Safety Data Sheet
Temozolomide Capsules
Strength: 5 mg, 20 mg, 100 mg, 140 mg, 180 mg and 250 mg
Pack Size: 5's and 14's Tablets per glass bottle

Revision No.: 00

EMERGENCY OVERVIEW
Each Temozolomide Capsules intended for oral administration contains Temozolomide and excipients generally considered to be non- toxic and non-hazardous in small quantities and under conditions of normal occupational exposure.

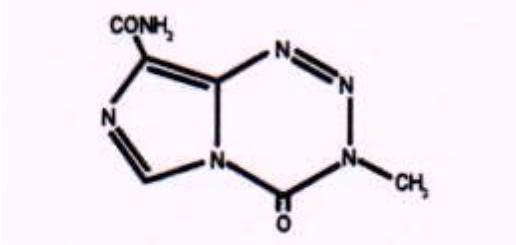
Section 1. Identification

Identification of the product

Product Name: Temozolomide Capsules

Formula: $C_6H_6N_6O_2$

Chemical Name:



3,4-Dihydro-3-methyl-4-oxoimidazo[5,1-d]-as-tetrazine-8-carbox-amide [85622-93-1].

Manufacturer / supplier identification

Company: **Cadila Healthcare Ltd., Matoda, India**

Address: Cadila Healthcare Limited, Plot No- 1A/1 & 2, Pharmez Special Economic Zone, Sarkhej- Bavla N.H. No. 8A, Near Village Matoda, Tal. Sanand, Dist. Ahmedabad-382 213, India

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Emergency Telephone No. Tel: +91-79-26868101

Recommended use / Therapeutic Category Alkylatic Agent, it works by Slowing or Stopping the Growth of cancer cells in body.

Restriction on Use / Contraindications: Known hyper sensitivity to any Temozolomide or dacarbazine

Section 2. Hazard(s) Identification	
Dose and Administration	Newly Diagnosed GBM: 75 mg/m^2 for 42 days concomitant with focal radiotherapy followed by initial maintenance dose of 150 mg/m2 once daily for Days 1 to 5 of a 28-day cycle of temozolomide for 6 cycles. (2.1) • Refractory Anaplastic Astrocytoma: Initial dose 150 mg/m^2 once daily for 5 consecutive days per 28-day treatment
Adverse Effects	The following adverse reactions have been identified during post approval use of temozolomide. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to the drug exposure. Dermatologic disorders: Toxic epidermal necrolysis and Stevens-Johnson syndrome Immune system disorders: Allergic reactions, including anaphylaxis. Erythema multiforme, which resolved after discontinuation of temozolomide and, in some cases, recurred upon rechallenge. Hematopoietic disorders: Prolonged pancytopenia, which may result in aplastic anemia and fatal outcomes. Hepatobiliary disorders: Fatal and severe hepatotoxicity, elevation of liver enzymes, hyperbilirubinemia, cholestasis, and hepatitis Infections and infestations: Opportunistic infections including Pneumocystis pneumonia (PCP) primary and reactivated cytomegalovirus (CMV), and reactivation of hepatitis B infections including some cases with fatal outcomes, and herpes simplex encephalitis including cases with fatal outcomes. Pulmonary disorders: Interstitial pneumonitis, pneumonitis, alveolitis, and pulmonary fibrosis. Endocrine disorders: Diabetes insipidus

Over Dose Effect	Doses of 500, 750, 1000, and 1250 mg/m^2 (total dose per cycle over 5 days) have been evaluated clinically in patients. Dose-limiting toxicity was hematologic and was reported with any dose but is expected to be more severe at higher doses. An overdose of 2000 mg per day for 5 days was taken by one patient and the adverse reactions reported were pancytopenia, pyrexia, multi-organ failure, and death. There are reports of patients who have taken more than 5 days of treatment (up to 64 days), with adverse reactions reported including bone marrow suppression, which in some cases was severe and prolonged, and infections and resulted in death. In the event of an overdose, hematologic evaluation is needed. Supportive measures should be provided as necessary.
Contraindications	Hypersensitivity Temozolomide is contraindicated in patients who have a history of hypersensitivity reaction (such as urticaria, allergic reaction including anaphylaxis, toxic epidermal necrolysis, and Stevens-Johnson syndrome) to any of its components. Temozolomide is also contraindicated in patients who have a history of hypersensitivity to dacarbazine (DTIC), since both drugs are metabolized to 5-(3-methyltriazen-1-yl)-imidazole-4-carboxamide (MTIC).
Pregnancy Comments	Pregnancy Temozolomide can cause fetal harm when administered to a pregnant woman. Five consecutive days of oral temozolomide administration of 0.38 and 0.75 times the highest recommended human dose (75 and 150 mg/m2) in rats and rabbits, respectively, during the period of organogenesis caused numerous malformations of the external and internal soft tissues and skeleton in both species. Doses equivalent to 0.75 times the highest recommended human dose (150 mg/m2) caused embryolethality in rats and rabbits as indicated by increased resorptions. There are no adequate and well-controlled studies in pregnant women. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus. Women of childbearing potential should be advised to avoid becoming pregnant during therapy with temozolomide.
Pregnancy Category	D

