Safety Data Sheet
Tizanidine Hydrochloride Capsules
Strength: 2 mg, 4 mg and 6 mg
Pack Size: 150's and 500's Capsule per bottle , Unit Dose blister Cartons of 100 (10 x10) unit dose capsule

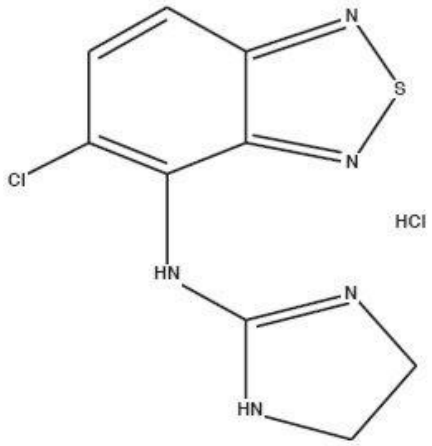
Revision No.: 00

EMERGENCY OVERVIEW
Each Tizanidine hydrochloride capsules intended for oral administration contains Tizanidine hydrochloride 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:	Tizanidine Hydrochloride
Formula:	C9H8ClN5S-HCl
Chemical Name:	5-chloro-4-(2-imidazolin-2-ylamino)-2,1,3-benzothiodiazole hydrochloride.



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
Contact for information:	Tel: +91-79-26868100 Fax: +91-79-26868533
Emergency Telephone No.	Tel: +91-79-26868101
Recommended use / Therapeutic Category	Anti-hypertensive
Restriction on Use / Contraindications:	Patient with orthostatic hypotension Tizanidine with fluvoxamine or with ciprofloxacin, potent inhibitors of CYP1A2, is contraindicated

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Section 2. Hazard(s) Identification	
Dose and Administration	A single dose of 8 mg of tizanidine reduces muscle tone in patients with spasticity for a period of several hours. The effect peaks at Approximately 1 to 2 hours and dissipates between 3 to 6 hours. Effects are dose-related. Although single doses of less than 8 mg have not been demonstrated to be effective in controlled clinical studies, the dose-related nature of tizanidine's common adverse events make it prudent to begin treatment with single oral doses of 4 mg. Increase the dose gradually (2 to 4 mg steps) to optimum effect (satisfactory reduction of muscle tone at a tolerated dose). The dose can be repeated at 6 to 8 hour intervals, as needed, to a maximum of three doses in 24 hours. The total daily dose should not exceed 36 mg. Experience with single doses exceeding 8 mg and daily doses exceeding 24 mg is limited. There is essentially no experience with repeated, single, daytime doses greater than 12 mg or total daily doses greater than 36 mg Food has complex effects on tizanidine pharmacokinetics, which differ with the different formulations. These pharmacokinetic differences may result in clinically significant differences when [1] switching administration of the capsule between the fed or fasted state, [2] switching between the tablet and capsule in the fed state, or [3] switching between the intact capsule and sprinkling the contents of the capsule on applesauce. These changes may result in increased adverse events or delayed/more rapid onset of activity, depending upon the nature of the switch. For this reason, the prescriber should be thoroughly familiar with the changes in kinetics associated with these different conditions

Adverse Effects	Forty-five of 264 (17%) patients receiving tizanidine and 13 of 261 (5%) of patients receiving placebo in three multiple dose, placebo controlled clinical studies, discontinued treatment for adverse events. When patients withdrew from the study, they frequently had more than one reason for discontinuing. The adverse events most frequently leading to withdrawal of tizanidine treated patients in the controlled clinical studies were asthenia (weakness, fatigue and/or tiredness) (3%), somnolence (3%), dry mouth (3%), increased spasm or tone (2%), and dizziness (2%). In multiple dose, placebo-controlled clinical studies involving 264 patients with spasticity, the most frequent adverse effects were dry mouth, somnolence /sedation, asthenia (weakness, fatigue and/or tiredness) and dizziness. Three-quarters of the patients rated the events as mild to moderate and one-quarter of the patients rated the events as being severe. These events appeared to be dose related. In the single dose, placebo-controlled study involving 142 patients with spasticity, the patients were specifically asked if they had experienced any of the four most common adverse events: dry mouth, somnolence (drowsiness), asthenia (weakness, fatigue and/ or tiredness) and dizziness. In addition, hypotension and bradycardia were observed. frequent adverse events are those occurring on one or more occasions in at least 1/100 patients (only those not already listed in the tabulated results from placebo-controlled studies appear in this listing); infrequent adverse events are those occurring in 1/100 to 1/1000 patients; rare adverse events are those occurring in fewer than 1/1000 patients. **BODY AS A WHOLE** Frequent: Fever Infrequent: Allergic reaction, moniliasis, malaise, abscess, neck pain, sepsis, cellulites, death, overdose Rare: Carcinoma, congenital anomaly, suicide attempt **CARDIOVASCULAR SYSTEM** Infrequent: Vasodilatation, postural hypotension, syncope, migraine, arrhythmia Rare: Angina pectoris, coronary artery disorder, heart failure, myocardial infarct, phlebitis, pulmonary embolus, ventricular extrasystoles, ventricular tachycardia **DIGESTIVE SYSTEM** Frequent: Abdomen pain, diarrhea, dyspepsia Infrequent: Dysphagia, cholelithiasis, fecal impaction, flatulence, gastrointestinal hemorrhage, hepatitis, melena

