DISCLAIMER

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Amantadine Hydrochloride Oral Solution, USP 50 mg/5 mL Rx Only

DESCRIPTION:
Amantadine Hydrochloride, USP is designated generically as amantadine hydrochloride and chemically as 1-adamantylamine hydrochloride.

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

Amantadine hydrochloride has pharmacological actions as both an anti-Parkinson and an antiviral drug.

Amantadine hydrochloride oral solution contains 50 mg of amantadine hydrochloride per 5 mL and has the following inactive ingredients: artificial raspberry flavor, citric acid, methylparaben, propylparaben, purified water, and sorbitol solution.

CLINICAL PHARMACOLOGY
Pharmacodynamics
Mechanism of Action: Antiviral The mechanism by which amantadine exerts its antiviral activity is not clearly understood. It appears to mainly prevent the release of infectious viral nucleic acid 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 immunogenicity of inactivated influenza A virus vaccine.

Antiviral Activity: Amantadine inhibits the replication of influenza A virus isolates from each of the subtypes, i.e., H1N1, H2N2 and H3N2. It has very little or no activity against influenza B virus isolates. A quantitative relationship between the in vitro susceptibility of influenza A virus to amantadine and the clinical response to therapy has not been established in man. Sensitivity test results, expressed as the concentration of amantadine required to inhibit by 50% the growth of virus (ED50) in tissue culture vary greatly (from 0.1 mcg/mL to 25.0 mcg/mL) depending upon the assay protocol used, size of virus inoculum, isolates of influenza A virus strains tested, and the cell type used. Host cells in tissue culture readily tolerated amantadine up to a concentration of 100 mcg/mL.

Drug Resistance: Influenza A variants with reduced in vitro sensitivity to amantadine have been isolated from epidemic strains in areas where amantadine derivatives are being used. Influenza virus strains with reduced in vitro sensitivity have been shown to be transmissible and to cause typical influenza illness. The quantitative relationship between the in vitro sensitivity of influenza A variants to amantadine and the clinical response to therapy has not been established.

Mechanism of Action: Parkinson's Disease The mechanism of action of amantadine in the treatment of Parkinson's disease and drug-induced extrapyramidal reactions is not known. Data from earlier animal studies suggest that amantadine hydrochloride may have direct and indirect effects on dopamine neurons. More recent studies have demonstrated that amantadine is a weak, non-competitive NMDA receptor antagonist (K0 = 10μM). Although amantadine has not been shown to possess direct anticholinergic activity in animal studies, clinically, it exhibits anticholinergic-like side effects such as dry mouth, urinary retention, and constipation.

Pharmacokinetics: Amantadine hydrochloride is well absorbed orally. Maximum plasma concentrations are directly related to dose for doses up to 200 mg/day. Doses above 200 mg/day may result in a greater than proportional increase in maximum plasma concentrations. It is not known whether any change is exchanged in the urine by glomerular filtration and tubular secretion. Eight metabolites of amantadine have been identified in human urine. One metabolite, a N-acetylated compound, was quantified in human urine and accounted for 5 to 15% of the administered dose. Plasma acetylamantadine accounted for up to 80% of the concurrent amantadine plasma concentration in 5 of 12 healthy volunteers following the ingestion of a 200 mg dose of amantadine. Acetylamantadine was not detected in the plasma of the remaining seven volunteers. The contribution of this metabolite to efficacy or toxicity is not known.

There appears to be a relationship between plasma amantadine concentrations and toxicity. As concentration increases, toxicity seems to be more prevalent, however, absolute values of amantadine concentrations associated with adverse effects have not been fully defined.

Amantadine pharmacokinetics were determined in 24 normal adult male volunteers after the oral administration of a single amantadine hydrochloride 100 mg soft gel capsule. The mean ± SD maximum plasma concentration (Cmax) was 0.24 ± 0.04 mcg/mL and ranged from 0.18 to 0.28 mcg/mL.

After 15 days of amantadine 100 mg b.i.d., the Cmax was 0.47 ± 0.11 mcg/mL in four of the five volunteers. The administration of amantadine tablets as a 200 mg single dose to 6 healthy volunteers resulted in a Cmax of 0.51 ± 0.14 mcg/mL. Across studies, the time to Cmax (Tmax) averaged about 2 to 4 hours.

