SAFETY DATA SHEET

Temozolomide Injection Formulation

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Temozolomide Injection Formulation

Manufacturer or supplier’s details
Company : MSD
Address : Rua Treze de Maio, 1161
Campinas, São Paulo, Brazil 13106-054
Telephone : 908-740-4000
Emergency telephone : 55 19 3758 2000
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 in accordance with ABNT NBR 14725 Standard

Acute toxicity (Oral) : Category 3
Serious eye damage : Category 1
Germ cell mutagenicity : Category 2
Carcinogenicity : Category 2
Reproductive toxicity : Category 1B
Specific target organ systemic toxicity - repeated exposure (Oral) : Category 1 (Bone marrow, thymus gland, Lymph nodes, spleen)

GHS label elements in accordance with ABNT NBR 14725 Standard

Hazard pictograms : 

Signal Word : Danger
Hazard Statements : H301 Toxic if swallowed.
H318 Causes serious eye damage.
H341 Suspected of causing genetic defects.
H351 Suspected of causing cancer.
H360FD May damage fertility. May damage the unborn child. 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.
P260 Do not breathe dust. 
P280 Wear protective gloves/ protective clothing/ eye protection/ face protection.

Response:
P301 + P310 + P330 IF SWALLOWED: Immediately call a POISON CENTER/doctor. Rinse mouth. 
P305 + P351 + P338 + P310 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a POISON CENTER/doctor. 
P308 + P313 IF exposed or concerned: Get medical advice/ attention.

Other hazards which do not result in classification
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>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temozolomide</td>
<td>85622-93-1</td>
</tr>
<tr>
<td>Hydrochloric acid</td>
<td>7647-01-0</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 immediately.

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 damage.
- 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.

**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.

**Notes to physician:**
Treat symptomatically and supportively.

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**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 for fire-fighters:**
In the event of fire, wear self-contained breathing apparatus.
Use personal protective equipment.

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**SECTION 6. ACCIDENTAL RELEASE MEASURES**

**Personal precautions, protective equipment and emergency procedures:**
Use personal protective equipment. Follow safe handling advice and personal protective equipment recommendations.

**Environmental precautions:**
Discharge into the environment must be avoided. Prevent further leakage or spillage if safe to do so. Retain and dispose of contaminated wash water. Local authorities should be advised if significant spillages cannot be contained.

**Methods and materials for**
Sweep up or vacuum up spillage and collect in suitable
containment and cleaning up: 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: 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. Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment. Keep container tightly closed. Minimize dust generation and accumulation. Keep container closed when not in use. Keep away from heat and sources of ignition. Take precautionary measures against static discharges. Take care to prevent spills, waste and minimize release to the environment.

Hygiene measures: Ensure that eye flushing systems and safety showers are located close to the working place. When using do not eat, drink or smoke. Wash contaminated clothing before re-use.

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)</th>
<th>Control parameters / Permissible</th>
<th>Basis</th>
</tr>
</thead>
</table>

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Exposure concentration limits:

<table>
<thead>
<tr>
<th>Substance</th>
<th>CAS Registry Number</th>
<th>Exposure</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temozolomide</td>
<td>85622-93-1</td>
<td>TWA</td>
<td>0.1 ug/m^3 (OEB 5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wipe limit</td>
<td>1 µg/100 cm^2</td>
</tr>
<tr>
<td>Hydrochloric acid</td>
<td>7647-01-0</td>
<td>C</td>
<td>2 ppm</td>
</tr>
</tbody>
</table>

**Engineering measures**

Minimize workplace exposure concentrations. Apply measures to prevent dust explosions. Ensure that dust-handling systems (such as exhaust ducts, dust collectors, vessels, and processing equipment) are designed in a manner to prevent the escape of dust into the work area (i.e., there is no leakage from the equipment). Use with local exhaust ventilation.

**Personal protective equipment**

**Respiratory protection**

Use respiratory protection unless adequate local exhaust ventilation is provided or exposure assessment demonstrates that exposures are within recommended exposure guidelines. If combined particulates and acidic gas/vapor type

**Hand protection**

Material: Chemical-resistant gloves

Remarks: Choose gloves to protect hands against chemicals depending on the concentration specific to place of work. Breakthrough time is not determined for the product. Change gloves often!
For special applications, recommend clarifying the resistance to chemicals of the aforementioned protective gloves with the glove manufacturer. Wash hands before breaks and at the end of workday.

**Eye protection**

Wear the following personal protective equipment:
Chemical resistant goggles must be worn.
If splashes are likely to occur, wear:
Face-shield

**Skin and body protection**

Select appropriate protective clothing based on chemical resistance data and an assessment of the local exposure potential.
Skin contact must be avoided by using impervious protective clothing (gloves, aprons, boots, etc).

**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**

No data available
Evaporation rate : No data available
Flammability (solid, gas) : May form explosive dust-air mixture during processing, handling or other means.
Flammability (liquids) : No data available
Upper explosion limit / Upper flammability limit : No data available
Lower explosion limit / Lower flammability limit : No data available
Vapor pressure : No data available
Relative vapor density : No data available
Relative density : No data available
Density : 1 g/cm³
Solubility(ies) 
Water solubility : No data available
Partition coefficient: n-octanol/water : No data available
Autoignition temperature : No data available
Decomposition temperature : No data available
Viscosity 
Viscosity, kinematic : No data available
Explosive properties : Not explosive
Oxidizing properties : The substance or mixture is not classified as oxidizing.
Molecular weight : No data available
Particle size : No data available

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: 243.59 mg/kg
  - Method: Calculation method

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

Hydrochloric acid:
Acute inhalation toxicity:
- LC50 (Rat): 8.3 mg/l
  - Exposure time: 30 min
  - Test atmosphere: dust/mist

Skin corrosion/irritation:
Not classified based on available information.

