Amantadine Hydrochloride Tablets are indicated for chemoprophylaxis in the treatment of Parkinson’s disease and drug-induced extrapyramidal reactions.

**Mechanism of Action:** Antiviral - The mechanism by which amantadine exerts its antiviral activity is not clearly understood. It appears to prevent the release of the viral nucleic acid into the host cell. The ensuing viral replication is blocked and viral progeny are not released.

**Antiviral Activity:** Amantadine inhibits the replication of influenza A viruses from each of the subtypes, i.e., H1N1, H2N2, and H3N2. It has little or no effect against influenza B viruses.

**Mechanism of Action:** Amantadine has a high affinity for viral matrix (M2) proteins of influenza A viruses. These proteins are located on the surface of the viral particle and are associated with the viral proton channels. Amantadine binds to this channel and blocks the proton conduction, inhibiting the uncoating and subsequent viral replication.

**Indications:** Amantadine Hydrochloride Tablets are indicated for prophylaxis and treatment of influenza A infections.

**Contraindications:** Amantadine Hydrochloride Tablets should not be used in patients with acute or chronic renal failure, or in those with a history of drug-induced extrapyramidal reactions.

**Warnings:** Amantadine Hydrochloride Tablets should be used with caution in patients with liver disease. Rare instances of reversible elevation of liver enzymes have been reported in patients receiving amantadine hydrochloride, though a specific relationship between the drug and such changes has not been established.

**Side Effects:** Amantadine Hydrochloride Tablets may cause side effects such as dizziness, lightheadedness, blurred vision, difficulty in urination, and constipation.

**Pharmacokinetics:** Amantadine Hydrochloride Tablets are rapidly absorbed orally. Maximum plasma concentrations are reached within 2 hours to 4 hours.

** Elimination:** Amantadine Hydrochloride Tablets are metabolized in the liver and excreted in the urine. Amantadine itself is not excreted in the urine. The primary metabolite is amantadine N-oxide, which is formed by liver microsomal enzymes.

** Drug-Drug Interactions:** Amantadine Hydrochloride Tablets may interact with other drugs that are excreted via the same pathways, such as tricyclic antidepressants or metoprolol. This interaction can result in increased levels of amantadine and increased risk of side effects.

** Adverse Effects:** Amantadine Hydrochloride Tablets have been associated with adverse effects such as dizziness, lightheadedness, blurred vision, difficulty in urination, and constipation.

**Overdose:** Amantadine Hydrochloride Tablets should not be administered in overdose. The management of an overdose should include supportive care such as monitoring of vital signs, ensuring adequate airway, and managing any specific symptoms that arise.

Because Amantadine Hydrochloride Tablets have anticholinergic effects and may cause mydriasis, it should not be given to patients with uncontrolled glaucoma.

**Precautions:** Amantadine Hydrochloride Tablets should not be administered in patients with Parkinson’s disease since a few patients have experienced a paradoxical response, i.e., a worsening of tremor and rigidity due to anticholinergic effects. The best management of this condition is not clearly established. When this medication was suddenly stopped, the dose of anticholinergic drugs or of another antiparkinson medication should be reduced if drug interactions appear when these drugs are used concurrently. Abrupt discontinuation may also precipitate disorientation, agitation, delusions, hallucinations, paranoid ideation, alteration of speech, and auditory and visual hallucinations.

**Neuroleptic Malignant Syndrome:** Sporadic cases of possible Neuroleptic Malignant Syndrome (NMS) have been reported in association with the use of Amantadine Hydrochloride therapy. Therefore, patients should be observed carefully when the dosage of amantadine hydrochloride is reduced or abruptly discontinued, especially if the patient is receiving neuroleptics.

**Liver Disease:** Because amantadine hydrochloride is excreted mainly in the urine, it is accumulated in the plasma and in the body in which renal function declines. Thus, the dose of amantadine hydrochloride should be reduced in patients with renal impairment and in individuals who are 60 years of age or older (see DOSAGE AND ADMINISTRATION: Dosage for Impaired Renal Function).

**Impulse Control/Compulsive Behaviors:** Patients who have a history of impulse control or compulsive behaviors should be monitored closely during treatment with Amantadine Hydrochloride Tablets. Although anticholinergic-type side effects have been noted with the use of antiparkinson drugs, there is a lower incidence of these side effects than that observed with the anticholinergic antiparkinson drugs.

**Drug-Induced Extrapyramidal Reactions:** Amantadine Hydrochloride Tablets are indicated in the treatment of drug-induced extrapyramidal reactions. Although anticholinergic-type side effects were noted in patients with Parkinson’s disease, they were not observed in patients treated with Amantadine Hydrochloride Tablets.