Pharmacokinetics:
Amantadine plasma clearance ranged from 0.2 to 0.3 L/hr/kg after the administration of 5 mg to 25 mg intravenous doses of amantadine to 15 healthy volunteers.
In six healthy volunteers, the ratio of amantadine renal clearance to apparent oral plasma clearance was 0.79 ± 0.17 (mean ± SD).

The volume of distribution determined after the intravenous administration of amantadine to 15 healthy subjects was 3 to 8 L/kg, suggesting tissue binding. Amantadine, after single oral 200 mg doses to 6 healthy young subjects and to 6 healthy elderly subjects has been found in nasal mucus at mean ± SD concentrations of 0.15 ± 0.16, 0.28 ± 0.26, and 0.39 ± 0.34 mcg/g at 1, 4, and 8 hours after dosing, respectively. These concentrations represented 31 ± 33%, 59 ± 61%, and 95 ± 86% of the corresponding plasma amantadine concentrations.

Amantadine is approximately 67% bound to plasma proteins over a concentration range of 0.1 to 2.0 mcg/mL. Following the administration of amantadine 100 mg as a single dose, the mean ± SD red blood cell to plasma ratio ranged from 2.7 ± 0.5 in 6 healthy subjects to 1.4 ± 0.2 in 8 patients with renal insufficiency.

The apparent plasma clearance of amantadine is reduced and the plasma half-life and plasma concentrations are increased in healthy elderly individuals age 60 and older. After single dose administration of 25 to 75 mg to 7 healthy, 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) and the half-life was 29 ± 7 hours (range 20 to 41 hours). Whether these changes are due to renal function or other age related factors is not known.

In a study of young healthy subjects (n=20), mean renal clearance of amantadine, normalized for body mass index, was 1.5 fold higher in males compared to females (p<0.032). Compared with otherwise healthy adult individuals, the clearance of amantadine is significantly reduced in adult patients with renal insufficiency. The elimination half-life increases two to three fold or greater when creatinine clearance is less than 40 mL/min/1.73 m2 and averages eight days in patients on chronic maintenance hemodialysis. Amantadine is removed in negligible amounts by hemodialysis.

The pH of the urine has been reported to influence the excretion rate of amantadine hydrochloride. Since the excretion rate of amantadine hydrochloride increases rapidly when the urine is acidic, the administration of urine acidifying drugs may increase the elimination of the drug from the body.

INDICATIONS AND USAGE
Amantadine hydrochloride is indicated for the prophylaxis and treatment of signs and symptoms of infection caused by various strains of influenza A virus. Amantadine hydrochloride is also used in the treatment of signs and symptoms of influenza B virus infection. Amantadine pharmacokinetics have not been fully defined.

Influenza A Prophylaxis: Amantadine hydrochloride is indicated for chemoprophylaxis against signs and symptoms of influenza A virus infection. Because amantadine hydrochloride does not completely prevent the host immune response to influenza A infection, individuals who take this drug may still develop immune responses to natural disease or vaccination and may be protected when later exposed to antigenically related viruses. Following vaccination during an influenza A outbreak, amantadine hydrochloride prophylaxis should be considered for the 2- to 4-week postvaccination period to help prevent secondary transmission of influenza A virus.

Influenza A Treatment: Amantadine hydrochloride is also indicated in the treatment of uncomplicated respiratory tract illness caused by influenza A virus strains especially when administered early in the course of illness. There are no well-controlled clinical studies demonstrating that treatment with amantadine hydrochloride 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 is effective in the prophylaxis or treatment of viral respiratory tract illnesses other than those caused by influenza A virus strains.

The following points should be considered before initiating or prophylaxis with amantadine hydrochloride:

- Amantadine hydrochloride is not 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 viruses change over time. Emergence of resistance mutations could diminish clinical benefit of antiviral drugs. Prescribers should consider available information on influenza drug susceptibility patterns and treatment effects when deciding whether to use amantadine hydrochloride.

Parkinson's Disease/Syndrome: Amantadine hydrochloride is indicated in the treatment of idiopathic Parkinson's disease (Paralysis Agitans), postencephalitic parkinsonism, and symptomatic parkinsonism which may follow injury to the nervous system by carbon monoxide intoxication. It is indicated in these patients believed to develop parkinsonism in association with cerebral arteriosclerosis. In the treatment of Parkinson's disease, amantadine hydrochloride is less effective than levodopa, (-)-3-(3,4-dihydroxyphenyl)-L-alanine, and its efficacy in comparison with the anticholinergic antiparkinson drugs has not yet been established.

