SAFETY DATA SHEET

Temozolomide Injection Formulation

SECTION 1: Identification of the substance/mixture and of the company/undertaking

1.1 Product identifier
   Trade name : Temozolomide Injection Formulation

1.2 Relevant identified uses of the substance or mixture and uses advised against
   Use of the Substance/Mixture : Pharmaceutical

1.3 Details of the supplier of the safety data sheet
   Company : MSD
             117 16th Road
             07033 Halfway house, Midrand, South Africa
   Telephone : +27 11 655 3000
   Telefax : 908-735-1496
   E-mail address of person responsible for the SDS : EHSDATASTEWARD@msd.com

1.4 Emergency telephone number
   1-908-423-6000

SECTION 2: Hazards identification

2.1 Classification of the substance or mixture
   Classification (REGULATION (EC) No 1272/2008)
      Acute toxicity, Category 3 : H301: Toxic if swallowed.
      Serious eye damage, Category 1 : H318: Causes serious eye damage.
      Germ cell mutagenicity, Category 2 : H341: Suspected of causing genetic defects.
      Carcinogenicity, Category 2 : H351: Suspected of causing cancer.
      Reproductive toxicity, Category 1B : H360FD: May damage fertility. May damage the unborn child.
      Specific target organ toxicity - repeated exposure, Category 2 : H373: May cause damage to organs through prolonged or repeated exposure.

2.2 Label elements
   Labelling (REGULATION (EC) No 1272/2008)
      Hazard pictograms :
                        
                        
                        
      Signal word : Danger
      Hazard statements : H301 Toxic if swallowed.
                          H318 Causes serious eye damage.
                          H341 Suspected of causing genetic defects.
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.

Hazardous components which must be listed on the label:
- Temozolomide
- Hydrochloric acid

**2.3 Other hazards**
- May form explosive dust-air mixture during processing, handling or other means.

### SECTION 3: Composition/information on ingredients

#### 3.2 Mixtures

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>EC-No.</th>
<th>Index-No.</th>
<th>Classification</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temozolomide</td>
<td>85622-93-1</td>
<td></td>
<td></td>
<td>Acute Tox.2; H300 Muta.2; H341 Carc.2; H351 Repr.1B; H360FD STOT RE1; H372</td>
<td>&gt;= 1 - &lt; 10</td>
</tr>
<tr>
<td>Hydrochloric acid</td>
<td>7647-01-0</td>
<td>231-595-7</td>
<td>017-002-01-X</td>
<td>Met. Corr.1; H290 Skin Corr.1A; H314 Eye Dam.1; H318 STOT SE3; H335</td>
<td>&gt;= 3 - &lt; 5</td>
</tr>
</tbody>
</table>

For explanation of abbreviations see section 16.
SECTION 4: First aid measures

4.1 Description of 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.

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.

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 centre immediately. Rinse mouth thoroughly with water. Never give anything by mouth to an unconscious person.

4.2 Most important symptoms and effects, both acute and delayed

Risks: Toxic if swallowed. Causes serious eye damage. 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.

4.3 Indication of any immediate medical attention and special treatment needed

Treatment: Treat symptomatically and supportively.

SECTION 5: Firefighting measures

5.1 Extinguishing media

Suitable extinguishing media: Water spray Alcohol-resistant foam Carbon dioxide (CO2) Dry chemical
5.2 Special hazards arising from the substance or mixture

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

5.3 Advice for firefighters

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

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.

SECTION 6: Accidental release measures

6.1 Personal precautions, protective equipment and emergency procedures

Personal precautions: Use personal protective equipment. Follow safe handling advice and personal protective equipment recommendations.

6.2 Environmental precautions

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.

6.3 Methods and material for containment and cleaning up

Methods for 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 deter-
mine which regulations are applicable. Sections 13 and 15 of this SDS provide information regarding certain local or national requirements.

6.4 Reference to other sections
See sections: 7, 8, 11, 12 and 13.

SECTION 7: Handling and storage

7.1 Precautions for safe 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: 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.

7.2 Conditions for safe storage, including any incompatibilities

Requirements for storage areas and containers: Keep in properly labelled containers. Store locked up. Keep tightly closed. Store in accordance with the particular national regulations.

Advice on common storage: Do not store with the following product types: Strong oxidizing agents Organic peroxides Explosives Gases

7.3 Specific end use(s)

Specific use(s): No data available

No data available
SECTION 8: Exposure controls/personal protection

8.1 Control parameters

**Occupational Exposure Limits**

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters</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>
<tr>
<td>Hydrochloric acid</td>
<td>7647-01-0</td>
<td>STEL OEL-RL</td>
<td>5 ppm 7 mg/m³</td>
<td>ZA OEL</td>
</tr>
<tr>
<td>Further information</td>
<td>Recommended Limit</td>
<td>STEL 10 ppm 15 mg/m³</td>
<td>2000/39/EC</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA 5 ppm 8 mg/m³</td>
<td>2000/39/EC</td>
<td></td>
</tr>
</tbody>
</table>

**Derived No Effect Level (DNEL) according to Regulation (EC) No. 1907/2006:**

<table>
<thead>
<tr>
<th>Substance name</th>
<th>End Use</th>
<th>Exposure routes</th>
<th>Potential health effects</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrochloric acid</td>
<td>Workers</td>
<td>Inhalation</td>
<td>Long-term local effects</td>
<td>8 mg/m3</td>
</tr>
<tr>
<td>Workers</td>
<td>Inhalation</td>
<td>Acute local effects</td>
<td>15 mg/m3</td>
<td></td>
</tr>
</tbody>
</table>

8.2 Exposure controls

**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 local exhaust ventilation.

**Personal protective equipment**

**Eye protection**

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

**Hand protection**

Material: Chemical-resistant gloves

Remarks: Choose gloves to protect hands against chemicals depending on the concentration and quantity of the hazardous substance and specific to place of work. Breakthrough time is not determined for the product. Change gloves often! For special applications, we 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.

