SAFETY DATA SHEET

TOPIRAMATE EXTENDED-RELEASE CAPSULES

1. IDENTIFICATION

Manufacturer:
Ascent Pharmaceuticals Inc
400 S. Technology Drive

Central Islip, NY 11722

Emergency Phone:
1-855-221-1622

Common Name: Topiramate Extended-Release Capsules

Synonym(s): No data available.

Chemical Name: 2,3:4,5-Di-*O*- isopropylidene-β-D- fructopyranose sulfamate

Trade Name(s): Topiramate Extended-Release Capsules, USP 25 mg, 50 mg, 100 mg & 200 mg.

Molecular formula: $C_{12}H_{21}NO_8S$ **Molecular Weight:** 339.36

2.HAZARDS IDENTIFICATION

Not considered hazardous when handled under normal conditions.

EMERGENCY OVERVIEW

Caution Statement:
Each Topiramate Extended-Release Capsules intended for oral administration contains Topiramate, USP and excipients generally considered to be non-toxic and non-hazardous in small quantities and under conditions of normal occupational exposure.

Routes of Entry: Oral

Effects of Overexposure: Extended-Release Capsules are intended for human consumption under guidance of a physician. Intact Extended-Release Capsules are not considered hazardous under normal handling procedures.

Medical conditions Aggravated by Long Term Exposure: Liver impairment, Kidney impairment, Kidney stones, Glaucoma, Respiratory disorders, Osteoporosis, Mental depression, Metabolic acidosis.

Carcinogenicity: Topiramate - Not listed by IARC, NTP and OSHA.

3.COMPOSITION / INFORMATION ON INGREDIENTS

Ingredient	CAS #	Concentration % (Approx)
Topiramate, USP	97240-79-4	≈4 %
Excipients	NA	≈96 %

Contains no hazardous components (one percent or greater) or carcinogens (one-tenth percent or greater) not listed above.

* All Concentrations are percent by weight.

4. FIRST AID MEASURES

Inhalation: Move in to fresh air and keep at rest. For breathing difficulties, Oxygen may be necessary. Get medical attention. If breathing stops, provide artificial respiration.

Skin Contact: Wash skin thoroughly with soap and water. Get medical attention if irritation persists after washing. Remove contaminated clothing and shoes. Wash contaminated clothing before reuse. Destroy or thoroughly clean contaminated shoes.

Eye Contact: Immediately flush with plenty of water for at least 15 minutes. If easy to do, remove contact lenses. Get medical attention.

Ingestion: Do not induce vomiting unless directed to do so by medical personnel. Never give liquid to an unconscious person. Get medical attention.

Notes to the Physician:
The precise mechanisms by which topiramate exerts its anticonvulsant and other effects are unknown; however, preclinical studies have revealed four properties that may contribute to topiramate's efficacy for epilepsy. Electrophysiological and biochemical evidence suggests that topiramate, at pharmacologically relevant concentrations, blocks voltage-dependent sodium channels, augments the activity of the neurotransmitter gamma-amino butyrate at some subtypes of the GABA-A receptor, antagonizes the AMPA/kainate subtype of the glutamate receptor, and inhibits the carbonic anhydrase enzyme, particularly isozymes II and IV.

Overdose Treatment:
In acute topiramate overdose, if the ingestion is recent, the stomach should be emptied immediately by lavage or by induction of emesis. Activated charcoal has been shown to adsorb topiramate in vitro. Treatment should be appropriately supportive. Hemodialysis is an effective means of removing topiramate from the body.

5.FIRE-FIGHTING MEASURES

Extinguishing Media: Water spray, CO2, dry chemical or alcohol resistant foam.

Unusual Fire & Explosion Hazards: Emits toxic fumes under fire conditions.

Special Fire Fighting Procedures: Self-Contained breathing apparatus and full protective clothing must be worn in case of fire.

Protective Measures: Prevent runoff from fire control or dilution from entering streams, sewers, or drinking water supply.

6.ACCIDENTAL RELEASE MEASURES

Personal precautions: Use personal protective equipment. Immediately contact emergency personnel. Keep unnecessary personnel away. Follow all firefighting procedures.

Environmental precautions: Do not release in to the environment.

Spill Cleanup methods: Use a vacuum cleaner. If not possible, moisten dust with water before it is collected with shovel, broom or the like. Collect in containers and seal securely. For waste disposal, see section 13 of the SDS.

7.HANDLING AND STORAGE

Handling: Do not breathe dust. Avoid contact with eyes, skin, and clothing. Wash thoroughly after handling.

Storage: Keep container tightly closed in a cool, well-ventilated place. Keep away from heat and direct sun light.