Drug-Induced Extrapyramidal Reactions: Amantadine hydrochloride is indicated in the treatment of drug-induced extrapyramidal reactions. Although anticholinergic-type side effects have been noted with amantadine hydrochloride when used in patients with drug-induced extrapyramidal reactions, there is a lower incidence of these side effects than that observed with the anticholinergic antiparkinson drugs.

CONTRAINDICATIONS
Amantadine hydrochloride is contraindicated in patients with known hypersensitivity to amantadine hydrochloride or to any of the other ingredients in amantadine hydrochloride.

WARNINGS:
Deaths: Deaths have been reported from overdose with amantadine hydrochloride. The lowest reported acute lethal dose was 1 gram. Acute toxicity may be attributable to the anticholinergic effects of this drug. Deaths have been reported in one patient with renal impairment, who was prescribed higher than recommended doses of amantadine hydrochloride for their level of renal function (see DOSAGE AND ADMINISTRATION; Dosage of Impaired Renal Function and OVERDOSAGE).

Suicide Attempts: Suicide attempts, some of which have been fatal, have been reported in patients with amantadine hydrochloride, many of whom received short courses for influenza treatment or prophylaxis. The incidence of suicide attempts is not known and the pathophysiologic mechanism is not understood. Suicide attempts and suicidal ideation have
been reported in patients with and without prior history of psychiatric illness. Amantadine hydrochloride can exacerbate mental problems in patients with a history of psychiatric disorders or substance abuse. Patients who attempt suicide may exhibit abnormal mental states which include disorientation, confusion, depression, personality changes, agitation, aggressive behavior, hallucinations, paranoia, other psychotic reactions, and somnolence or insomnia. Because of the possibility of serious adverse effects, caution should be observed when prescribing amantadine hydrochloride to patients being treated with drugs having CNS effects, or for whom the potential risks outweigh the benefit of treatment.

CNS Effects: Patients with a history of epilepsy or other “seizures” should be observed closely for possible increased seizure activity.

Patients receiving amantadine hydrochloride who note central nervous system effects or blurring of vision should be cautioned against driving or working in situations where alertness and adequate motor coordination are important.

Other: Patients with a history of congestive heart failure or peripheral edema should be followed closely as there are patients who developed congestive heart failure while receiving amantadine hydrochloride.

Patients with Parkinson’s disease improving on amantadine hydrochloride should resume normal activities gradually and cautiously, consistent with other medical considerations, such as the presence of ostitis or phlebitis trombosis.

Because amantadine hydrochloride has anticholinergic effects and may cause mydriasis, it should not be given to patients with untreated angle closure glaucoma.

PRECAUTIONS

Amantadine hydrochloride should not be discontinued abruptly in patients with Parkinson’s disease since a few patients have experienced a parkinsonian crisis, i.e., a sudden marked clinical deterioration, when this medication was suddenly stopped. The dose of anticholinergic drugs or of amantadine hydrochloride should be reduced if antiparkinson-like effects appear when these drugs are used concomitantly. Confusion may also occur, and in some cases, delirium, agitation, delusions, hallucinations, paranoid reaction, stupor, anxiety, depression and slurred speech.

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

NMS is an uncommon but life-threatening syndrome characterized by fever or hyperthermia; neurologic findings including muscle rigidity, involuntary movements, altered consciousness; mental status changes; other disturbances such as autonomic dysfunction, tachycardia, tachypnea, hyper- or hypotension; laboratory findings such as creatine phosphokinase elevation, leukocytosis, myoglobinuria, and increased serum myoglobin.

The early diagnosis of this condition is important for the appropriate management of these patients. Considering NMS as a possible diagnosis and ruling out other acute illnesses (e.g., pneumonia, systemic infection, etc.) is essential. This may be especially critical if the clinical presentation includes both serious medical illness and untreated or inadequately treated extrapyramidal signs and symptoms (EPS). Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever and primary central nervous system (CNS) pathology.

