavera Corp Centre, Macquarie Park
          New South Wales, 2113 Australia
Telephone : (61)-02-8988-8000
Emergency telephone number : (61)-02-8988-8000
E-mail address : EHSDATASTEWARD@msd.com
Telefax : 908-735-1496

Recommended use of the chemical and restrictions on use

Recommended use : Pharmaceutical

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification

Acute toxicity (Oral) : Category 3
Serious eye damage/eye irritation : Category 1
Germ cell mutagenicity : Category 2
Carcinogenicity : Category 2
Reproductive toxicity : Category 1B
Specific target organ toxicity - repeated exposure (Oral) : Category 2 (Bone marrow, thymus gland, Lymph nodes, spleen)

GHS label elements

Hazard pictograms : 

Signal word : Danger
Hazard statements : H301 Toxic if swallowed.
H318 Causes serious eye damage.
H341 Suspected of causing genetic defects.
H351 Suspected of causing cancer.
H360FD May damage fertility. May damage the unborn child.
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Temozolomide Injection Formulation

Version 5.6  Revision Date: 04/24/2019  SDS Number: 27548-00014  Date of last issue: 07.02.2019

Date of first issue: 03.11.2014

H373 May cause damage to organs (Bone marrow, thymus gland, Lymph nodes, spleen) through prolonged or repeated exposure if swallowed.

Precautionary statements:

Prevention:
P201 Obtain special instructions before use.
P202 Do not handle until all safety precautions have been read and understood.
P260 Do not breathe dust.
P264 Wash skin thoroughly after handling.
P270 Do not eat, drink or smoke when using this product.
P280 Wear eye protection/face protection.
P281 Use personal protective equipment as required.

Response:
P301 + P310 + P330 IF SWALLOWED: Immediately call a POISON CENTER or doctor/physician. Rinse mouth.
P305 + P351 + P338 + P310 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a POISON CENTER or doctor/physician.
P308 + P313 IF exposed or concerned: Get medical advice/attention.

Storage:
P405 Store locked up.

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

Other hazards which do not result in classification
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>Temozolomide</td>
<td>85622-93-1</td>
<td>&gt;= 1 - &lt; 10</td>
</tr>
<tr>
<td>Hydrochloric acid</td>
<td>7647-01-0</td>
<td>&gt;= 3 - &lt; 5</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: In case of contact, immediately flush skin with soap and plenty
of water.
Remove contaminated clothing and shoes.
Get medical attention.
Wash clothing before reuse.
Thoroughly clean shoes before reuse.

In case of eye contact:
In case of contact, immediately flush eyes with plenty of water for at least 15 minutes.
If easy to do, remove contact lens, if worn.
Get medical attention immediately.

If swallowed:
If swallowed, DO NOT induce vomiting.
Call a physician or poison control centre immediately.
Rinse mouth thoroughly with water.
Never give anything by mouth to an unconscious person.

Most important symptoms and effects, both acute and delayed:
Toxic if swallowed.
Causes serious eye damage.
Suspected of causing genetic defects.
Suspected of causing cancer.
May damage fertility. May damage the unborn child.
May cause damage to organs through prolonged or repeated exposure if swallowed.

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. 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
- Nitrogen oxides (NOx)
- Metal oxides
- Chlorine compounds

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.

SECTION 6. ACCIDENTAL RELEASE MEASURES

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

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.

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.

Static electricity may accumulate and ignite suspended dust causing an explosion. Provide adequate precautions, such as electrical grounding and bonding, or inert atmospheres.

Use with local exhaust ventilation.

Do not get on skin or clothing. Do not breathe dust. Do not swallow. Do not get in eyes. Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment. Keep container tightly closed. 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.

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.

Keep in properly labelled containers. Store locked up. Keep tightly closed. Store in accordance with the particular national regulations.