8.EXPOSURE CONTROLS / PERSONAL PROTECTION

Capsules are not considered hazardous under normal handling procedures and protective equipment is not required. The following are recommended for manufacturing or other situations where exposure to the powder may occur.

Protective Measures: Minimize open handling. Containment technologies suitable for controlling compounds are required to control at source and to prevent migration of the compound to uncontrolled areas.

Respiratory Protection: Use a NIOSH approved respirator or an alternate approved dust mask should be used.

Hand Protection: Chemical resistant gloves.

Eye Protection: Wear safety glasses with side shields (or goggles). If the work environment or activity involves dusty conditions, mist or aerosols, wear the appropriate goggles. Wear a face shield 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: 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: Wash skin thoroughly with soap and water.

9.PHYSICAL AND CHEMICAL PROPERTIES

Physical Properties:

Physical State: Solid

Form: Extended-Release Capsules

10. STABILITY AND REACTIVITY

Possibility of hazardous reactions: Stable under ordinary conditions of use and storage.

Conditions to avoid: Excessive heat & Moisture.

Incompatible materials: Strong oxidizers, Strong Bases and Strong Acids.

Hazardous Decomposition products: Thermal decomposition or combustion may liberate irritating gases or vapors.

11.TOXICOLOGICAL INFORMATION

General information: The information presented below pertains to the individual ingredients (Topiramate, USP), and not to the mixture(s) or final formulations.

Inhalation: No data available.

Ingestion: No data available.

Skin Corrosion/ irritation: No data available.

Serious eye damage/eye irritation: No data available.

Respiratory sensitizer/Skin sensitizer: No data available.

Carcinogenesis:

An increase in urinary bladder tumors was observed in mice given topiramate (20 mg, 75 mg, 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/ m2 basis).

Mutagenesis:

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.

Impairment of Fertility:
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/ m2 basis).

Other information:

Medically adverse effects reported with Topiramate Extended-Release Capsuless include: Any vision problems, especially blurred vision, double vision, eye pain, or rapidly decreasing vision, burning, prickling, or tingling sensations, clumsiness or unsteadiness, confusion, continuous, uncontrolled back-and-forth or rolling eye movements, dizziness, drowsiness, eye redness, generalized slowing of mental and physical activity, increased eye pressure, memory problems, menstrual changes, menstrual pain, nervousness, speech or language problems, trouble in concentrating or paying attention, unusual tiredness or weakness.

12.ECOLOGICAL INFORMATION

General information: The information presented below pertains to the individual ingredients (Topiramate, USP), and not to the mixture(s) or final formulations.

Ecotoxicity Effects:

Acute toxicity to Fish: No data available.

Acute toxicity to Aquatic Invertebrates: No data available.

Toxicity to Aquatic Plants: No data available.

Bioaccumulation: No data available.

Mobility: No data available.

13.DISPOSAL CONSIDERATIONS

Waste Disposal: Dispose of waste must be in accordance with all applicable Federal, State and local laws.

Measures for Avoidance and Recovery: Incineration is the most effective method of disposal in most instances. Do not allow runoff to sewer, waterway or ground. Operations that involve the crushing or shredding of waste materials or returned goods should take into account recommended exposure limits where they exist.

14.TRANSPORT INFORMATION

DOT: Not Regulated

IMDG: Not regulated

ICAO/IATA: Not Regulated

IMO: Not Regulated

15.REGULATORY INFORMATION

Stated regulatory information chosen primarily for possible usage of Ascent Pharmaceutical, Inc. This section is not a complete analysis or reference to all applicable regulatory information. Please consider all applicable laws and regulations for your country/state.

CERLA Hazardous Substance List (40 CFAscentR 302.4): None

TSCA : None

SARA Title III

Section 302 Extremely Hazardous Substance (40 CFR 355, Appendix A): None

Section 313 Toxic Release Inventory (40 CFR 372): None

16.OTHER INFORMATION

SDS Sections Revised:
New

GLOSSARY:

SDS	Safety Data Sheet
NA	Not Applicable
CAS Number	Chemical Abstract Service Registry Number
NTP	National Toxicology Program
NIOSH	National Institute for Occupational Safety and Health
DOT	Department of Transportation
IMDG	International Maritime Dangerous Goods Code
ICAO	International Civil Aviation Organization
IATA	International Air Transport Association
IMO	International Maritime Organization
TSCA	Toxic Substances Control Act
CERCLA	Comprehensive Environmental Response, Compensation, and Liability Act
SARA	Superfund Amendments and Reauthorization Act
OSHA	Occupational Safety and Health Administration

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