SAFETY DATA SHEET

Temozolomide Injection Formulation

SECTION 1. IDENTIFICATION

Product name : Temozolomide Injection Formulation
Other means of identification : No data available

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

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

Restrictions on use : Not applicable

SECTION 2. HAZARDS IDENTIFICATION

GHS classification in accordance with the Hazardous Products Regulations
Acute toxicity (Oral) : Category 3
Eye irritation : Category 2A
Germ cell mutagenicity : Category 2
Carcinogenicity : Category 2
Reproductive toxicity : Category 1B
Specific target organ toxicity - repeated exposure (Oral) : Category 1 (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.
H372 Causes 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 and face protection.

**Response:**
- P301 + P310 + P330 IF SWALLOWED: Immediately call a POISON CENTER. 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 attention.
- P337 + P313 If eye irritation persists: Get medical attention.

**Storage:**
- P405 Store locked up.

**Disposal:**
- P501 Dispose of contents and container to an approved waste disposal plant.

**Other hazards**
Contact with dust can cause mechanical irritation or drying of the skin.
May form explosive dust-air mixture during processing, handling or other means.

### SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Mixture</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Components</th>
<th></th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citric acid</td>
<td>2-hydroxypropane-1,2,3-tricarboxylic acid</td>
<td>77-92-9</td>
</tr>
<tr>
<td>Temozolomide</td>
<td>No data available</td>
<td>85622-93-1</td>
</tr>
</tbody>
</table>

*Actual concentration or concentration range is withheld as a trade secret*

### 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.
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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. Causes 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.

SECTION 5. FIRE-FIGHTING MEASURES

Suitable extinguishing media: Water spray
Alcohol-resistant foam
Carbon dioxide (CO2)
Dry chemical

Unsuitable extinguishing media: None known.

Specific hazards during fire fighting: 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: In the event of fire, wear self-contained breathing apparatus.
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for fire-fighters

Use personal protective equipment.

SECTION 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.

SECTION 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 labeled 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
- Organic peroxides
- Explosives
- Gases

## SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

### Ingredients 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/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**: Chemical-resistant gloves

**Remarks**: Consider double gloving.

**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 faceshield 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**: Work uniform or laboratory coat. 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.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

- **Appearance**: powder
- **Color**: white
- **Odor**: No data available
- **Odor 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
- **Vapor pressure**: Not applicable
- **Relative vapor density**: Not applicable
- **Relative density**: No data available
- **Density**: No data available
- **Solubility(ies)**
  - **Water solubility**: soluble
- **Partition coefficient: n-**: Not applicable
SECTION 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.

SECTION 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: 241.75 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
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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 sensitization

Skin sensitization
Not classified based on available information.

Respiratory sensitization
Not classified based on available information.

Components:
Temozolomide:
Test Type: Maximization Test
Routes of exposure: Dermal
Species: Guinea pig
Result: negative

Germ cell mutagenicity
Suspected of causing genetic defects.

Components:
Citric acid:
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES)
Result: negative
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<table>
<thead>
<tr>
<th>Test Type</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>in vitro micronucleus test</td>
<td>positive</td>
</tr>
<tr>
<td>Bacterial reverse mutation assay (AMES)</td>
<td>negative</td>
</tr>
</tbody>
</table>

#### Genotoxicity in vivo
- **Test Type:** Mutagenicity (in vivo mammalian bone-marrow cytogenetic 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:** 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 fetal 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 fetal development: Test Type: Embryo-fetal development
Species: Rat
Application Route: Oral
Embryo-fetal 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
Causes damage to organs (Bone marrow, thymus gland, Lymph nodes, spleen) through prolonged or repeated exposure if swallowed.

Components:

**Temozolomide:**

<table>
<thead>
<tr>
<th>Routes of exposure</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>
</tbody>
</table>
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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, Diarrhea, anorexia, Fatigue, hair loss

SECTION 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 (Onchorhynchus 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
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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

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.

Domestic regulation

TDG
Not regulated as a dangerous good

SECTION 15. REGULATORY INFORMATION

The ingredients of this product are reported in the following inventories:
AICS : not determined
DSL : not determined
IECSC : not determined

SECTION 16. OTHER INFORMATION

Full text of other abbreviations

AIIIC - 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 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 Organization for Standardization; KECI - 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; NOELR - No Observable Effect Loading Rate; NOM - Official Mexican Norm; NTP - National Toxicology Program; NZIoC - New Zealand Inventory of Chemicals; OECD - Organization for Economic Co-operation and Development; OPPTS - Office of Chemical Safety and Pollution Prevention; PBT - Persistent, Bioaccumulative and Toxic substance; PICCS - Philippines Inventory of Chemicals and Chemical Substances; (Q)SAR - (Quantitative) Structure Activity Relationship; REACH - Regulation (EC) No
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Date of first issue: 11/03/2014

1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; SADT - Self-Accelerating Decomposition Temperature; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance Inventory; TDG - Transportation of Dangerous Goods; TSCA - Toxic Substances Control Act (United States); UN - United Nations; UNRTDG - United Nations Recommendations on the Transport of Dangerous Goods; vPvB - Very Persistent and Very Bioaccumulative; WHMIS - Workplace Hazardous Materials Information System

Sources of key data used to compile the Material Safety Data Sheet:

Revision Date: 03/22/2021
Date format: mm/dd/yyyy

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

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.

CA / Z8