The management of NMS should include: 1) intensive symptomatic treatment 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 NMS, however, their effectiveness has not been demonstrated in controlled studies.

Renal Disease: Because amantadine hydrochloride is mainly excreted in the urine, it may accumulate in the plasma and in the body when renal function declines. Thus, the dose of amantadine hydrochloride should be reduced in patients with renal impairment and in individuals who have underlying renal disease, such as those with creatinine clearance of 20 mL/min or less. If renal function is markedly decreased, amantadine hydrochloride should be administered at a reduced dosage of 100 mg twice daily or at a dosage of 100 mg once daily. In patients with severe renal impairment, amantadine hydrochloride should be administered cautiously and the dosage adjusted according to the clinical response.

Liver Disease: Care should be exercised when administering amantadine hydrochloride to 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.

Impulse Control/Compulsive Behaviors: Postmarketing reports suggest that patients treated with anti-Parkinson medications can experience intense urges to gamble, increased sexual urges, intense urges to spend money uncontrollably, and other intense urges. Patients may be unable to control these urges with standard methods of treating such behaviors. Although the true incidence of these behaviors is generally unknown, the data are consistent with the possibility that amantadine hydrochloride may be a cause for some of these behavioral changes.

For the reasons stated above, patients and providers are advised to monitor for melanomas frequently and on a regular basis when using amantadine hydrochloride for any indication. Ideally, periodic skin examinations should be performed by appropriately qualified individuals (e.g., dermatologists).

Other: The dose of amantadine hydrochloride may need careful adjustment in patients with congestive heart failure, peripheral edema, or orthostatic hypotension. Care should be exercised when administering amantadine hydrochloride to patients with a history of recurrent exacerbation of chronic obstructive pulmonary disease. Cardiovascular maldevelopment (atresia) was associated with maternal exposure to amantadine (100 mg/d) administered during the first 2 weeks of pregnancy. Amantadine hydrochloride should be used during pregnancy only if the potential benefit justifies the potential risk to the embryo or fetus.
Amantadine hydrochloride is excreted in human milk. Use is not recommended in nursing mothers.

Pediatric Use: The safety and efficacy of amantadine hydrochloride in newborn infants and infants below the age of 1 year have not been established.

Usage in the Elderly: Because amantadine hydrochloride is primarily excreted in the urine, it accumulates in the plasma and in the body when renal function declines. Thus, the dose of amantadine hydrochloride may need to be reduced in patients with renal impairment and in individuals who are 65 years of age or older. The dose of amantadine hydrochloride may need to be reduced in patients with congestive heart failure, peripheral edema, or orthostatic hypotension (see DOSE AND ADMINISTRATION).

ADVERSE REACTIONS
To report SUSPECTED ADVERSE REACTIONS, contact Hi-Tech Pharmacal Co., Inc. at 1-800-262-9010 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

The adverse reactions reported most frequently at the recommended dose of amantadine hydrochloride (5 to 10%) are: nausea, dizziness, (lightheadedness), and insomnia.

Less frequently (1 to 5%) reported adverse reactions are: depression, anxiety and irritability, hallucinations, confusion, anorexia, dry mouth, constipation, ataxia, livedo reticularis, peripheral edema, orthostatic hypotension, headache, somnolence, nervousness, dream abnormality, agitation, dry nose, diarrhea and fatigue.

Infrequently (0.1 to 1%) occurring adverse reactions are: congestive heart failure, psychosis, urinary retention, BUN, creatinine, vomiting, weakness, slurred speech, euphoria, thinking abnormalities, amnesia, hypokinesia, hypertonia, decreased libido, and visual disturbance, including punctate subepithelial or corneal opacities, corneal edema, decreased visual acuity, sensitivity to light, and optic nerve palsy.

Rare (less than 0.1%) occurring adverse reactions are: instances of convulsion, leukopenia, neutropenia, exanthematosis, oligocytic episodes, suicidal attempt, suicide, and suicidal ideation (see WARNINGS).

Other adverse reactions reported during postmarketing experience with amantadine hydrochloride usage include:

Nervous System/Psychiatric - coma, stupor, delirium, hypokinesia, hypertonia, delusions, aggressive behavior, paranoid reaction, maniac reaction, involuntary muscle contractions, gait abnormalities, paresthesias, EEG changes, and tremor. Abrupt discontinuation may also precipitate delirium, agitation, delusions, hallucinations, paranoid reaction, stupor, anxiety, depression and slurred speech.