**Drug Resistance:** Influenza A variants with reduced sensitivity to amantadine have been isolated from patients treated with Amantadine Hydrochloride Tablets. Resistance to amantadine may be due to mutations in the viral M2 gene.

**Contraindications:** Amantadine Hydrochloride Tablets are contraindicated in patients with known hypersensitivity to amantadine hydrochloride or to any of the other ingredients in Amantadine Hydrochloride Tablets.

**Warnings:** Amantadine Hydrochloride Tablets have been reported from overdose with amantadine hydrochloride. The lowest reported acute lethal dose in humans was 300 mg, and the usual fatal dose was 400 mg.

**Side Effects:** Amantadine Hydrochloride Tablets may cause side effects such as dizziness, lightheadedness, blurred vision, difficulty in urination, and constipation.

**Overdose:** Amantadine Hydrochloride Tablets should not be administered in overdose. The management of an overdose should include supportive care such as monitoring of vital signs, ensuring adequate airway, and managing any specific symptoms that arise.

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Dosage for the Concomitant Therapy: Some patients who do not respond to anticholinergic
oral dopaminergic therapy may exhibit improved response to adjunctive Amantadine. When Amantadine Hydrochloride Tablets or anticholinergic/antiparkinsonian drugs are each used with marginal benefit, concomitant use may produce additional benefit.

When Amantadine Hydrochloride Tablets and levodopa are initiated concurrently, the patient can occasionally experience hypotriglyceridemic action. The doses of Amantadine Hydrochloride Tablets may need to be adjusted to provide additional benefit may result in improvement which sometimes occurs in patients on levodopa alone. Patients who require a reduction in their usual dose of levodopa may benefit because of development of disturbances or possible regulatory benefit with the addition of Amantadine Hydrochloride Tablets.

Dosage for Drug-Induced Extrapyramidal Reactions:

Adult: The usual dose of Amantadine Hydrochloride Tablets is 100 mg twice a day. Occasionally, patients whose responses have not responded to Amantadine tablets in divided doses may benefit from an increase up to 300 mg daily in divided doses.

Dosage for Impaired Renal Function:

Depending upon creatinine clearance, the following dosage adjustments are recommended. The recommended dosage for patients on hemodialysis is 200 mg every 7 days.

<table>
<thead>
<tr>
<th>Creatinine Clearance (mL/min)</th>
<th>Amantadine Hydrochloride Tablets Doseage</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 to 19</td>
<td>100 mg every 4 days</td>
</tr>
<tr>
<td>15 to 29</td>
<td>100 mg every 7 days</td>
</tr>
<tr>
<td>&gt; 20</td>
<td>100 mg every 14 days</td>
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</tbody>
</table>

For patients on peritoneal dialysis, the total daily dose administered should not exceed 200 mg.

HMG SUPPLIED

Amantadine Hydrochloride Tablets are available as peach, compressed tablets, round, debossed “82” on one side and “AM” on the other side as follows:

Bottles of 500 (NDC 0382-0111-50)

Store at controlled room temperature 20° to 25°C (68° to 77°F). Excursions permitted to 15° to 30° C (59° to 86°F). [See USP control test information].

Dispense in a light-resistant container as defined in the USP, with child-resistant (os) as required. Keep out of reach of children.


Manufactured by:

SMITH LABORATORIES, INC.

10016-03-02

Revised 04/12

Dosage for Prophylaxis and Treatment of Uncomplicated Influenza A Virus Illness:

Adult: The daily adult dose of Amantadine Hydrochloride Tablets is 100 mg every 12 hours for uncomplicated influenza A virus infection. This dose may be administered in two daily oral doses of 100 mg each.

Children: The total daily dose is divided into two equal or two unequal oral doses. The total daily dose must be administered within 48 hours of the first onset of symptoms.

Dosage for the Prevention of Influenza A Virus Illness:

Adult: The daily adult dose of Amantadine Hydrochloride Tablets is 100 mg every 12 hours for uncomplicated influenza A virus infection. This dose may be administered in two daily oral doses of 100 mg each.

Children: The total daily dose is divided into two equal or two unequal oral doses. The total daily dose must be administered within 48 hours of the first onset of symptoms.

Both adults and children can benefit from Amantadine Hydrochloride Tablets. The recommended dosage is 100 mg twice a day, regardless of age. Flulike symptoms have been reported in children given this dosage, and they may continue to develop for several days after the drug is discontinued.

Dosage for Prophylaxis:

Adult: The daily adult dose of Amantadine Hydrochloride Tablets is 100 mg every 12 hours for uncomplicated influenza A virus infection. This dose may be administered in two daily oral doses of 100 mg each.

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