SAFETY DATA SHEET

Temozolomide Injection Formulation

Version 4.6
Revision Date: 04/24/2019
SDS Number: 27571-00014
Date of last issue: 2019/02/07
Date of first issue: 2014/11/03

1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Temozolomide Injection 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
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.
  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 protective gloves/ protective clothing/ eye protection/ face protection.

**Response:**
- P301 + P310 + P330 IF SWALLOWED: Immediately call a POISON CENTER/doctor. 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/doctor.
- 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**

Important symptoms and outlines of the emergency assumed:
- 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>
<th>ENCS No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temozolomide</td>
<td>85622-93-1</td>
<td>&gt;= 1 - &lt; 10</td>
<td></td>
</tr>
<tr>
<td>Hydrochloric acid</td>
<td>7647-01-0</td>
<td>&gt;= 3 - &lt; 5</td>
<td>1-215</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.
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.
**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.

## 7. HANDLING AND STORAGE

### Handling

<table>
<thead>
<tr>
<th>Technical measures</th>
<th>Static electricity may accumulate and ignite suspended dust causing an explosion. Provide adequate precautions, such as electrical grounding and bonding, or inert atmospheres.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local/Total ventilation</td>
<td>Use with local exhaust ventilation.</td>
</tr>
<tr>
<td>Advice on safe handling</td>
<td>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.</td>
</tr>
</tbody>
</table>

### 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.

### Storage

- Keep in properly labelled containers.
Store locked up.  
Keep tightly closed.  
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>Temozolomide</td>
<td>85622-93-1</td>
<td>TWA</td>
<td>0.1 ug/m³ (OEB 5)</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wipe limit</td>
<td>1 µg/100 cm²</td>
<td>Internal</td>
</tr>
<tr>
<td>Hydrochloric acid</td>
<td>7647-01-0</td>
<td>OEL-C</td>
<td>2 ppm</td>
<td>JP OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3 mg/m³</td>
<td>JSOH</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: 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.
Skin contact must be avoided by using impervious protective clothing (gloves, aprons, boots, etc).

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.
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.

11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure:
- 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

**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: Saccharomyces cerevisiae, mitotic recombination
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
12. ECOLOGICAL INFORMATION

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

Hazardous to the ozone layer:
Not applicable
### 12. 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**: 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**
Refer to section 15 for specific national regulation.

### 15. REGULATORY INFORMATION

**Related Regulations**

- **Fire Service Law**: Not applicable to dangerous materials / designated flammables.
- **Chemical Substance Control Law**: Not applicable for Specified Chemical Substance, Monitoring Chemical Substance and Priority Assessment Chemical Substance.
- **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

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>Number</th>
<th>Concentration (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-Methyl-4-oxo-3,4-dihydroimidazo[5,1-d][1,2,3,5]tetrazine-8-carboxamide</td>
<td>98</td>
<td>&gt;=1 - &lt;10</td>
</tr>
<tr>
<td>3-Methyl-4-oxo-3,4-dihydroimidazo[5,1-d][1,2,3,5]tetrazine-8-carboxamide</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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>Hydrogen chloride</td>
<td>98</td>
<td>&gt;=1 - &lt;10</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>Hydrogen chloride</td>
<td>98</td>
</tr>
</tbody>
</table>

Ordinance on Prevention of Hazards Due to Specified Chemical Substances - Group 3 Substance

<table>
<thead>
<tr>
<th>Chemical name</th>
</tr>
</thead>
<tbody>
<tr>
<td>hydrogen chloride</td>
</tr>
</tbody>
</table>

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
Not regulated as a dangerous good

Aviation Law
Not regulated as a dangerous good

Marine Pollution and Sea Disaster Prevention etc Law
Bulk transportation : Noxious liquid substance(Category Y)
Pack transportation : Not 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 Sheet:

Date format:
- yyyy/mm/dd

**Full text of other abbreviations**
- **ACGIH** : USA. ACGIH Threshold Limit Values (TLV)

**ACGIH / C** : Ceiling limit
**JP OEL JSOH / OEL-C** : Occupational Exposure Limit-Ceiling

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% response; EmS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; ERG - Emergency Response Guide; GHS - Globally Harmonized System; GLP - Good Laboratory Practice; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; IBC - International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk; IC50 - Half maximal inhibitory concentration; ICAO - International Civil Aviation Organization; IECSC - Inventory of Existing Chemical Substances in China; IMDG - International Maritime Dangerous Goods; IMO - International Maritime Organization; ISHL - Industrial Safety and Health Law (Japan); ISO - International Organisation for Standardization; KECl - Korea Existing Chemicals Inventory; LC50 - Lethal Concentration to 50% of a test population; LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose); MARPOL - International Convention for the Prevention of Pollution from Ships; n.o.s. - Not Otherwise Specified; Nch - Chilean Norm; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level;
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