Components:
Hydrochloric acid:
Method:
- EPISKIN Human Skin Model Test
Result:
- Corrosive after 3 minutes or less of exposure

Serious eye damage/eye irritation:
Causes serious eye damage.

Components:
Hydrochloric acid:
Result:
- Irreversible effects on the eye
Method:
- OECD Test Guideline 437

Respiratory or skin sensitization:
Skin sensitization:
Not classified based on available information.
Respiratory sensitization:
Not classified based on available information.
Components:

Temozolomide:

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Maximization Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Routes of exposure</td>
<td>Dermal</td>
</tr>
<tr>
<td>Species</td>
<td>Guinea pig</td>
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<tr>
<td>Result</td>
<td>negative</td>
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</table>

Hydrochloric acid:

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Maximization Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Routes of exposure</td>
<td>Skin contact</td>
</tr>
<tr>
<td>Species</td>
<td>Guinea pig</td>
</tr>
<tr>
<td>Method</td>
<td>OECD Test Guideline 406</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
</tbody>
</table>

Germ cell mutagenicity

Suspected of causing genetic defects.

Components:

Temozolomide:

Genotoxicity in vitro:

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Bacterial reverse mutation assay (AMES)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Result: positive</td>
</tr>
</tbody>
</table>

Genotoxicity in vitro:

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Chromosome aberration test in vitro</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test system</td>
<td>Human lymphocytes</td>
</tr>
<tr>
<td>Result</td>
<td>positive</td>
</tr>
</tbody>
</table>

Germ cell mutagenicity - Assessment:

Positive results from in vitro mammalian mutagenicity assays, chemical structure activity relationship to known germ cell mutagens

Hydrochloric acid:

Genotoxicity in vitro:

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Saacharomyces cerevisiae, miotic recombination assay (in vitro)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
</tbody>
</table>

Carcinogenicity

Suspected of causing cancer.

Components:

Temozolomide:

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>6 Months</td>
</tr>
<tr>
<td>Result</td>
<td>4 mg/kg body weight</td>
</tr>
<tr>
<td>Target Organs</td>
<td>positive</td>
</tr>
</tbody>
</table>

Carcinogenicity - Assessment:

Limited evidence of carcinogenicity in animal studies
Hydrochloric acid:
Species: Rat
Application Route: Inhalation
Exposure time: 128 weeks
Result: negative

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

Components:

Temozolomide:
Effects on fertility: Test Type: Fertility/early embryonic development
Species: Rat, male
Application Route: Oral
Fertility: LOAEL: 8.5 mg/kg body weight
Result: positive

Effects on 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.

Components:

Hydrochloric acid: May cause respiratory irritation.

STOT-repeated exposure
Causes 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:

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:

Temozolomide:
Toxicity to fish: LC50 (Oncorhynchus mykiss (rainbow trout)): > 100 mg/l  
Exposure time: 96 h  
Method: OECD Test Guideline 203

Toxicity to daphnia and other aquatic invertebrates: EC50 (Daphnia magna (Water flea)): > 100 mg/l  
Exposure time: 48 h  
Method: OECD Test Guideline 202

Toxicity to algae/aquatic plants: EC50 (Pseudokirchneriella subcapitata (green algae)): > 90 mg/l  
Exposure time: 72 h  
Method: OECD Test Guideline 201
NOEC (Pseudokirchneriella subcapitata (green algae)): 40 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201

Toxicity to microorganisms:
EC50: > 100 mg/l
Exposure time: 3 h
Test Type: Respiration inhibition
Method: OECD Test Guideline 209

Persistence and degradability
Components:

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

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

Bioaccumulative potential
Components:

Temozolomide:
Partition coefficient: n-octanol/water: log Pow: 1,35

Mobility in soil
No data available

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
Transit in bulk according to Annex II of MARPOL 73/78 and the IBC Code
Not applicable for product as supplied.

Domestic regulation

ANTT
Not regulated as a dangerous good

SECTION 15. REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture
National List of Carcinogenic Agents for Humans - (LINACH) : Not applicable
Brazil. Ordinance No. 1274 on the control and monitoring of chemicals. : Hydrochloric acid

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

Full text of other abbreviations
ACGIH : USA. ACGIH Threshold Limit Values (TLV)
ACGIH / C : Ceiling limit

AICS - Australian Inventory of Chemical Substances; ANTT - National Agency for Transport by Land of Brazil; ASTM - American Society for the Testing of Materials; bw - Body weight; CMR - Carcinogen, Mutagen or Reproductive Toxicant; CPR - Controlled Products Regulations; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; ELx - Loading rate associated with x% response; EmS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; ERG - Emergency Response Guide; GHS - Globally Harmonized System; GLP - Good Laboratory Practice; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; IBC - International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk; IC50 - Half maximal inhibitory concentration; ICAO - International Civil Aviation Organization; IECSC - Inventory of Existing Chemical Substances in China; IMDG - International Maritime Dan-
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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