Do not store with the following product types: Explosives
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>Temozolomide</td>
<td>85622-93-1</td>
<td>TWA</td>
<td>0.1 ug/m^3 (OEB 5)</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wipe limit</td>
<td>1 µg/100 cm^2</td>
<td>Internal</td>
</tr>
<tr>
<td>Hydrochloric acid</td>
<td>7647-01-0</td>
<td>Peak limit</td>
<td>5 ppm 7.5 mg/m^3</td>
<td>AU OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C</td>
<td>2 ppm</td>
<td>ACGIH</td>
</tr>
</tbody>
</table>

Engineering measures:
- Minimize workplace exposure concentrations.
- Apply measures to prevent dust explosions.
- Ensure that dust-handling systems (such as exhaust ducts, dust collectors, vessels, and processing equipment) are designed in a manner to prevent the escape of dust into the work area (i.e., there is no leakage from the equipment). Use with local exhaust ventilation.

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: Combined particulates and acidic gas/vapour type

Hand protection:
- Material: Chemical-resistant gloves
- Remarks: Choose gloves to protect hands against chemicals depending on the concentration and quantity of the hazardous substance and specific to place of work. Breakthrough time is not determined for the product. Change gloves often! For special applications, we recommend clarifying the resistance to chemicals of the aforementioned protective gloves with the glove manufacturer. Wash hands before breaks and at the end of workday.

Eye protection:
- Wear the following personal protective equipment: Chemical resistant goggles must be worn. If splashes are likely to occur, wear: Face-shield

Skin and body protection:
- Select appropriate protective clothing based on chemical resistance data and an assessment of the local exposure potential. Skin contact must be avoided by using impervious protective clothing (gloves, aprons, boots, etc).

SECTION 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: No data available
Evaporation rate: No data available
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: No data available
Relative vapour density: No data available
Relative density: No data available
Density: 1 g/cm³
Solubility(ies)
  Water solubility: No data available
Partition coefficient: n-octanol/water: No data available
Auto-ignition temperature: No data available
Decomposition temperature: No data available
Viscosity
  Viscosity, kinematic: No data available
Explosive properties: Not explosive
Oxidizing properties: The substance or mixture is not classified as oxidizing.
Molecular weight: No data available
Particle size: No data available

SECTION 10. STABILITY AND REACTIVITY
SAFETY DATA SHEET

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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
Toxic if swallowed.

Product:
Acute oral toxicity: Acute toxicity estimate: 243.59 mg/kg
Method: Calculation method

Components:

Temozolomide:
Acute oral toxicity: LD50 (Dog): 19 mg/kg
LD50 (Rat): 315 mg/kg
LD50 (Mouse): 205 mg/kg

Hydrochloric acid:
Acute inhalation toxicity: LC50 (Rat): 8.3 mg/l
Exposure time: 30 min
Test atmosphere: dust/mist

Skin corrosion/irritation
Not classified based on available information.

Components:

Hydrochloric acid:
Method: EPISKIN Human Skin Model Test
Result: Corrosive after 3 minutes or less of exposure

Serious eye damage/eye irritation
Causes serious eye damage.
Components:

Hydrochloric acid:
Result : Irreversible effects on the eye
Method : OECD Test Guideline 437

Respiratory or skin sensitisation

Skin sensitisation
Not classified based on available information.

Respiratory sensitisation
Not classified based on available information.

Components:

Temozolomide:
Test Type : Maximisation Test
Exposure routes : Dermal
Species : Guinea pig
Result : negative

Hydrochloric acid:
Test Type : Maximisation Test
Exposure routes : Skin contact
Species : Guinea pig
Method : OECD Test Guideline 406
Result : negative

Chronic toxicity

Germ cell mutagenicity
Suspected of causing genetic defects.

Components:

Temozolomide:
Genotoxicity in vitro : Test Type: Bacterial reverse mutation assay (AMES)
Result: positive
Test Type: Chromosome aberration test in vitro
Test system: Human lymphocytes
Result: positive

Germ cell mutagenicity - Assessment
Positive results from in vitro mammalian mutagenicity assays, chemical structure activity relationship to known germ cell mutagens

Hydrochloric acid:
Genotoxicity in vitro : Test Type: Saacharomyces cerevisiae, miotic recombination assay (in vitro)
Result: negative
Carcinogenicity
Suspected of causing cancer.