Cardiovascular - cardiac arrest, arrhythmias including malignant arrhythmias, hypotension, and tachycardia.

Respiratory - acute respiratory failure, pulmonary edema, and tachypnea.

Gastrointestinal - dysphagia.

Hematologic - leukocytosis; agranulocytosis.

Special Senses - keratitis and mydriasis.

Skin and Appendages - pruritus and diaphoresis; Miscellaneous - neuroleptic malignant syndrome (see WARNINGS), allergic reactions including anaphylactic reactions, edema and fever.

Laboratory Test - elevated: CPK, BUN, serum creatinine, alkaline phosphatase, LDH, bilirubin, GGT, SGOT, and SGPT.

OVERDOSAGE
Deaths have been reported from overdose with amantadine hydrochloride. The lowest reported acute lethal dose was 1 gram. Because some patients have attempted suicide by overdose with amantadine, prescriptions should be written for the smallest quantity consistent with good patient management.

Acute toxicity may be attributable to the anticholinergic effects of amantadine. Drug overdose has resulted in cardiac, respiratory, renal or central nervous system toxicity. Cardiac dysfunction includes arrhythmia, tachycardia and hypertension. Pulmonary edema and respiratory distress (including adult respiratory distress syndrome-ARDS) have been reported; renal dysfunction including increased creatinine clearance and renal insufficiency can occur. Central nervous system effects that have been reported include insomnia, anxiety, agitation, aggressive behavior, hypokinesia, ataxia, gait abnormality, tremor, confusion, disorientation, depersonalization, fear, delirium, hallucinations, psychotic reactions, lethargy, somnolence and coma. Seizures may be exacerbated in patients with prior history of seizure disorders. Hyperthermia has also been observed in cases where a drug overdose has occurred.

There is no specific antidote for an overdose of amantadine hydrochloride. However, slowly administered intravenous physostigmine in 1 and 2 mg doses in an adult of 1 to 2 hour intervals and 0.5 mg doses in a child of 5 to 10 minute intervals up to a maximum of 2 mg/hour have been reported to be effective in the control of central nervous system toxicity caused by amantadine hydrochloride. For acute overdosing, general supportive measures should be employed along with immediate gastric lavage or induction of emesis. Fluids should be forced, and if necessary, given intravenously. The pH of the urine has been reported to influence the excretion rate of amantadine hydrochloride. Since the excretion rate of amantadine hydrochloride increases rapidly when the urine is acidic, the administration of urine acidifying drugs may increase the elimination of the drug from the body. The blood pressure, pulse, respiration and temperature should be monitored. The patient should be observed for hyperactivity and convulsions; if required, sedation, and anticonvulsant therapy should be administered. The patient should be observed for the possible development of arrhythmias and hypotension; if required, appropriate antihypertensive and arrhythmogenic therapy should be given. Electrocardiographic monitoring may be required after ingestion, since malignant tachyarrhythmias can appear after overdose.

Care should be exercised when administering adrenergic agents, such as isoproterenol, to patients with an amantadine hydrochloride overdose, since the dopaminergic activity of amantadine hydrochloride has been reported to induce malignant arrhythmias.

The blood electrolytes, urine pH and urinary output should be monitored. If there is no record of recent voiding, catheterization should be done.

DOSE AND ADMINISTRATION
The dose of amantadine hydrochloride, USP may need reduction in patients with congestive heart failure, peripheral edema, orthostatic hypotension, or impaired renal function (see DOSAGE for Impaired Renal Function).

Dosing for Prophylaxis and Treatment of Uncomplicated Influenza A Virus Illness:
Adult: The adult daily dosage of amantadine hydrochloride is 200 mg; four teaspoonsful of oral solution twice a day. The total daily dosage may be split into two teaspoonsfuls of oral solution given every 12 hours. If central nervous system effects develop in a once-a-day dosage, a split dosage schedule may reduce such complaints. In persons 65 years of age or older, the daily dosage of amantadine hydrochloride is 100 mg. A 100 mg daily dose has also been shown in experimental challenge studies to be effective as prophylaxis in healthy adults who are not at high risk for influenza-related complications. However, it has not been demonstrated that a 100 mg daily dose is as effective as a 200 mg daily dose for prophylaxis, nor has the 100 mg daily dose been studied in the treatment of acute influenza. If central nervous system effects develop in a once-a-day dosing, the incidence of central nervous system (CNS) side effects associated with the 100 mg daily dose was at or near the level of placebo. The 100 mg dose is recommended for persons who have demonstrated intolerance of 200 mg of amantadine hydrochloride daily because of CNS or other toxicities.