Rare: Gastroenteritis, hematemesis, hepatoma, intestinal obstruction, liver damage

HEMIC AND LYMPHATIC SYSTEM

Infrequent: Ecchymosis, hypercholesteremia, anemia, hyperlipemia, leukopenia, leukocytosis, sepsis

Rare: Petechia, purpura, thrombocythemia, thrombocytopenia

METABOLIC AND NUTRITIONAL SYSTEM

Infrequent: Edema, hypothyroidism, weight loss

Rare: Adrenal cortex insufficiency, hyperglycaemia, hypokalaemia, hypernatremia, hypoproteinemia, respiratory acidosis

MUSCULOSKELETAL SYSTEM

Frequent: Myasthenia, back pain

Infrequent: Pathological fracture, arthralgia, arthritis, bursitis

NERVOUS SYSTEM

Frequent: Depression, anxiety, paresthesia

Infrequent: Tremor, emotional liability, convulsion, paralysis, thinking abnormal, vertigo, abnormal dreams, agitation, depersonalization, euphoria, migraine, stupor, dysautonomia, neuralgia

Rare: Dementia, hemiplegia, neuropathy

RESPIRATORY SYSTEM

Infrequent: Sinusitis, pneumonia, bronchitis

Rare: Asthma

SKIN AND APPENDAGES

Frequent: Rash, sweating, skin ulcer

Infrequent: Pruritus, dry skin, acne, alopecia, urticaria

Rare: Exfoliative dermatitis, herpes simplex, herpes zoster, skin carcinoma

SPECIAL SENSES

Infrequent: Ear pain, tinnitus, deafness, glaucoma, conjunctivitis, eye pain, optic neuritis, otitis media, retinal hemorrhage, visual field defect

Rare: Iritis, keratitis, optic atrophy

UROGENITAL SYSTEM

Infrequent: Urinary urgency, cystitis, menorrhagia, pyelonephritis, urinary retention, kidney calculus, uterine fibroids enlarged, vaginal moniliasis, vaginitis

Rare: Albuminuria, glycosuria, hematuria, metrorrhagia

Over Dose Effect	Review of the safety surveillance database revealed cases of intentional and accidental tizanidine overdose. Some of the cases resulted in fatality and many of the intentional overdoses were with multiple drugs including CNS depressants. The clinical manifestations of tizanidine overdose were consistent with its known pharmacology. In the majority of cases a decrease in sensorium was observed including lethargy, somnolence, confusion and coma. Depressed cardiac function are also observed including most often bradycardia and hypotension. Respiratory depression is another common feature of tizanidine overdose. Should overdose occur, basic steps to ensure the adequacy of an airway and the monitoring of cardiovascular and respiratory systems should be undertaken. In general, symptoms resolve within one to three days following discontinuation of tizanidine and administration of appropriate therapy. Due to the similar mechanism of action, symptoms and management of tizanidine overdose are similar to those following clonidine overdose. For the most recent information concerning the management of overdose, contact a poison control center.
Contraindications	Concomitant use of tizanidine with fluvoxamine or with ciprofloxacin, potent inhibitors of CYP1A2, is contraindicated. Significantalterations of pharmacokinetic parameters of tizanidine including increased AUC, t1/2, Cmax, increased oral bioavailability and decreased plasma clearance have been observed with concomitant administration of either fluvoxamine or ciprofloxacin. This pharmacokinetic interaction can result in potentially serious adverse events.
Pregnancy Comments	Reproduction studies performed in rats at a dose of 3 mg/kg, equal to the maximum recommended human dose on a mg/m2 basis, and in rabbits at 30 mg/kg, 16 times the maximum recommended human dose on a mg/m2 basis, did not show evidence of teratogenicity. Tizanidine at doses that are equal to and up to 8 times the maximum recommended human dose on a mg/m2 basis increased gestation duration in rats. Prenatal and postnatal pup loss was increased and developmental retardation occurred. Post-implantation loss was increased in rabbits at doses of 1 mg/kg or greater, equal to or greater than 0.5 times the maximum recommended human dose on a mg/m2 basis. Tizanidine has not been studied in pregnant women. Tizanidine should be given to pregnant women only if clearly needed.

