1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Temozolomide Injection Formulation

Manufacturer or supplier's details
Company : Merck & Co., Inc
Address : 2000 Galloping Hill Road
Kenilworth - New Jersey - U.S.A. 07033
Telephone : 908-740-4000
Emergency telephone number : 1-908-423-6000
E-mail address : EHSDATASTEWARD@msd.com

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 2A
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:
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>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mixture</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citric acid</td>
<td>77-92-9</td>
<td>&gt;= 10 -&lt; 30</td>
</tr>
<tr>
<td>Temozolomide</td>
<td>85622-93-1</td>
<td>&gt;= 1 -&lt; 10</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 center 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.

Special protective equipment for firefighters: In the event of fire, wear self-contained breathing apparatus.
Use personal protective equipment.
SAFETY DATA SHEET

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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

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.

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: Explosives.
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 µg/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

Eye protection: Remarks: Consider double gloving.

Skin and body protection: 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.

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

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</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>pH</td>
<td>No data available</td>
</tr>
<tr>
<td>Melting point/freezing point</td>
<td>No data available</td>
</tr>
<tr>
<td>Initial boiling point and boiling range</td>
<td>No data available</td>
</tr>
<tr>
<td>Flash point</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Evaporation rate</td>
<td>Not applicable</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>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>Vapour pressure</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Relative vapour density</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Relative density</td>
<td>No data available</td>
</tr>
<tr>
<td>Density</td>
<td>No data available</td>
</tr>
<tr>
<td>Solubility(ies) Water solubility</td>
<td>soluble</td>
</tr>
<tr>
<td>Partition coefficient: n-octanol/water</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Auto-ignition temperature</td>
<td>No data available</td>
</tr>
<tr>
<td>Decomposition 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>
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

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:
<table>
<thead>
<tr>
<th>Species</th>
<th>Rabbit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Method</td>
<td>OECD Test Guideline 404</td>
</tr>
<tr>
<td>Result</td>
<td>No skin irritation</td>
</tr>
</tbody>
</table>

Serious eye damage/eye irritation
Causes serious eye irritation.

Components:

Citric acid:
<table>
<thead>
<tr>
<th>Species</th>
<th>Rabbit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Result</td>
<td>Irritation to eyes, reversing within 21 days</td>
</tr>
<tr>
<td>Method</td>
<td>OECD Test Guideline 405</td>
</tr>
</tbody>
</table>

Respiratory or skin sensitisation

Skin sensitisation
Not classified based on available information.

Respiratory sensitisation
Not classified based on available information.

Components:

Temozolomide:
<table>
<thead>
<tr>
<th>Test Type</th>
<th>Maximisation Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure routes</td>
<td>Dermal</td>
</tr>
<tr>
<td>Species</td>
<td>Guinea pig</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
</tbody>
</table>

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 cytogenetic test, chromosomal analysis) |
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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: positive
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:
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:

<table>
<thead>
<tr>
<th>Exposure routes</th>
<th>Ingestion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Target Organs</td>
<td>Bone marrow, thymus gland, Lymph nodes, spleen</td>
</tr>
<tr>
<td>Assessment</td>
<td>Causes damage to organs through prolonged or repeated exposure</td>
</tr>
</tbody>
</table>

Repeated dose toxicity

Components:

Citric acid:

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>4,000 mg/kg</td>
</tr>
<tr>
<td>LOAEL</td>
<td>8,000 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Ingestion</td>
</tr>
<tr>
<td>Exposure time</td>
<td>10 Days</td>
</tr>
</tbody>
</table>

Temozolomide:

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat, female</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>4 mg/kg</td>
</tr>
<tr>
<td>LOAEL</td>
<td>21 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>6 Months</td>
</tr>
<tr>
<td>Target Organs</td>
<td>Lymph nodes, thymus gland, Bone marrow, Reproductive organs</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat, male</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>8.5 mg/kg</td>
</tr>
<tr>
<td>LOAEL</td>
<td>34 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>6 Months</td>
</tr>
<tr>
<td>Target Organs</td>
<td>Lymph nodes, thymus gland, Bone marrow, male reproductive organs, Gastrointestinal tract</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Dog</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>2.5 mg/kg</td>
</tr>
<tr>
<td>LOAEL</td>
<td>6.3 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>6 Months</td>
</tr>
</tbody>
</table>
11. 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

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.

15. REGULATORY INFORMATION

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

Minister of Industry Regulation No. 23/M-IND/PER/4/2013 concerning the Revision of Minister of Industry Regulation No. 87/M-IND/PER/9/2009 concerning Globally Harmonized System of Classification and Labelling of Chemicals.

Regulation of the Minister of Health No. 472 of 1996 on the Safeguarding of Substances Hazardous to Health
Hazardous substances that must be registered : Not applicable

Government Regulation No. 74 of 2001 on the Management of Hazardous and Toxic Substances
Hazardous substances approved for use : Not applicable
Prohibited substances : Not applicable
Restricted substances : Not applicable

Regulation of the Minister of Trade No. 44 of 2009 on Procurement, Distribution and Supervision of Hazardous Materials
Type of Hazardous Materials Restricted to Import, Distribution and Supervision : 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

Items where changes have been made to the previous version are highlighted in the body of this document by two vertical lines.

Date format : yyyy/mm/dd
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.

ID / EN