Amantadine HCI Tablets

Description
Amantadine hydrochloride is a stable white or nearly white crystalline powder, freely soluble in water and insoluble in alcohol.

Amantadine hydrochloride has pharmacological actions both as an anti-Parkinson's disease agent and a chemical antiviral.

Each tablet is intended for oral administration contains 100 mg amantadine hydrochloride and has the following inactive ingredients: starch, magnesium stearate, and hydroxypropyl methylcellulose.

CNS Effects:

Drug-related CNS effects, including restlessness, insomnia, anxiety, nervousness, agitation, confusion, hallucinations, depression, mania, and suicidal ideation. Higher incidence in adults with idiopathic Parkinson's disease than in other age groups. It is unknown if these effects are due to anticholinergic toxicity or other factors. A small number of reports have described atypical parkinsonian syndromes in patients treated with amantadine.

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

Amantadine hydrochloride is effective in the treatment of Parkinson's disease and drug-induced extrapyramidal reactions. Its mechanism of action appears to be related to its ability to block the action of dopamine on dopamine receptors. It is also effective in reducing extrapyramidal side effects of levodopa therapy.

Amantadine is a non-competitive NMDA receptor antagonist (Ki = 10µM). Although amantadine has not been shown to block the action of glutamate on other receptors, it is possible that amantadine may also have other actions.

Amantadine hydrochloride is well absorbed orally. Maximum plasma concentrations are directly related to dose for doses up to 150 mg, but may result in a greater than proportional increase in maximum plasma concentrations. It is primarily excreted unchanged in the urine by glomerular filtration and tubular secretion. Eight metabolites of amantadine have been identified in human urine. One metabolite, an acetylated compound, was quantitated in human urine and accounted for 5 to 15% of the administered dose. Plasma pharmacokinetics are unchanged at doses of up to 200 mg of amantadine HCl.

Amantadine is not extensively bound to plasma proteins; approximately 20% at steady state. The volume of distribution determined after the intravenous administration of amantadine to 15 healthy volunteers was 0.79 ± 0.17 L/kg (mean ± SD).

The terminal elimination half-life of amantadine is about 10 hours. The elimination rate constant is about 0.12 per hour. The total clearance of amantadine is about 0.28 L/kg per hour. The apparent oral bioavailability of amantadine HCl is about 85%.

Amantadine HCI Tablets are a substitute for early vaccination on an annual basis as recommended by the Centers for Disease Control and Prevention Advisory Committee on Immunization Practices.

Influenza virus change over time. Emergence of resistance mutations could decrease drug effectiveness. Other factors (for example, changes in viral fitness) might also decrease clinical benefit of antiviral drugs. Prescriptions should consider available information on influenza drug and treatment effects when deciding whether to use Amantadine Hydrochloride Tablets or Oseltamivir Phosphate tablets for prophylaxis or treatment. It is generally accepted that prophylaxis with Amantadine Hydrochloride Tablets will avoid the development of influenza A virus pneumonitis or other complications in high-risk patients. There is no clinical evidence indicating that Amantadine Hydrochloride Tablets are effective in the prophylaxis or treatment of respiratory tract influenza A virus infections other than those caused by influenza A virus strains.

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Deaths: Deaths have been reported from overdose with amantadine hydrochloride. The lowest reported lethal dose is 50 mg, but lethal doses range from 150 to 300 mg. After 15 days of amantadine therapy (100 mg/day), there were still significant amantadine levels in the plasma of patients who died. Amantadine hydrochloride should be reduced if atropine-like effects appear when these drugs are used concurrently.

Reconstruction of a possible Neuroleptic Malignant Syndrome (NMS) has been reported in association with clozapine withdrawal of amantadine hydrochloride. Therefore, patients should be observed carefully when the dosage of amantadine hydrochloride is reduced abruptly or discontinued, especially if the patient is receiving neuroleptic agents.

NMS is an uncommon but life-threatening syndrome characterized by fever, hyperthermia, autonomic instability, muscle stiffness, mental status changes, other disturbances such as autonomic dysfuncion, delirium, polyneuropathy, myoglobinuria, and increased serum creatine phosphokinase. NMS should be considered in the differential diagnosis of any event associated with anticholinergic toxicity, fever, and primary central nervous system pathology.

The management of MMS should include: 1) intravenous symptomatic therapy and medical monitoring, and 2) treatment of any concomitant serious medical problems for which specific treatments are available. Dopamine agonists, such as bromocriptine, and muscle relaxants, such as dantrolene are often used in the treatment of MMS, however, their effectiveness has not been demonstrated in controlled studies.

Renal disease: Because amantadine hydrochloride is rapidly excreted in the urine, it accumulates in the plasma and in the body when renal function declines. Thus, the dosage of amantadine hydrochloride should be reduced in patients with renal impairment and in individuals who are 65 years of age or older (see DOSAGE AND ADMINISTRATION: Dosage for Impaired Renal Function).

Liver disease: Care should be exercised when administering amantadine hydrochloride to patients with liver disease. Any instance of morbid elevation of liver enzymes has been reported in patients receiving amantadine hydrochloride, through a specific relationship between the drug and such changes has not been established.

Imputable Compl/Compulsive Behaviors: Postmarketing reports suggest that patients treated with anticholinergic agents can experience alterations in gait, increased sexual urges, and sexual thoughts.

Gastrointestinal: Anticholinergic agents may decrease gastrointestinal motility and may cause constipation. Anticholinergic agents may also cause an increase in the incidence of gastrointestinal adverse events.

Cardiovascular: Anticholinergic agents may cause an increase in systolic blood pressure and heart rate. Anticholinergic agents may also cause an increase in the incidence of cardiovascular adverse events.

Respiratory: Anticholinergic agents may cause an increase in the incidence of respiratory adverse events.

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Coadministration of thrombolytics has been reported to increase the risk of oculogyric crisis in patients with Parkinson's disease. However, it is not known if other thrombolytic products provide protection.

Coadministration of spironolactone with amantadine was shown to reduce the renal clearance of amantadine by about 39%.

The concurrent use of amantadine hydrochloride with live attenuated influenza vaccine (LAIV) has not been evaluated. However, because of the potential for interference between these products, LAIV should not be administered within 2 weeks before or 48 hours after administration of amantadine hydrochloride, even if administered as an oral or nasal spray.

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