EMERGENCY OVERVIEW
Each Pramipexole Dihydrochloride tablet intended for oral administration contains Pramipexole Dihydrochloride 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: Pramipexole Dihydrochloride Tablets

Formula: C₁₀H₁₁N₃S · 2HCl · H₂O

Chemical Name: (S)-2-amino-4,5,6, 7-tetrahydro-6-(propylamino) benzothiazole dihydrochloride monohydrate.

Manufacturer / supplier identification

Company: Cadila Healthcare Ltd. Ahmedabad, India


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

Emergency Telephone No. Tel.: +91 79 6868100

Recommended use / Therapeutic Category Vitamin D Analog Anticoagulant

Restriction on Use / Contraindications Pramipexole dihydrochloride tablets are contraindicated in patients who have demonstrated hypersensitivity to the drug or its ingredients.
Section 2. Hazard(s) 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:

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

Discontinuation of Treatment:
It is recommended that pramipexol 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 unevaleuable, Fever.

**Digestive System:**
Nausea, Constipation, Anorexia, Dysphagia.

**Metabolic & Nutritional System:**
Peripheral Edema, Decreased Weight.
Nervous System:
Dizziness, Somnolence, Insomnia, Hallucinations, Confusion, Amnesia, Dystonia, Akathisia, Thinking abnormalities, Decreased Libido

Special Senses:
Visible abnormalities.

Urogenital System:
Impotence

Over Dose Effects
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.

Medical Condition
• Falling asleep during activities of daily living: Sudden onset of sleep may occur without warning. Advise patients to report symptoms to the prescriber.
• Symptomatic orthostatic hypotension. Monitor during dose escalation
• Impulse control/Compulsive behaviors: Patients may experience compulsive behaviors and other intense urges.
• Hallucinations: May occur. Risk increases with age.
• Dyskinesia: May be caused or exacerbated by pramipexole Dihydrochloride.
• Renal Impairment: Requires dose reduction.
• Events reported with dopaminergic therapy: Include withdrawal-emergent hyperpyrexia and confusion, fibrotic complications, and melanoma.

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 3. Composition / information on ingredient

<table>
<thead>
<tr>
<th>Component</th>
<th>Exposure Limit</th>
<th>CAS No.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Principle Component:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pramipexol Dihydrochloride</td>
<td>Not Found</td>
<td>104632-25-9</td>
</tr>
<tr>
<td><strong>Inactive Ingredients:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colloidal silicon dioxide</td>
<td>Not Found</td>
<td>7631-86-9</td>
</tr>
<tr>
<td>Mannitol</td>
<td>Not Found</td>
<td>69-65-8</td>
</tr>
<tr>
<td>Magnesium Stearate</td>
<td>Not Found</td>
<td>557-04-0</td>
</tr>
</tbody>
</table>
Section 4. First-aid measures

General
Remove from exposure. Remove contaminated 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

Auto-Ignition Temperature: Not Found

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. Firefighter should use self-contained breathing equipment and protective clothing.
Safety Data Sheet
Pramipexole Dihydrochloride Tablets

**Strength:** 0.125/0.25/0.5/111.5mg.  **Pack Size:** 90/500/1000 Tablets  **Revision No.:** 02

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### Section 6. Accidental Release Measures

**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.

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### Section 7. Handling and Storage

**Storage**

Store at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature]. Protect from light. Dispense in a tight, light-resistant container.

**Incompatibilities:**

No data available.

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### Section 8. Exposure controls / 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.

**Engineering Control**

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.

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### Section 9. Physical and chemical properties

**Appearance**

Pramipexole Dihydrochloride Tablets, 0.125 mg are pink color, capsule-shaped, flat, beveled-edged, uncoated tablets debossed with ‘P1’ on one side and plain on other side.

Pramipexole Dihydrochloride Tablets, 0.25 mg are pale blue color, round, flat, beveled-edged, uncoated tablets debossed with ‘P2’ on one side and break line on other side.

Pramipexole Dihydrochloride Tablets, 0.5 mg are lavender, capsule-shaped, flat, beveled-edged, uncoated tablets debossed with ‘P’ breakline ‘3’ on one side and plain on other side.
Pramipexole Dihydrochloride Tablets

**Strength:** 0.125/0.25/0.5/111.5mg.  **Pack Size:** 90/500/1000 Tablets  **Revision No.:** 02

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Pramipexole Dihydrochloride Tablets, 1 mg are light peach to peach, round, flat, beveled-edged, uncoated tablets debossed with ‘P4’ on one side and break line on other side.

Pramipexole Dihydrochloride Tablets, 1.5 mg are yellow color, round, flat, beveled-edged, uncoated tablets debossed with ‘P5’ on one side and break line on other side.

**Solubility in water**  Freely soluble in Methanol  **Odour**  Odourless

**Boiling point**  No Data Available  **Melting Point**  296° to 301°C

**Evaporation rate**  No Data Available  **Vapour density**  No Data Available

**Reactivity in water**  No Data Available  **Evaporation rate**  No Data Available

**% Volatile by volume**  No Data Available  **Specific gravity**  No Data Available

**Vapour pressure**  No Data Available

**Other information**  Pramipexole Dihydrochloride Tablets contain Pramipexole Dihydrochloride and its molecular formula is C\textsubscript{10}H\textsubscript{17}N\textsubscript{3}S\textsubscript{2}HCl·H\textsubscript{2}O, and its molecular weight is 302.26. Pramipexole dihydrochloride USP is a white to almost white crystalline powder and it is freely soluble in water, soluble in methanol, slightly soluble in alcohol and practically insoluble in methylene chloride.

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**Section 10. Stability and Reactivity**

**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.

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**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 specific formulation.

**Target organ**  Eye contact, Skin contact and inhalation is not great risk as this product is Tablets.
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 12. Ecological information

Do not allow product to enter drinking water supplies, waste water or soil.

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).

**Section 15. Regulatory Information**

Generic Medicine. Approved by USFDA & the ANDA Number is 078920

**Section 16. Other Information**

None

**Date of issue:** 28/05/2015  
**Supersedes edition of:** 01

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.