SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Temozolomide Injection Formulation

Manufacturer or supplier’s details
Company : MSD
Address : 855 Leandro N. Alem St., 8 Floor
Buenos Aires, Argentina C1001AFB
Telephone : 908-740-4000
Emergency telephone : 1-908-423-6000
E-mail address : EHSDATASTEWARD@msd.com
Telefax : 908-735-1496

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

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification
Acute toxicity (Oral) : Category 3
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 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 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.

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>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; 20</td>
</tr>
<tr>
<td>Sodium chloride</td>
<td>7647-14-5</td>
<td>&gt;= 10 - &lt; 20</td>
</tr>
<tr>
<td>Temozolomide</td>
<td>85622-93-1</td>
<td>&gt;= 5 - &lt; 10</td>
</tr>
</tbody>
</table>

SECTION 4. FIRST AID MEASURES

General advice:
In the case of accident or if you feel unwell, seek medical advice immediately.
When symptoms persist or in all cases of doubt seek medical advice.
If inhaled: If inhaled, remove to fresh air. Get medical attention.

In case of skin contact: In case of contact, immediately flush skin with soap and plenty of water. Remove contaminated clothing and shoes. Get medical attention. Wash clothing before reuse. Thoroughly clean shoes before reuse.

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

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.

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.
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

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 toxicity
Sodium chloride:
Acute oral toxicity: LD50 (Rat): 3.550 mg/kg
Acute inhalation toxicity: LC50 (Rat): > 42 mg/l
   Exposure time: 1 h
   Test atmosphere: dust/mist
Acute dermal toxicity: LD50 (Rabbit): > 5.000 mg/kg

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

Sodium chloride:
Species: Rabbit
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

Sodium chloride:
Species: Rabbit
Result: No eye irritation

Respiratory or skin sensitization

Skin sensitization
Not classified based on available information.
**Respiratory sensitization**
Not classified based on available information.

**Components:**

**Sodium chloride:**
- **Test Type:** Local lymph node assay (LLNA)
- **Routes of exposure:** Skin contact
- **Species:** Mouse
- **Result:** negative

**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
  - **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)
    - **Species:** Rat
    - **Application Route:** Ingestion
    - **Result:** negative

**Sodium chloride:**
- **Genotoxicity in vitro:**
  - **Test Type:** In vitro mammalian cell gene mutation test
    - Result: positive
  - **Test Type:** Bacterial reverse mutation assay (AMES)
    - Result: negative
  - **Test Type:** Saccharomyces cerevisiae, gene mutation assay (in vitro)
    - Result: positive
  - **Test Type:** DNA damage and repair, unscheduled DNA synthesis in mammalian cells (in vitro)
    - Result: positive
Test Type: Chromosome aberration test in vitro
Result: positive

Test Type: Chromosome aberration test in vitro
Result: negative

Genotoxicity in vivo:
- Test Type: In vivo micronucleus test
  - Species: Mouse
  - Application Route: Intraperitoneal injection
  - Result: negative

Test Type: Mutagenicity (in vivo mammalian bone-marrow cytogenetic test, chromosomal analysis)
- Species: Rat
- Application Route: Intraperitoneal injection
- Result: positive

Germ cell mutagenicity - Assessment:
- Weight of evidence does not support classification as a germ cell mutagen.

**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:**

**Sodium chloride:**
-Species: Rat
- Application Route: Ingestion
- Exposure time: 2 Years
- Result: negative

**Temozolomide:**
- Species: Rat
- Application Route: Oral
- Exposure time: 6 Months
  - 4 mg/kg body weight
- 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
May cause damage to organs (Bone marrow, thymus gland, Lymph nodes, spleen) through prolonged or repeated exposure if swallowed.

Components:

Temozolomide:
Routes of exposure: 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
Sodium chloride:
Species: Rat
LOAEL: 2.533 mg/kg
Application Route: Ingestion
Exposure time: 2 y

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, 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

**Sodium chloride:**
  Toxicity to fish: LC50 (Lepomis macrochirus (Bluegill sunfish)): 5.840 mg/l
  Exposure time: 96 h

  Toxicity to daphnia and other aquatic invertebrates: EC50 (Daphnia magna (Water flea)): 4.136 mg/l
  Exposure time: 48 h

  Toxicity to algae/aquatic plants: EC50: > 2.000 mg/l
  Exposure time: 96 h

  Toxicity to fish (Chronic toxicity): NOEC (Pimephales promelas (fathead minnow)): 252 mg/l
  Exposure time: 33 d

  Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity): NOEC (Daphnia pulex (Water flea)): 314 mg/l
  Exposure time: 21 d

  Toxicity to microorganisms: EC10: > 1.000 mg/l

**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

**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**
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.

**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.

**SECTION 15. REGULATORY INFORMATION**

Safety, health and environmental regulations/legislation specific for the substance or mixture
- Argentina. Carcinogenic Substances and Agents Registry: Not applicable
- Control of precursors and essential chemicals for the preparation of drugs: Not applicable

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

**SECTION 16. OTHER INFORMATION**

Further information
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.

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