Amantadine Hydrochloride Tablets

**DESCRIPTION**

Amantadine Hydrochloride USP is designated generally as amantadine hydrochloride and chemically as 1-adamantanehydrochloride.

**Mechanisms of Action**

**Antiviral**

The mechanism by which amantadine exerts its antiviral activity is not clearly understood. It appears to primarily interfere with the release of infective viral nucleocapsid into the host cell by interfering with the function of the transmembrane domain of the viral M2 protein. In certain cases, amantadine is also known to prevent virus assembly during virus replication. It does not appear to interfere with the immunopathology associated with influenza A virus infections.

**Pharmacokinetics**

**Absorption**

Amantadine Hydrochloride is well absorbed orally. Maximum plasma concentrations are directly related to dose for doses up to 200 mg. Above 200 mg, drug metabolism may result in greater than proportional increases in maximum plasma concentrations. It is primarily excreted unchanged in the urine by glomerular filtration and tubular secretion. The plasma elimination half-life of amantadine is 2 to 3 hours.

**Distribution**

Intravenous amantadine has been identified in human urine. One metabolite, 1-hydroxyamantadine, has been quantified in human urine and accounted for 15% of the administered dose. Plasma and amantadine plasma concentration for up to 72% of healthy volunteers following the ingestion of a 200 mg dose of amantadine. Amantadine was not detected in the plasma of the remaining seven volunteers. The contribution of this metabolite to the efficacy or toxicity is unknown.

**Metabolism**

There appears to be a relationship between plasma amantadine concentrations and toxicity. As concentration increases, both CNS effects and antiviral activity increase. Absolute oral bioavailability of amantadine has not been fully defined. As concentration increases, absolute oral bioavailability decreases in normal adult volunteers, but is unchanged in patients with renal failure.

**Excretion**

Amantadine is metabolized and excreted as unchanged, in sodium bicarbonate. The mean 24-hour plasma clearance was 26.8 L/hr. The plasma clearance of amantadine in 12 healthy volunteers following the ingestion of a 200 mg dose of amantadine was 26.8 L/hr. Amantadine was not detected in the plasma of the remaining seven volunteers. The contribution of this metabolite to the efficacy or toxicity is unknown.

**Volume of Distribution**

The volume of distribution determined after the intravenous administration of amantadine to 15 healthy subjects was 3

1.0

**CLINICAL PHARMACOLOGY**

**Packaging and Storage**

Amantadine Hydrochloride Tablets are packaged in bottles of 100 tablets. On one side of each tablet, the imprint “AR” is scored, and on the other side, the imprint “100mg.” The tablets are white, square, scored tablets in a fiberboard box with a plastic tray liner. The product is supplied in bottles of 100 tablets. The tablets are stable under usual storage conditions.

**ADVERSE REACTIONS**

**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**

**Drug-Induced Extrapyramidal Reactions**

Amantadine Hydrochloride Tablets are contraindicated in patients with a history of extrapyramidal reactions.

**OVERDOSE**

**CNS Antidepressants**

Amantadine Hydrochloride Tablets are contraindicated in patients with a history of CNS depression or any of the other ingredients in Amantadine Hydrochloride Tablets.

**Suicide Attempts**

Amantadine Hydrochloride Tablets are contraindicated in patients with a history of CNS depression or any of the other ingredients in Amantadine Hydrochloride Tablets.

**CONTRAINDICATIONS**

Amantadine Hydrochloride Tablets are contraindicated in patients with a history of CNS depression or any of the other ingredients in Amantadine Hydrochloride Tablets.

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**Drug-Induced Extrapyramidal Reactions**

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Amantadine Hydrochloride Tablets are contraindicated in patients with a history of CNS depression or any of the other ingredients in Amantadine Hydrochloride Tablets.

**CONTRAINDICATIONS**

Amantadine Hydrochloride Tablets are contraindicated in patients with a history of CNS depression or any of the other ingredients in Amantadine Hydrochloride Tablets.
Avoid excessive alcohol usage, since it may increase the potential for CNS effects such as dizziness, confusion, sedation, and anticholinergic effects.

