SAFETY DATA SHEETS

This SDS packet was issued with item:

078700147

N/A

MATERIAL SAFETY DATA SHEET

1. IDENTIFICATION OF THE SUBSTANCE AND THE COMPANY

Material: **Topiramate Tablets**
25 mg, 50 mg, 100 mg and 200 mg

Manufacturer: Torrent Pharmaceuticals Limited
Ahmedabad- Mehsana Highway
Taluka- Kadi, Dist. Mehsana
Indrad-382 721, Gujarat, INDIA

Distributor: Torrent Pharma Inc.
Kalamazoo, MI 49009

2. COMPOSITION / INFORMATION ON INGREDIENTS

Ingredients	CAS #	Quantity
Topiramate	97240-79-7	Topiramate 25 mg; 50 mg; 100 mg; and 200 mg
Non-hazardous ingredients	----------	q.s.

3. HAZARDOUS IDENTIFICATION

WARNING: This is a pharmaceutical product available only with a prescription – use only as directed by physician.

Major health hazards: Hypersensitivity to the material of product and/or severe low blood pressure.
Target Organ(s): Cardiovascular System.

Potential health effects:

Skin and Eye Effects: May cause sensitization or irritation by skin contact. Causes irritation if come in contact with eye.

Inhalation: The effects of inhaling airborne dust generated while breaking tablets, may be irritating to the respiratory tract and allergic reaction.

Environment	No information is available about the potential of this product to produce adverse environmental effects.

4. FIRST AID MEASURES

Ingestion	Do not induce vomiting. If vomiting occurs, keep head lower than hips to help prevent aspiration. Do not induce evacuation of stomach unless directed by medical personnel. Wash out mouth with water and obtain medical attention.
Inhalation	Dust containing drug substance could be inhaled if tablets are broken. If dust is inhaled, remove to fresh air. If breathing is difficult, give oxygen and seek medical attention if respiratory irritation develops.
Skin Contact	Remove contaminated clothing. Wash affected areas with plenty of water and soap if available, for several minutes until no evidence of chemical remains. Seek medical attention if irritation or rash develops and persists.
Eye Contact	In case of contact with dust from crushed or broken tablets, hold eyelids open. Get medical attention immediately. Flush eyes with large amounts of running water or with normal saline, until no evidence of chemical remains.
Antidotes	No specific antidote exists.

5. FIRE-FIGHTING MEASURES

Hazardous Combustion Products	Emits thermal decomposition products or combustion when the product is exposed to fire.
Fire Fighting Instructions	Move container from fire area if it can be done without risk. Wear approved positive pressure, self contained breathing apparatus and full protective turn out gear. Use fire extinguishing agents appropriate for surrounding fire. Stay upwind and keep out of low areas.

Extinguisher to Use	Use carbon dioxide, dry chemical powder, water spray or appropriate foam.
Large fires	Use regular foam or flood with fine water spray.

6. ACCIDENTAL RELEASE MEASURES

Occupational Spill	Collect spilled material into a labeled container for disposal. Clean spill thoroughly with detergent and water. Avoid breathing dust.

7. HANDLING AND STORAGE

General Handling	Keep away from heat. Avoid creating dust when handling. Use with adequate ventilation. If tablets are crushed and/or broken, avoid contact with eyes, skin and clothing. Avoid breathing dust. When handling use proper personal protective equipment specified in section 8.
Storage	Store at 20°-25° C (68°-77°F); excursions permitted to 15°-30° C (59°-86° F) [see USP Controlled Room Temperature]. Protect from Moisture.

