1. PRODUCT AND COMPANY IDENTIFICATION

Chemical product name  :  Temozolomide Injection Formulation

Supplier's company name, address and phone number
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 of chemical product
Acute toxicity (Oral)  :  Category 3
Serious eye damage/eye irritation  :  Category 2
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.
H319 Causes serious eye irritation.
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
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 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P308 + P313 IF exposed or concerned: Get medical advice/ attention.
P337 + P313 If eye irritation persists: 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:
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

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Mixture</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Components</strong></td>
<td></td>
</tr>
<tr>
<td>Chemical name</td>
<td>CAS-No.</td>
</tr>
<tr>
<td>Citric acid</td>
<td>77-92-9</td>
</tr>
<tr>
<td>Temozolomide</td>
<td>85622-93-1</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 : 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.

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 irritation. 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. Contact with dust can cause mechanical irritation or drying of the skin.

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
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.
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Date of last issue: 2020/06/11
Date of first issue: 2014/11/03

6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures: Use personal protective equipment. Follow safe handling advice (see section 7) and personal protective equipment recommendations (see section 8).

Environmental precautions: Avoid release to the environment. 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

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: If sufficient ventilation is unavailable, use with local exhaust ventilation.

Advice on safe handling: Do not get on skin or clothing. Do not breathe dust. Do not swallow. Do not get in eyes. Wash skin thoroughly after handling. 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. Do not eat, drink or smoke when using this product. Take care to prevent spills, waste and minimize release to the environment.
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Avoidance of contact
Hygiene measures
   : Oxidizing agents
   : 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.

Storage
Conditions for safe 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>
</tbody>
</table>

Engineering measures
   : Use closed processing systems or containment technologies to control at source (e.g., glove boxes/isolators) and to prevent leakage of compounds into the workplace.
   : All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment.
   : No open handling permitted.
   : Totally enclosed processes and materials transport systems are required.
   : Operations require the use of appropriate containment technology designed to prevent leakage of compounds into the workplace.

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
9. PHYSICAL AND CHEMICAL PROPERTIES

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical state</td>
<td>powder</td>
</tr>
<tr>
<td>Colour</td>
<td>white</td>
</tr>
<tr>
<td>Odour</td>
<td>No data available</td>
</tr>
<tr>
<td>Odour Threshold</td>
<td>No data available</td>
</tr>
<tr>
<td>Melting point/freezing point</td>
<td>No data available</td>
</tr>
<tr>
<td>Boiling point, initial boiling point and boiling range</td>
<td>No data available</td>
</tr>
<tr>
<td>Flammability (solid, gas)</td>
<td>May form explosive dust-air mixture during processing, handling or other means.</td>
</tr>
<tr>
<td>Flammability (liquids)</td>
<td>No data available</td>
</tr>
<tr>
<td>Lower explosion limit and upper explosion limit / flammability limit</td>
<td>No data available</td>
</tr>
<tr>
<td>Upper explosion limit / Upper flammability limit</td>
<td>No data available</td>
</tr>
<tr>
<td>Lower explosion limit / Lower flammability limit</td>
<td>No data available</td>
</tr>
<tr>
<td>Flash point</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Decomposition temperature</td>
<td>No data available</td>
</tr>
<tr>
<td>pH</td>
<td>No data available</td>
</tr>
<tr>
<td>Evaporation rate</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Auto-ignition temperature</td>
<td>No data available</td>
</tr>
<tr>
<td>Viscosity</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Viscosity, kinematic</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>
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:

Citric acid:
Acute oral toxicity : LD50 (Mouse): 5,400 mg/kg
Acute dermal toxicity : LD50 (Rat): > 2,000 mg/kg
Method: OECD Test Guideline 402
Assessment: The substance or mixture has no acute dermal toxicity

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

Skin corrosion/irritation
Not classified based on available information.

Components:

Citric acid:
Species : Rabbit
Method : OECD Test Guideline 404
Result : No skin irritation

Serious eye damage/eye irritation
Causes serious eye irritation.

Components:

Citric acid:
Species : Rabbit
Result : Irritation to eyes, reversing within 21 days
Method : OECD Test Guideline 405

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

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Germ cell mutagenicity
Suspected of causing genetic defects.