Drug Interactions

Central nervous system depression may be enhanced by the concomitant use of amantadine hydrochloride and other CNS depressants, including alcohol, sedatives, hypnotics, narcotics, and antidepressants. CNS depression, respiratory depression, and anticholinergic effects may be observed with concomitant use of amantadine hydrochloride and MAO-inhibitor antidepressants. Amantadine hydrochloride has been associated with a low incidence of orthostatic hypotension which may be potentiated by antihypertensive agents. Amantadine hydrochloride also has been associated with an increased risk of suicide when used concomitantly with a tricyclic antidepressant. 

Overdosage

In several cases of overdosage with amantadine, the following symptoms were reported: gastrointestinal disturbances (including anorexia, nausea, vomiting, diarrhea, abdominal distention, dyspepsia), psychotic reactions, hallucinations, delirium, agitation, tremors, hyperreflexia, and coma. 

Signs of toxicity may be eliminated by emesis or gastric lavage. Normal saline or other appropriate fluid may be used for the purpose of increasing the volume of distribution and decreasing the peak plasma concentration. 

The use of antidotes is not recommended in amantadine overdosage since the therapeutic index is quite wide. Hemodialysis or peritoneal dialysis are not expected to be of value since the drug is not protein-bound.

Dosage in Renal Impairment

The safety and efficacy of amantadine hydrochloride in patients with various degrees of renal impairment have not been formally evaluated. However, the pharmacokinetics of amantadine hydrochloride in healthy adults and in patients with moderate renal impairment were similar. Based on this information, it is recommended that dose adjustment of amantadine hydrochloride be based on the creatinine clearance (mL/min).


Creatinine Clearance

Dosage

In renal failure, the dose of Amantadine Hydrochloride Tablets should be reduced to one half to two thirds of the normal dosage as determined by the creatinine clearance. 

In patients with moderate renal impairment (creatinine clearance 30 to 50 mL/min), Amantadine Hydrochloride Tablets should be administered at a dose of 100 mg twice daily. 

In patients with severe renal impairment (creatinine clearance less than 30 mL/min), Amantadine Hydrochloride Tablets should be administered at a dose of 100 mg once daily. 

Dosage adjustment is not needed in patients with end-stage renal disease who are undergoing dialysis. 

DOSAGE AND ADMINISTRATION

The daily dosage of Amantadine Hydrochloride Tablets should be taken orally in the morning and evening. 

The initial dose of Amantadine Hydrochloride Tablets in adults is 100 mg once daily, at bedtime. 

The recommended dosage for patients on hemodialysis is 200 mg every 7 days.

HOW SUPPLIED

Amantadine Hydrochloride Tablets 100 mg are available as Peach colored, round shaped, flat, beveled edge tablet, with debossed logo as "S" on one side and "502" on other side as follow: 

<table>
<thead>
<tr>
<th>Size</th>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>100mg</td>
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</tr>
<tr>
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<td></td>
</tr>
<tr>
<td>Tablets</td>
<td>100 tablets</td>
<td></td>
</tr>
</tbody>
</table>

 kept under tight, light-resistant container as defined in USP, with child-resistant closures. 

Keep out of reach of children.

REFERENCES

4. Dopamine is a registered trademark of Bristol-Myers Squibb. 
5. Vensun Pharmaceuticals, Inc., Yardley, PA 19067 
6. Strides Shasun Limited, India 

D33-PD-002-9-F-06-00

ARTWORK DETAIL LABEL

Product

Amantadine Hydrochloride Tablets, USP 100mg

Buyer/Country

Vensun / USA

Component

Outlet

Vensun / USA

Dimensions

Open Size 380 x 275 mm, Fold Size : 33 x 34mm

New Item Code

1034833

Old Item Code

NA

No. of Colours

1

Control Change No.

NA

Design/Style

Front & Back side printing

Pharmacode

NA

Substrate

As per specification

Additional Special Instructions

Printing clarity should be clear and sharp.

Autocontentor Requirements

NA

Caution to the Printer: Before processing, please ensure that the ARTWORK received for printing is exactly in line with APPROVED ARTWORK provided to you. In case of any FORMS/DESIGN are Mis-matching with the APPROVED ARTWORK, please inform PD for further action. DO NOT MAKE ANY CHANGE TO THE ARTWORK WITHOUT WRITTEN INSTRUCTIONS FROM PD.