Material Safety data sheet

PRAMIPEXOL DIHYDROCHLORIDE TABLETS

Strength: 0.125/0.25/0.5/1/1.5 mg **Pack Size:** Bottles of 90/500/1000 Tablets **Revision No:** 00

EMERGENCY OVERVIEW

Pramipexole Dihydrochloride tablet intended for oral administration contains 0.125 mg, 0.25 mg, 0.5 mg, 1 mg, or 1.5 mg of pramipexole dihydrochloride monohydrate I and excipients generally considered to be non- toxic and non-hazardous in small quantities and under conditions of normal occupational exposure.

Section 1. Identification of the substance

Identification of the product

Product name: Pramipexol Dihydrochloride Tablets
Formula: $C_{10}H_{17}N_3S \cdot 2HCl \cdot H_2O$
Chemical Name: (*S*)-2-amino-4,5,6,7-tetrahydro-6-(propylamino) benzothiazole dihydrochloride monohydrate
Therapeutic Category Vitamin D Analog

Manufacturer / Supplier Identification

Company: Cadila Healthcare Ltd. Ahmedabad, India

Contact for information: Tel.: +91 79 6868100 Fax: +91 79 3750319

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Section 2. Composition / information on ingredients

Component	Exposure Limit	CAS No.
Principle Component :		
Pramipexol Dihydrochloride	Not Found	104632-25-9
Inactive Ingredients :		
colloidal silicon dioxide	Not Found	7631-86-9
mannitol	Not Found	69-65-8
magnesium stearate	Not Found	557-04-0
pregelatinized starch	Not Found	9005-25-8
povidone	Not Found	9003-39-8
D&C red no. 27 aluminum lake	Not Found	NA

FD&C blue no. 1 aluminum lake	Not Found	NA
FD&C blue no. 1 aluminum lake	Not Found	NA
D&C red no. 27 aluminum lake	Not Found	NA
ferric oxide yellow	Not Found	90452-21-4

Section 3. Health Hazards Information

Dose and Administration

Dosing in Patients with Normal Renal Function:

Initial Treatment:

Dosages should be increased gradually from a starting dose of 0.375 mg/day given in three divided doses and should not be increased more frequently than every 5 to 7 days.

Maintenance Treatment:

Pramipexole dihydrochloride tablets were effective and well tolerated over a dosage range of 1.5 to 4.5 mg/day administered in equally divided doses three times per day with or without concomitant levodopa (approximately 800 mg/day).

Dosing in Patients with Renal Impairment:

Renal Status	Starting Dose (mg)	Maximum Dose (mg)
Normal to mild impairment (creatinine Cl > 60 mL/min)	0.125 TID	1.5 TID
Moderate impairment (creatinine Cl = 35 to 59 mL/min)	0.125 BID	1.5 BID
Severe impairment (creatinine Cl = 15 to 34 mL/min)	0.125 QD	1.5 QD
Very severe impairment (creatinine Cl < 15 mL/min and hemodialysis patients)	The use of pramipexole dihydrochloride has not been adequately studied in this group of patients.	

Discontinuation of Treatment:

It is recommended that pramipexole dihydrochloride tablets be discontinued over a period of 1 week; in some studies, however, abrupt discontinuation was uneventful.

Adverse Effects

Body as a whole:
Asthenia, General edema, Malaise, Reaction unevaluable, Fever.

Digestive System:
Nausea, Constipation, Anorexia, Dysphagia.

Metabolic & Nutritional System:
Peripheral Edema, Decreased Weight.

Nervous System:
Dizziness, Somnolescence, Insomnia, Hallucinations, Confusion, Amnesia, Dystonia, Akathisia, Thinking abnormalities, Decreased Libido

Special Senses:
Visible abnormalities.

Urogenital System:
Impotence

Over Dose Effect

There is no clinical experience with massive overdosage. One patient, with a 10-year history of schizophrenia, took 11 mg/day of pramipexole for 2 days in a clinical trial to evaluate the effect of pramipexole in schizophrenic patients. No adverse events were reported related to the increased dose. Blood pressure remained stable although pulse rate increased to between 100 and 120 beats/minute. The patient withdrew from the study at the end of week 2 due to lack of efficacy.

There is no known antidote for overdosage of a dopamine agonist. If signs of central nervous system stimulation are present, a phenothiazine or other butyrophenone neuroleptic agent may be indicated; the efficacy of such drugs in reversing the effects of overdosage has not been assessed. Management of overdose may require general supportive measures along with gastric lavage, intravenous fluids, and electrocardiogram monitoring.

Contraindications

Pramipexole dihydrochloride tablets are contraindicated in patients who have demonstrated hypersensitivity to the drug or its ingredients.

Pregnancy Comments	There are no studies of pramipexole in human pregnancy. Because animal reproduction studies are not always predictive of human response, pramipexole should be used during pregnancy only if the potential benefit outweighs the potential risk to the fetus. Nursing Mothers: A single-dose, radio-labeled study showed that drug-related materials were excreted into the breast milk of lactating rats. Concentrations of radioactivity in milk were three to six times higher than concentrations in plasma at equivalent time points. Other studies have shown that pramipexole treatment resulted in an inhibition of prolactin secretion in humans and rats. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from pramipexole, a decision should be made as to whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.
Pregnancy Category	**C**

Section 4. First aid measures

General	Remove from exposure. Remove contiminated Clothing. Person developing serious hypersensitivity reaction must receive medical attention
Overdose Treatment	Tertiary anticholinergics such as atropine may be used as an antidote for donepezil hydrochloride overdosage. Intravenous atropine sulfate titrated to effect is recommended: an initial dose of 1.0 to 2.0 mg IV with subsequent doses based upon clinical response.