**Components:**

**Citric acid:**
Genotoxicity in vitro : Test Type: Bacterial reverse mutation assay (AMES)
Result: negative

Test Type: in vitro micronucleus test
Result: positive

Test Type: Bacterial reverse mutation assay (AMES)
Result: negative

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

**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

Carcinogenicity
Suspected of causing cancer.

**Components:**

**Temozolomide:**
Species : Rat
Application Route : Oral
Exposure time : 6 Months
Result : 4 mg/kg body weight
Target Organs : Mammary gland

Carcinogenicity - Assessment : Limited evidence of carcinogenicity in animal studies

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

**Components:**

**Citric acid:**
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Effects on foetal development:
Test Type: One-generation reproduction toxicity study
Species: Rat
Application Route: Ingestion
Result: negative

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.

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:

Citric acid:
Species: Rat
NOAEL: 4,000 mg/kg
LOAEL: 8,000 mg/kg
Application Route: Ingestion
Exposure time: 10 Days

Temozolomide:
Species: Rat, female
NOAEL: 4 mg/kg
LOAEL: 21 mg/kg
Application Route: Oral
# SAFETY DATA SHEET

## Temozolomide Injection Formulation

<table>
<thead>
<tr>
<th>Version</th>
<th>Revision Date:</th>
<th>SDS Number:</th>
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<tbody>
<tr>
<td>7.1</td>
<td>2020/10/16</td>
<td>27571-00018</td>
<td>2020/06/11</td>
</tr>
</tbody>
</table>

### 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:

#### Citric acid:

**Toxicity to fish**
- LC50 (Pimephales promelas (fathead minnow)): > 100 mg/l
  - Exposure time: 96 h

**Toxicity to daphnia and other aquatic invertebrates**
- EC50 (Daphnia magna (Water flea)): 1,535 mg/l
  - Exposure time: 24 h

#### 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:

Citric acid:
Biodegradability: Result: Readily biodegradable.
Biodegradation: 97 %
Exposure time: 28 d
Method: OECD Test Guideline 301B

Temozolomide:
Biodegradability: Result: rapidly degradable
Biodegradation: 83 %
Exposure time: 35 d

Stability in water: Degradation half life (DT50): < 1 d

Bioaccumulative potential

Components:

Citric acid:
Partition coefficient: n-octanol/water: log Pow: -1.72

Temozolomide:
Partition coefficient: n-octanol/water: log Pow: 1.35

Mobility in soil
No data available

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 2811
- Proper shipping name: TOXIC SOLID, ORGANIC, N.O.S. (Temozolomide)
- Class: 6.1
- Packing group: III
- Labels: 6.1

IATA-DGR
- UN/ID No.: UN 2811
- Proper shipping name: Toxic solid, organic, n.o.s. (Temozolomide)
- Class: 6.1
- Packing group: III
- Labels: Toxic
- Packing instruction (cargo aircraft): 677
- Packing instruction (passenger aircraft): 670

IMDG-Code
- UN number: UN 2811
- Proper shipping name: TOXIC SOLID, ORGANIC, N.O.S. (Temozolomide)
- Class: 6.1
- Packing group: III
- Labels: 6.1
- EmS Code: F-A, S-A
- Marine pollutant: no

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.

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
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

| Chemical name | 3-Methyl-4-oxo-3,4-dihydroimidazo[5,1-d][1,2,3,5]tetrazine-8-carboxamide |

Substances Subject to be Notified Names
Not applicable

Substances Subject to be Indicated Names
Not applicable

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
Toxic and infectious substances (Article 2 and 3 of rules on shipping and storage of dangerous goods and its Attached Table 1)

Aviation Law
Toxic and infectious substances (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 Y)
Pack transportation : Not classified as marine pollutant

Narcotics and Psychotropics Control Act
Narcotic or Psychotropic Raw Material (Export / Import Permission)
Not applicable

Specific Narcotic or Psychotropic Raw Material (Export / Import permission)
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
Date format : yyyy/mm/dd

Full text of other abbreviations
AIIC - Australian Inventory of Industrial Chemicals; 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
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.