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Ventilation	Local exhaust ventilation is adequate unless the process generates airborne dust or fumes.
Eye Protection	Required under normal and foreseeable conditions of use. It is suggestive to wear safety glasses with side shields or goggles where risk of eye exposure exists.
Skin Protection	Required under normal and foreseeable conditions of use. It is suggestive to wear chemical resistant gloves.
Respiratory Protection	Required under normal and foreseeable conditions of use. Use dust mask for dusty conditions also.
Environmental Exposure Controls:	Special care should be taken to ensure that contaminated clothing, equipment, and surfaces are properly cleaned after use. Wash hands and other

areas of skin contact thoroughly after handling this material. Contaminated clothing should be cleaned or disposed off.

9. PHYSICAL & CHEMICAL PROPERTIES

Physical Forms	Tablets
Appearance	**25mg;** White to off white, round, biconvex, film coated tablets debossed with '1031' on one side and '25' on other side.
	50mg; Yellow colored, round, biconvex, film coated tablets debossed with '1032' on one side and '50' on other side.
	100mg; Light yellow colored, round, biconvex, film coated tablets debossed with '1033' on one side and '100' on other side.
	200mg; Peach colored, round, biconvex, film coated tablets debossed with '1034' on one side and '200' on other side.

10. STABILITY AND REACTIVITY

Stable under recommended storage conditions.

11. TOXICOLOGICAL INFORMATION

Eye	May cause irritation.
Skin	May cause irritation.
Inhalation	May cause irritation to respiratory tract.
Ingestion	Ingestion of between 6 and 40 g topiramate has been reported in a few patients. Signs and symptoms included: headache, agitation, drowsiness, lethargy, metabolic acidosis and hypokalemia. The clinical consequences were not severe. All patients recovered. A patient who

ingested a dose calculated to be between 96 and 110 g topiramate was admitted to hospital with coma lasting 20-24 hours followed by full recovery after 3 to 4 days.

Mutagenicity

Topiramate did not demonstrate genotoxic potential when tested in a battery of in vitro and in vivo assays. Topiramate was not mutagenic in the Ames test or the in vitro mouse lymphoma assay; it did not increase unscheduled DNA synthesis in rat hepatocytes in vitro; and it did not increase chromosomal aberrations in human lymphocytes in vitro or in rat bone marrow in vivo.

Acute Toxicity

Acute toxicity studies included topiramate oral (1000 to 4500 mg/kg) and i.p. (500 to 2250 mg/kg) administration to mice and rats and oral (250 to 400 mg/kg) administration to dogs. Rodents tolerated topiramate well; high acute doses were required to cause death. No death occurred among dogs, which were, however, more sensitive to the acute toxic effects of topiramate than were rodents. The acute toxicity was primarily CNS related: ataxia, decreased motor activity, tremors, and clonic convulsions.

Chronic Toxicity

Chronic toxicity studies also showed additional dose-dependent effects, including lower body weight and reduced body weight gain occasionally associated with decreased food efficiency, central nervous system clinical signs, shifts in fluid and electrolyte levels related to diuresis, and higher urine pH.

Long Term Toxicity

Long-term toxicity was evaluated by 3- and 12-month oral multiple-dose treatments of rats and dogs. Increased liver weights and liver cell hypertrophy, elevated serum gastrin levels and gastric mucosal hyperplasia, and renal pelvis and urinary bladder epithelium hyperplasia were seen at the highest doses of topiramate in rats. Hyperplasia of the gastric epithelial and endothelial cells did not progress to neoplasia after lifetime exposure of rats and mice to topiramate. Moreover, no changes in gastric histology or gastrin levels were noted in humans receiving therapeutic doses of topiramate.