**Skin and body protection**

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

Respiratory protection: Use respiratory protection unless adequate local exhaust ventilation is provided or exposure assessment demonstrates that exposures are within recommended exposure guidelines.

Filter type: Combined particulates and acidic gas/vapour type (E-P)

**SECTION 9: Physical and chemical properties**

9.1 Information on basic physical and chemical properties

- **Appearance**: powder
- **Colour**: white
- **Odour**: No data available
- **Odour 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.
- **Upper explosion limit / Upper flammability limit**: No data available
- **Lower explosion limit / Lower flammability limit**: No data available
- **Vapour pressure**: No data available
- **Relative vapour 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
  - Auto-ignition temperature: No data available
  - Decomposition temperature: No data available
- **Viscosity**
  - Viscosity, kinematic: No data available
9.2 Other information
- Flammability (liquids): No data available
- Molecular weight: No data available
- Particle size: No data available

SECTION 10: Stability and reactivity

10.1 Reactivity
- Not classified as a reactivity hazard.

10.2 Chemical stability
- Stable under normal conditions.

10.3 Possibility of hazardous reactions
- Hazardous reactions: May form explosive dust-air mixture during processing, handling or other means. Can react with strong oxidizing agents.

10.4 Conditions to avoid
- Conditions to avoid: Heat, flames and sparks. Avoid dust formation.

10.5 Incompatible materials
- Materials to avoid: Oxidizing agents

10.6 Hazardous decomposition products
- No hazardous decomposition products are known.

SECTION 11: Toxicological information

11.1 Information on toxicological effects
- 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:**
- **Method**
  - OECD Test Guideline 437
- **Result**
  - Irreversible effects on the eye

**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

**Hydrochloric acid:**
- **Test Type**
  - Maximisation Test
- **Exposure routes**
  - Skin contact
- **Species**
  - Guinea pig
- **Method**
  - OECD Test Guideline 406
**Germ cell mutagenicity**
Suspected of causing genetic defects.

**Components:**

**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

**Hydrochloric acid:**
Genotoxicity in vitro
Test Type: Saacharomyces cerevisiae, mitotic recombination assay (in vitro)
Result: negative

**Carcinogenicity**
Suspected of causing cancer.

**Components:**

**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

**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 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.

Components:

Hydrochloric acid:
Assessment: May cause respiratory irritation.

STOT - repeated exposure
May cause damage to organs through prolonged or repeated exposure.

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:

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
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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

SECTION 12: Ecological information

12.1 Toxicity

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

12.2 Persistence and degradability

Components:

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

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

12.3 Bioaccumulative potential

Components:

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

12.4 Mobility in soil
No data available

12.5 Results of PBT and vPvB assessment
Not relevant

12.6 Other adverse effects
No data available

SECTION 13: Disposal considerations

13.1 Waste treatment methods

Product: Dispose of in accordance with local regulations.
According to the European Waste Catalogue, Waste Codes
are not product specific, but application specific.
Waste codes should be assigned by the user, preferably in
discussion with the waste disposal authorities.

Contaminated packaging: Empty containers should be taken to an approved waste han-
dling site for recycling or disposal.
If not otherwise specified: Dispose of as unused product.

SECTION 14: Transport information

14.1 UN number
Not regulated as a dangerous good

14.2 UN proper shipping name
Not regulated as a dangerous good

14.3 Transport hazard class(es)
Not regulated as a dangerous good

14.4 Packing group
Not regulated as a dangerous good

14.5 Environmental hazards
Not regulated as a dangerous good

14.6 Special precautions for user
Not applicable

14.7 Transport in bulk according to IMO instruments
SECTION 15: Regulatory information

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

The components of this product are reported in the following inventories:

- AICS: not determined
- DSL: not determined
- IECSC: not determined

15.2 Chemical safety assessment
A Chemical Safety Assessment has not been carried out.

SECTION 16: Other information

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

Full text of H-Statements

- H290: May be corrosive to metals.
- H300: Fatal if swallowed.
- H314: Causes severe skin burns and eye damage.
- H318: Causes serious eye damage.
- H335: May cause respiratory 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 through prolonged or repeated exposure if swallowed.

Full text of other abbreviations

- Acute Tox.: Acute toxicity
- Carc.: Carcinogenicity
- Eye Dam.: Serious eye damage
- Met. Corr.: Corrosive to metals
- Muta.: Germ cell mutagenicity
- Repr.: Reproductive toxicity
- Skin Corr.: Skin corrosion
- STOT RE: Specific target organ toxicity - repeated exposure
- STOT SE: Specific target organ toxicity - single exposure
- ZA OEL: South Africa. Hazardous Chemical Substances Regulations, Occupational Exposure Limits
- 2000/39/EC / TWA: Limit Value - eight hours
- 2000/39/EC / STEL: Short term exposure limit
- ZA OEL / STEL OEL-RL: Short term occupational exposure limits - recommended limit
Further information

Classification of the mixture:

<table>
<thead>
<tr>
<th>Classification procedure</th>
<th>Acute Tox. 3 H301</th>
<th>Eye Dam. 1 H318</th>
<th>Muta. 2 H341</th>
<th>Carc. 2 H351</th>
<th>Repr. 1B H360FD</th>
<th>STOT RE 2 H373</th>
</tr>
</thead>
</table>

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 mate-
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.

ZA / EN