Amantadine Hydrochloride Tablets

DESCRIPTION

Amantadine hydrochloride is USP designated generically as amantadine hydrochloride and chemically as N1,N2-dimethyl-2-adamantanamine hydrochloride.

INDICATIONS AND USAGE

The principal indication for amantadine hydrochloride is the treatment of uncomplicated respiratory tract illness caused by various strains of influenza A virus. Amantadine hydrochloride Tablets are also indicated in the treatment of postencephalitic parkinsonism, and symptomatic parkinsonism which may follow injury to the nervous system by any cause, including head trauma.

Pharmacodynamics

Amantadine is absorbed orally with high bioavailability. The peak plasma concentration occurs 1 to 3 hours after a single 100 mg dose. Steady-state plasma concentrations are reached within 1 week of repeated-dose administration. The rate of amantadine hydrochloride increases rapidly when the urine is acidic, the administration of urine acidifying drugs may elevate the levels of amantadine hydrochloride in the plasma. The pH of the urine has been reported to influence the excretion rate of amantadine hydrochloride. Since the excretion of amantadine hydrochloride by patients has been shown to vary widely, it is recommended that amantadine hydrochloride levels be measured in plasma or urine to determine the correct dosage to achieve steady-state plasma concentrations of 0.15 to 0.30 mcg/mL. Thirty percent to 60% of the administered dose is removed in negligible amounts by hemodialysis.

Pharmacokinetics

In a study of young healthy subjects (n=20), mean renal clearance of amantadine, normalized for body mass index, was 0.09 ± 0.02 L/hr/kg (range 0.05 to 0.13 L/hr/kg). In elderly male volunteers, the apparent plasma clearance of amantadine was 0.10 ± 0.04 L/hr/kg (range 0.06 to 0.17 L/hr/kg). Across a range of renal function, the apparent plasma clearance of amantadine was 0.10 ± 0.04 L/hr/kg (range 0.06 to 0.17 L/hr/kg) in healthy volunteers with normal renal function, 0.04 ± 0.02 L/hr/kg (range 0.02 to 0.10 L/hr/kg) in subjects with moderate renal impairment (creatinine clearance > 30 to ≤ 60 mL/min), 0.04 ± 0.02 L/hr/kg (range 0.03 to 0.07 L/hr/kg) in subjects with a creatinine clearance ≤ 30 mL/min, and 0.03 ± 0.01 L/hr/kg (range 0.01 to 0.06 L/hr/kg) in patients on hemodialysis. Amantadine is removed completely by hemodialysis.

Time to Peak Concentration

At steady-state, the mean ± SD time to peak plasma concentration (Tmax) of amantadine 100 mg b.i.d., the Cmax was 0.24 ± 0.04 mcg/mL and ranged from 0.18 to 0.28 mcg/mL. Across all studies, the time to peak plasma concentration of amantadine after a single oral dose of 100 mg was 2 ± 1 hours, and the time to peak plasma concentration after 15 days of therapy was 3 ± 2 hours.

AUC

At steady-state, the mean ± SD AUC of amantadine after a single oral dose of 100 mg was 12 ± 4 mcg.hr/mL, and the AUC after 15 days of therapy was 15 ± 5 mcg.hr/mL. Across all studies, the time to maximum AUC (Tmax) of amantadine after a single oral dose of 100 mg was 2 ± 1 hours, and the time to maximum AUC after 15 days of therapy was 3 ± 2 hours.

Pharmacokinetic Parameters of Selected Populations

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CNS Effects

Sporadic cases of possible Neuroleptic Malignant Syndrome (NMS) have been reported in association with dose reduction or withdrawal of Amantadine Hydrochloride Tablets. Therefore, patients should be observed carefully when dose reduction or withdrawal of amantadine hydrochloride therapy. Therefore, patients should be observed carefully when dose reduction or withdrawal of amantadine hydrochloride therapy is considered. Patients should be observed carefully when dose reduction or withdrawal of amantadine hydrochloride therapy is considered. Patients should be observed carefully when dose reduction or withdrawal of amantadine hydrochloride therapy is considered. Patients should be observed carefully when dose reduction or withdrawal of amantadine hydrochloride therapy is considered. Patients should be observed carefully when dose reduction or withdrawal of amantadine hydrochloride therapy is considered. Patients should be observed carefully when dose reduction or withdrawal of amantadine hydrochloride therapy is considered. Patients should be observed carefully when dose reduction or withdrawal of amantadine hydrochloride therapy is considered. Patients should be observed carefully when dose reduction or withdrawal of amantadine hydrochloride therapy is considered. Patients should be observed carefully when dose reduction or withdrawal of amantadine hydrochloride therapy is considered. Patients should be observed carefully when dose reduction or withdrawal of amantadine hydrochloride therapy is considered. Patients should be observed carefully when dose reduction or withdrawal of amantadine hydrochloride therapy is considered. Patients should be observed carefully when dose reduction or withdrawal of amantadine hydrochloride therapy is considered. Patients should be observed carefully when dose reduction or withdrawal of amantadine hydrochloride therapy is considered. Patients should be observed carefully when dose reduction or withdrawal of amantadine hydrochloride therapy is considered. Patients should be observed carefully when dose reduction or withdrawal of amantadine hydrochloride therapy is considered. Patients should be observed carefully when dose reduction or withdrawal of amantadine hydrochloride therapy is considered. Patients should be observed carefully when dose reduction or withdrawal of amantadine hydrochloride therapy is considered. Patients should be observed carefully when dose reduction or withdrawal of amantadine hydrochloride therapy is considered. Patients should be observed carefully when dose reduction or withdrawal of amantadine hydrochloride therapy is considered. Patients should be observed carefully when dose reduction or withdrawal of amantadine hydrochloride therapy is considered. Patients should be observed carefully when dose reduction or withdrawal of amantadine hydrochloride therapy is considered. Patients should be observed carefully when dose reduction or withdrawal of amantadine hydrochloride therapy is considered. Patients should be observed carefully when dose reduction or withdrawal of amantadine hydrochloride therapy is considered. Patients should be observed carefully when dose reduction or withdrawal of amantadine hydrochloride therapy is considered. Patients should be observed carefully when dose reduction or withdrawal of amantadine hydrochloride therapy is consid
Intestinal for Patients

Patients should be advised of the following information about the risks of amantadine.

Anticholinergic effects

Cardiovascular

Cardiac slowing and/or impaired cardiac output may result in regaining benefit in some patients. A decision to use other antiparkinson drugs may be necessary.

Some patients who do not respond to anticholinergic antiparkinson drugs may respond to Amantadine Hydrochloride Tablets. The benefit may be regained by increasing the dose to 300 mg daily. Alternatively, patients who have improved with Amantadine Hydrochloride Tablets at 200 mg daily may benefit from an increase up to 400 mg daily in divided doses.

The usual dose of Amantadine Hydrochloride Tablets is 100 mg twice a day when used alone. Amantadine Hydrochloride Tablets are used chemoprophylactically in conjunction with inactivated influenza A virus vaccine (see PRECAUTIONS). The total daily dose is 200 mg given as one tablet of 100 mg twice a day. The 100 mg daily dose has not been studied in individuals with compromised immune function.

Amantadine hydrochloride is primarily excreted in the urine. It is recommended that the total daily dose not exceed 200 mg.

Hyperpyrexia

Tremor

Fever is not a contraindication to continuation of therapy; however, fever of 38.9°C (102°F) or higher (see DOSAGE AND ADMINISTRATION).

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