Carcinogenicity	An increase in urinary bladder tumors was observed in mice given topiramate (20, 75, and 300 mg/kg) in the diet for 21 months. The elevated bladder tumor incidence, which was statistically significant in males and females receiving 300 mg/kg, was primarily due to the increased occurrence of a smooth muscle tumor considered histomorphologically unique to mice. Plasma exposures in mice receiving 300 mg/kg were approximately 0.5 to 1 times steady-state exposures measured in patients receiving topiramate monotherapy at the recommended human dose (RHD) of 400 mg, and 1.5 to 2 times steady-state topiramate exposures in patients receiving 400 mg of topiramate plus phenytoin. The relevance of this finding to human carcinogenic risk is uncertain. No evidence of carcinogenicity was seen in rats following oral administration of topiramate for 2 years at doses up to 120 mg/kg (approximately 3 times the RHD on a mg/m^2 basis).
Reproductive Effects	No adverse effects on male or female fertility were observed in rats at doses up to 100 mg/kg (2.5 times the RHD on a mg/m^2 basis).
Teratogenicity	Teratology studies demonstrated that topiramate is teratogenic in mice, rats, and rabbits. In mice, fetal weights and skeletal ossification were reduced by topiramate at 500 mg/kg/d in conjunction with maternal toxicity. In rats, limb and digit defects were noted at 400 mg/kg/d and higher doses. In rabbits, rib and vertebral malformations occurred at 120 mg/kg/d. The teratogenic effects observed in rats and rabbits were similar to those seen with carbonic anhydrase inhibitors, which have not been associated with malformations in humans. Indeed, no abnormalities were evident in the infants of five women who received topiramate during pregnancy.

12. ECOLOGICAL INFORMATION

Prevent the product to enter in drinking water supplies, waste water or soil.

13. DISPOSAL CONSIDERATION

Waste disposal Method — Unused product and contaminated packaging should be disposed in accordance with applicable international, national, state, and / or local waste disposal regulations.

14. TRANSPORTATION INFORMATION

Contact Torrent Pharmaceuticals Limited or Torrent Pharma Inc. for transportation information. It has no known, significant hazards requiring special packaging or labeling for air, maritime, US or European ground transport purpose.

15. REGULATORY INFORMATION

No information available.

16. OTHER INFORMATION

The above information is believed to be correct but does not purport to be all-inclusive and shall be used only as a guide. Nothing herein shall be deemed to create any warranty, express or implied. It is the responsibility of the user to determine the applicability of this information and the suitability of the material or product for any particular purpose. The information in this sheet does not represent analytical specification.

Torrent shall not be held liable for any damage resulting from handling or from contact with the above product. Torrent reserves the right to revise this MSDS.

	PREPARED BY:	REVIEWED BY:		APPROVED BY:
Department	Formulation Development	Medicinal Chemistry Department	Clinical Research	Corporate Quality Assurance
Name	Sujay Rajhans	Ramaliya Dilip	Dr. Renu Jain	Hrushad Patil
Signature				
Date	24/11/08	24/11/08	24/11/08	24/11/08

SAFETY DATA SHEET (SDS)

HAZARD COMMUNICATION STATEMENT

This statement is prepared in accordance with OSHA requirements, 29 CFR 1910.1200(b)(6)(vii), as it relates to hazardous chemicals in the work place.

This regulation was implemented for the safety of the chemical operators who manufacture the finished dosage forms. As such, OSHA 29 CFR 1910.1200(b)(6)(vii) exempts the following:

"Any drug, as that term is defined in the Federal Food, Drug and Cosmetic Act (21 U.S.C. 301 et seq.), when it is in solid final form for direct administration to the patient (e.g. tablets or pills); drugs which are packaged by the chemical manufacturer for sale to consumers in retail establishment (e.g. over-the-counter drugs); and drugs intended for personal consumption by employees while in the work place (e.g. first aid supplies)."

Therefore this regulation does not apply to pharmaceutical solid finished dosage forms (i.e. tablets and capsules) only to liquids, ointments and creams where the patient has direct contact with the raw material ingredients.

Signed: Dawn Chitty

Dawn Chitty – VP, Strategy and Scientific Affairs

Torrent Pharma Inc.

Date: May 03, 2016

Torrent Pharma Inc. - 150 Allen Road, Suite 102, Basking Ridge, NJ 07920 – Tel: (908) 280-3346 – Fax: (908) 280-3396 – Email: customerservice@torrentpharma.us