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Section 3. Composition / information on ingredients		
Component	**Exposure Limit**	**CAS No.**
Principle Component:		
TEMOZOLOMIDE (USDMF)	1mcg/m^3 8-hour Time Weighted Average (8-hr TWA).	85622-93-1
Inactive Ingredients:		
ANHYDROUS LACTOSE	Not Found	63-42-3
COLLOIDAL SILICON DIOXIDE [AEROSIL 200 PHARMA]	Not Found	7631-86-9
SODIUM STARCH GLYCOLATE (TYPE B) (GLYCOLYS LOW PH) ROQUETTE.	Not Found	9063-38-1
NATURAL TARTARIC ACID L(+), SS , ICV (VERY FINE GRANULAR CODE SS)ICV	Not Found	133-37-9
STEARIC ACID (MALL INCKRODT)	Not Found	57-11-4

Section 4. First -aid measures

General

- **After inhalation:**
  Move to fresh air in case of accidental inhalation. assure fresh air breathing. If there are signs of intoxication, irritation, dizziness or nausea seek medical attention
- **After skin contact:**
  Rinse skin with Large Volume of water/Shoap
- **After eye contact:**
  Rinse with water while holding the eyes wide open. Contact lenses should be removed.
- **After swallowing:**
  Rinse mouth out with water
- **Information for doctor:**
- **Most important symptoms and effects, both acute and delayed-** No further relevant information available.
- **Indication of any immediate medical attention and special treatment needed-** No further relevant information available.

Overdose Treatment	Limited data are available related to overdosage in humans. If symptomatic hypotension occurs, initiate supportive treatment.
Section 5. Fire -fighting measures	
	Extinguishing media · **Suitable extinguishing agents:** Use extinguishing media appropriate for surrounding fire. Extinguishing blanket. Carbon dioxide. Dry powder **Special hazards arising from the substance or mixture** Stable under normal conditions. · **Advice for firefighters** Small amounts: Use normal individual fire protective equipment. Large amounts: Not · **Protective equipment:** Hand protection : Gloves Skin and body protection : Lab coat Respiratory protection : Quarter mask (DIN EN 140)
Specific hazards arising from the chemical	No additional information available
Special protective equipment and precautions for firefighters	Use normal individual fire protective equipment
General fire hazards	No unusual fire or explosion hazards noted
Section 6. Accidental Release Measures	
Personal precautions, protective equipment and emergency procedures	Avoid raising dust. Wear suitable protective clothing, gloves and eye or face protection.

Environmental precautions:	Do not discharge into drains or the environment, dispose to an authorised waste collection point. All personnel likely to be involved in antineoplastic (cytotoxic) spill must receive practical training in: i. Correct procedures in handling cytotoxic materials/drugs or waste in order to prevent and minimise the risk of spills. ii. The location of the spill kit in the area. iii. The arrangements for medical treatment of any affected personnel. iv. The procedure for containment of the spill, and decontamination of personnel and the environment, including the different procedures for major and minor spills. v. The procedures for waste disposal according to the nature and extent of the spill.
Methods and material for containment and cleaning up:	Sweep spilled substance into containers; if appropriate, moisten first to prevent dusting. Ensure waste is collected and contained. Clean thoroughly. Poorly soluble in water. Clean with the help of detergents.
Section 7. Handling and Storage	
Storage:	Store temozolomide capsule at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature]. Dispense the accompanying Patient Information to each patient. **Precautions for safe handling**: Keep it dry & in a cool, well ventilated place away from heat. Store in original container **Information about fire - and explosion protection:** No special measures required.