Pregnancy Category	Pregnancy Category C

Section 3. Composition / information on ingredients		
Component	**Exposure Limit**	**CAS No.**
Principle Component:		
Tizanidine Hydrochloride	Not available	64461-82-1
Inactive Ingredients:		
Lactose Monohydrate	Not available	64044-51-5
Microcrystalline Cellulose NF 101	Not available	9004-34-6
Crosscarmellose Sodium	Not available	7811-65-7
Hypromellose 5 CPS, 2910	Not available	9004-65-3
Colloidal Silicon Dioxide	Not available	112945-52-5
Stearic acid	Not available	57-11-4

Section 4. First -aid measures

General

- **After inhalation:**
  Move to fresh air in case of accidental inhalation. assure fresh air breathing.
- **After skin contact:**
  Rinse skin with water/shower
- **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	• For the most recent information concerning the management of overdose, contact a poison control enter.
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:	No additional information available
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 at 25°C (77°F); excursions permitted to 15–30°C (59–86°F) [see USP Controlled Room Temperature Dispense in containers with child resistant closure **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 Tizanidine Hydrochloride Capsules 2 mg** : "Light yellow to Yellow colored granular powder filled in size "5" empty hard gelatin capsule having light blue opaque colored cap imprinted with '1111' in black ink and light blue opaque colored body". **Description of Tizanidine Hydrochloride Capsules 4 mg** : "Light yellow to Yellow colored granular powder filled in size "3" empty hard gelatin capsule having violet opaque colored cap imprinted with '1112' in white ink and white opaque colored body". **Description of Tizanidine Hydrochloride Capsules 6 mg** : "Light yellow to Yellow colored granular powder filled in size "2" empty hard gelatin capsule having violet opaque colored cap imprinted with '1113' in white ink and violet opaque colored body".		
Solubility	Slightly soluble in water.	**Odour**	Odorless or faint characteristic odor.
Boiling point	Not available.	**Melting Point**	546.8 - 554 °F (286 - 290 °C)
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	None known.		
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	SOx, NOx, Cl-. Irritating and/or toxic fumes or gases. Emits		

	toxic fumes under fire conditions.
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	Harmful if swallowed
Symptoms related to the physical, chemical and Toxicological characteristics	Drowsiness. Fatigue. Weakness. Dizziness. Headache. Anxiety. Hallucinations. Insomnia. Burning or tingling sensations. Speech disturbances. Blurred vision. Dry mouth. Nausea. Vomiting. Indigestion. Stomach pain. Muscle pain. Back pain. Fever. Yellow eyes and/or skin. Painful or difficult urination. **Delayed and immediate effects of exposure:** Sedation. Low blood pressure. Orthostatic hypotension. Liver injury. Slow heartbeat. Irregular Heartbeat. Urinary tract infection. Respiratory failure. Coma. **Medical conditions aggravated by exposure:** Liver impairment. Kidney impairment. Hypotension. Heart disease. Use of oral contraceptives.
Information on toxicological effects	
Acute toxicity	Tizanidine Hydrochloride (CAS 64461-82-1) LD50 Mouse Oral **Acute** 235 mg/kg Rabbit 98 mg/kg Rat 414 mg/kg Carcinogenicity: Based on available data, the classification criteria are not met. This product is not considered to be a carcinogen by IARC, ACGIH, NTP, or OSHA. 4 / 6 Material name: Tizanidine Hydrochloride

	6762 Version #: 02 Revision date: 06-14-2013 Issue date: 04-17-2006 USP SDS US 16 mg/kg Long-term carcinogenicity study Result: No increase in tumor incidence. Species: Mouse Test Duration: 78 weeks 9 mg/kg Long-term carcinogenicity study Result: No increase in tumor incidence. Species: Rat Test Duration: 104 weeks
Further information	Specific target organ toxicity - single exposure Narcotic effects. Specific target organ toxicity - repeated exposure Based on available data, the classification criteria are not met. Aspiration hazard Based on available data, the classification criteria are not met.
Section 12. Ecological information	
	No ecotoxicity data noted for the ingredient(s).
Section 13. Disposal Consideration	
	This product, in its present state, when discarded or disposed of, is not a hazardous waste according to Federal regulations (40 CFR 261.4 (b)(4)). Under RCRA, it is the responsibility of the user of the product to determine, at the time of disposal, whether the product meets RCRA criteria for hazardous waste. Dispose in accordance with all applicable regulations.
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 208622
Section 16. Other information	
	None

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