Components:

Temozolomide:
Species: Rat
Application Route: Oral
Exposure time: 6 Months
Result: positive
Target Organs: Mammary gland

Carcinogenicity - Assessment: Limited evidence of carcinogenicity in animal studies

Hydrochloric acid:
Species: Rat
Application Route: Inhalation
Exposure time: 128 weeks
Result: negative

Reproductive toxicity
May damage fertility. May damage the unborn child.

Components:

Temozolomide:
Effects on fertility: Test Type: Fertility/early embryonic development
Species: Rat, male
Application Route: Oral
Fertility: LOAEL: 8.5 mg/kg body weight
Result: positive

Effects on foetal development: Test Type: Embryo-foetal development
Species: Rat
Application Route: Oral
Embryo-foetal toxicity: LOAEL: 13 mg/kg body weight
Result: positive, Malformations were observed.

Reproductive toxicity - Assessment: Clear evidence of adverse effects on sexual function and fertility, based on animal experiments., Clear evidence of adverse effects on development, based on animal experiments.

STOT - single exposure
Not classified based on available information.

Components:

Hydrochloric acid:
Assessment: May cause respiratory irritation.
STOT - repeated exposure
May cause damage to organs (Bone marrow, thymus gland, Lymph nodes, spleen) through prolonged or repeated exposure if swallowed.

Components:

Temozolomide:
Exposure routes: Ingestion
Target Organs: Bone marrow, thymus gland, Lymph nodes, spleen
Assessment: Causes damage to organs through prolonged or repeated exposure.

Repeated dose toxicity

Components:

Temozolomide:
Species: Rat, female
NOAEL: 4 mg/kg
LOAEL: 21 mg/kg
Application Route: Oral
Exposure time: 6 Months
Target Organs: Lymph nodes, thymus gland, Bone marrow, Reproductive organs

Species: Rat, male
NOAEL: 8.5 mg/kg
LOAEL: 34 mg/kg
Application Route: Oral
Exposure time: 6 Months
Target Organs: Lymph nodes, thymus gland, Bone marrow, male reproductive organs, Gastrointestinal tract

Species: Dog
NOAEL: 2.5 mg/kg
LOAEL: 6.3 mg/kg
Application Route: Oral
Exposure time: 6 Months
Target Organs: Bone marrow, spleen, male reproductive organs, Gastrointestinal tract, thymus gland

Aspiration toxicity
Not classified based on available information.

Experience with human exposure

Components:

Temozolomide:
Ingestion: Symptoms: Blood disorders, Nausea, Vomiting, Diarrhoea, anorexia, Fatigue, hair loss
Ecotoxicity

Components:

**Temozolomide:**
- 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
  - Method: OECD Test Guideline 202
- Toxicity to algae/aquatic plants: EC50 (Pseudokirchneriella subcapitata (green algae)): > 90 mg/l
  - Exposure time: 72 h
  - Method: OECD Test Guideline 201
  - NOEC (Pseudokirchneriella subcapitata (green algae)): 40 mg/l
  - Exposure time: 72 h
  - Method: OECD Test Guideline 201
- Toxicity to microorganisms: EC50: > 100 mg/l
  - Exposure time: 3 h
  - Test Type: Respiration inhibition
  - Method: OECD Test Guideline 209

Persistence and degradability

Components:

**Temozolomide:**
- Biodegradability: Result: rapidly degradable
  - Biodegradation: 83%
  - Exposure time: 35 d
- Stability in water: Degradation half life (DT50): < 1 d

Bioaccumulative potential

Components:

**Temozolomide:**
- Partition coefficient: n-octanol/water: log Pow: 1.35
- Mobility in soil: No data available
- 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
Not regulated as a dangerous good

IATA-DGR
Not regulated as a dangerous good

IMDG-Code
Not regulated as a dangerous good

Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code
Not applicable for product as supplied.

National Regulations

ADG
Not regulated as a dangerous good

SECTION 15. REGULATORY INFORMATION

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

Prohibition/Licensing Requirements: There is no applicable prohibition or notification/licensing requirements, including for carcinogens under Commonwealth, State or Territory legislation.

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

AICS: not determined
DSL: not determined
IECSC: not determined

SECTION 16. OTHER INFORMATION

Further information
Revision Date: 04/24/2019
Sources of key data used to: Internal technical data, data from raw material SDSs, OECD
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.

AU / EN