Section 5. Fire – fighting measures

Flash point	Not Found	**Upper Flammable Limit:**	Not Found
Auto-Ignition Temperature:	Not Found	**Lower Flammable**	Not Found

		Limit:	
Extinguishing Media	Water Spray, dry chemical, carbon dioxide or foam as appropriate for surrounding fire and material.	**Fire and Explosion Hazard**	This material is assumed to be combustible. As with all dry powders it is advisable to ground mechanical equipment in contact with the dry material to dissipate the potential build up of static electricity.

Fire Fighting Procedure As with all fires, evacuate personnel to a safe area. Fire fighter should use self- contained breathing equipment and protective clothing.

Section 6. Storage / Spill / Disposal Measures

Storage Store at 20° to 25°C (68° to 77°F). Protect from light. Dispense in a tight, light resistant container.

Spill Response Wear approved respiratory protection, chemically compatible gloves and protective clothing. Wipe up spillage or collect spillage using high efficiency vacuum cleaner. Avoid breathing dust. Place spillage in appropriately labelled container for disposal. Wash spill site.

Disposal Dispose the waste in accordance with all applicable Federal, State and local laws.

Section 7. Exposure controls and personal protection

Respiratory Protection Protection from inhalation is not normally necessary. If ventilation is inadequate or dust is likely to generate, use of suitable dust mask would be appropriate.

Skin Protection Skin protection is not normally necessary, however it is good practice to avoid contact with chemical to use suitable gloves when handling.

Eye protection Eye protection is not normally necessary. If concerned wear protective goggles or glasses. Wash hands prior to touching eye and in particular handling contact lenses.

Protective Clothing	Protective clothing is not normally necessary, however it is good practice to use apron.

Section 8. Physical and chemical properties

Appearance	white to off-white powder	**Odour**	No Data Available
Solubility in water	freely soluble in methanol.	**Melting Point**	296° to 301°C
Boiling point	No Data Available	**Vapour density**	No Data Available
Evaporation rate	No Data Available	**Evaporation rate**	No Data Available
Reactivity in water	No Data Available	**Specific gravity**	No Data Available
% Volatile by volume	No Data Available	**Vapour pressure**	No Data Available
Other information	Pramipexole dihydrochloride tablets contain pramipexole, a nonergot dopamine agonist. Its molecular weight is 302.27.		

Section 9. Physical Hazards

Condition to avoid	Avoid exposure to extreme heat, light and moisture.	**Stable**	Stable under normal ambient and anticipated storage and handling conditions.
Decomposition Products	No Data Available	**Hazardous Reaction**	No data available.
Incompatibilities	No data available.		

Section 10. Toxicological information

Handling of formulated product is not expected to cause any adverse affects. The data pertains to the ingredient in formulations, rather than this specie formulation.

Target organ

Eye contact, Skin contact and inhalation is not great risk as this product is tablet.

Other

Falling Asleep During Activities of Daily Living:
Patients treated with pramipexole dihydrochloride tablets have reported falling asleep while engaged in activities of daily living, including the operation of motor vehicles which sometimes resulted in accidents. Although many of these patients reported somnolence while on pramipexole dihydrochloride tablets, some perceived that they had no warning signs such as excessive drowsiness, and believed that they were alert immediately prior to the event. Some of these events had been reported as late as one year after the initiation of treatment.

Somnolence is a common occurrence in patients receiving pramipexole dihydrochloride tablets at doses above 1.5 mg/day (0.5 mg TID) for Parkinson's disease. Many clinical experts believe that falling asleep while engaged in activities of daily living always occurs in a setting of pre-existing somnolence, although patients may not give such a history. For this reason, prescribers should continually reassess patients for drowsiness or sleepiness, especially since some of the events occur well after the start of treatment. Prescribers should also be aware that patients may not acknowledge drowsiness or sleepiness until directly questioned about drowsiness or sleepiness during specific activities.

Before initiating treatment with pramipexole dihydrochloride tablets, patients should be advised of the potential to develop drowsiness and specifically asked about factors that may increase the risk with pramipexole dihydrochloride tablets such as concomitant sedating medications, the presence of sleep disorders, and concomitant medications that increase pramipexole plasma levels If a patient develops significant daytime sleepiness or episodes of falling asleep during activities that require active participation (e.g., conversations, eating, etc.), pramipexole dihydrochloride tablets should ordinarily be discontinued. If a decision is made to

continue pramipexole dihydrochloride tablets, patients should be advised to not drive and to avoid other potentially dangerous activities. While dose reduction clearly reduces the degree of somnolence, there is insufficient information to establish that dose reduction will eliminate episodes of falling asleep while engaged in activities of daily living.

Section 11. Ecological information

No data available on Ecotoxicity

Section 12. Other information

None

Date of issue: 27/08/2010 Supersedes edition of: New Edition

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