Section 8. Exposure controls / personal protection

Respiratory Protection	Quarter mask (DIN EN 140)
Skin protection	For prolonged or repeated skin contact use suitable protective gloves.
Eye/face protection	If contact is likely, safety glasses with side shields are recommended.
Protective Clothing	Protective clothing is not normally necessary, however it is good practice to use apron.
Biological limit values	No biological exposure limits noted for the ingredient(s).
Exposure guidelines	General ventilation normally adequate.
Thermal hazards	Wear appropriate thermal protective clothing, when necessary.
General hygiene considerations	Keep away from foodstuffs, beverages and feed. Wash hands before breaks and at the end of work. Routinely wash work clothing and protective equipment to remove contaminants. For advice on suitable monitoring methods, seek guidance from a qualified environment, health and safety professional.
Engineering controls	Engineering controls should be used as the primary means to control exposures. General room ventilation is adequate unless the process generates dust, mist or fumes. Keep airborne contamination levels below the exposure limits listed above in this section.

Section 9. Physical and chemical properties	
Appearance	Description of **Temozolomide Capsules 5 mg** : "White to off white to light pink /Light tan Granular Powder filled in size "5" Hard Gelatin Capsules with green colored cap and white colored body. The Capsule body is imprinted with "751"in black. Description of **Temozolomide Capsules 20 mg**: "White to off white to light pink /Light tan Granular Powder filled in size "5" Hard Gelatin Capsules with Yellow coloured cap and white colored body. The Capsule body is imprinted with "752"in black. Description of **Temozolomide Capsules 100 mg**: "White to off white to light pink /Light tan Granular Powder filled in size "3" Hard Gelatin Capsules with Pink coloured cap and white colored body. The Capsule body is imprinted with "753"in black. Description of **Temozolomide Capsules 140 mg**: "White to off white to light pink /Light tan Granular Powder filled in size "2" Hard Gelatin Capsules with blue coloured cap and white colored body. The Capsule body is imprinted with "754"in black. Description of **Temozolomide Capsules 180 mg**: "White to off white to light pink /Light tan Granular Powder filled in size "0" Hard Gelatin Capsules with Orange coloured cap and white colored body. The Capsule body is imprinted with "755"in black. Description of **Temozolomide Capsules 250 mg**: "White to off white to light pink /Light tan Granular Powder filled in size "00" Hard Gelatin Capsules with White coloured cap and white colored body. The Capsule body is imprinted with "756"in black

Solubility	Not available.	**Odour**	Not available.
Boiling point	Not available.	**Melting Point**	Not available.
Evaporation rate	Not available.	**Vapour density**	Not available.
Reactivity in water	Not available.	**Vapour pressure**	Not available.
% Volatile by volume	Not available.	**Specific gravity**	Not available.

Section 10. Stability and Reactivity

Conditions to avoid	Contact with incompatible materials.
Stable	**Reactivity** The product is stable and non-reactive under normal conditions of use, storage and transport. **Chemical stability** Material is stable under normal conditions.
Hazardous reactions	No dangerous reaction known under conditions of normal use.
Decomposition products	When heated to decomposition, emits dangerous fumes.
Incompatible materials	Strong Oxidizing agent

Section 11. Toxicological information

General	Handling of formulated product is not expected to cause any toxicological affects. The data pertains to the ingredient in formulations, rather than this specie formulation.
Ingestion	Health injuries are not known or expected under normal use. Expected to be a low ingestion hazard. However, ingestion is not likely to be a primary route of occupational exposure.
Other **Symptoms related to the physical, chemical and Toxicological characteristics**	Not available

Information on toxicological effects	
Acute toxicity	LD50/oral/rat: 315 mg/kg; LD50/oral/mouse: 330 mg/kg LD50/dermal/rat: N/A; LC50/inhalation/rat: N/A.
Further information	Not available
Section 12. Ecological information	
	Poorly soluble in water. No data available on ecotoxicity.
Section 13. Disposal Consideration	
	Dispose the waste in accordance with all applicable Federal, State and local laws.
Section 14. Transport Information	
	The product is not hazardous when shipping via air (IATA), ground (DOT), or sea (IMDG). In accordance with ADR / RID / IMDG / IATA / ADN
Section 15. Regulatory Information	
	Generic Medicine. Under Approval by USFDA & the ANDA Number is 206750
Section 16. Other information	
	None

Date of issue: 09/05/17 **Supersedes edition:** New Edition

The information contained herein is based on the state of our knowledge. It characterizes the product with regard to the appropriate safety precautions. It does not represent a guarantee of the properties of the product.