Pediatric Patients:
1 yr. to 9 yrs. of age: The total daily dose should be calculated on the basis of 2 to 4 mg/kg/day (4.4 to 8.8 mg/kg/day), but not to exceed 150 mg per day.
9 yrs. to 12 yrs. of age: The total daily dose is 200 mg given as two teaspoonsfuls of oral solution twice a day. The 100 mg daily dose has not been studied in this pediatric population. Therefore, there are no data which demonstrate that this dose is as effective as or is safer than the 200 mg daily dose in this patient population.

Prophylactic dosing should be started in anticipation of an influenza A outbreak and before or after contact with individuals with influenza A virus respiratory tract illness.

Amantadine hydrochloride should be continued daily for at least 10 days following a known exposure. If amantadine hydrochloride is used chemoprophylactically in conjunction with inactivated influenza A virus vaccine until protective antibody responses develop, then it should be administered for 2 to 4 weeks after the vaccine has been given. When inactivated influenza A virus vaccine is unavailable or contraindicated, amantadine hydrochloride should be administered for the duration of known influenza A in the community because of repeated and unknown exposure.

Treatment of influenza A virus illness should be started as soon as possible, preferably within 24 to 48 hours after onset of signs and symptoms, and should be continued for 24 to 48 hours after the disappearance of signs and symptoms.

Dosing for Parkinsonism:
Adult: The usual dose of amantadine hydrochloride is 100 mg twice a day when used alone. Amantadine hydrochloride has an onset of action usually within 48 hours. The initial dose of amantadine hydrochloride is 100 mg daily for patients with serious associated medical illnesses or who are receiving high doses of other antiparkinson drugs. After one to several weeks at 100 mg once daily, the dose may be increased to 100 mg twice daily, if necessary. Occasionally, patients whose responses are not optimal with amantadine hydrochloride at 200 mg daily may benefit from an increase up to 400 mg daily in divided doses. However, such patients should be supervised closely by their physicians.

Patients initially deriving benefit from amantadine hydrochloride not uncommonly experience a fall-off of effectiveness after a few months. Benefit may be regained by increasing the dose to 300 mg daily. Alternatively, temporary discontinuation of amantadine hydrochloride for several weeks, followed by reinitiation of the drug, may result in regaining benefit in some patients. A decision to use other antiparkinson drugs may be necessary.

Dosing for Concomitant Therapy: Some patients who do not respond to anticholinergic antiparkinson drugs may respond to amantadine hydrochloride. When amantadine hydrochloride or anticholinergic antiparkinson drugs are used with marginal benefit, concomitant use may produce additional benefit.

When amantadine hydrochloride and levodopa are initiated concurrently, the patient can exhibit rapid therapeutic benefits. Amantadine hydrochloride should be held constant at 100 mg daily or twice daily while the daily dose of levodopa is gradually increased to optimal benefit. When amantadine hydrochloride is added to optimal well-tolerated doses of levodopa, additional benefit may result, including smoothing out the fluctuations in improvement which sometimes occur in patients on levodopa alone. Patients who require a reduction in their usual dose of levodopa because of development of side effects may possibly regain lost benefit with the addition of amantadine hydrochloride.

Dosage for Drug-Induced Extrapyramidal Reactions:
Adult: The usual dose of amantadine hydrochloride is 100 mg twice a day. Occasionally, patients whose responses are not optimal with amantadine hydrochloride at 100 mg daily dose is recommended for persons who have demonstrated intolerance of 200 mg of amantadine hydrochloride daily because of CNS or other toxicities.

HOW SUPPLIED
Amanitadine Hydrochloride Oral Solution USP, 50 mg per 5 mL (1 teaspoonful) is supplied as a clear raspberry flavored oral solution supplied in a 16 fl oz (473 mL) container, and in 10 mL unit

DOSAGE
The recommended dosage for patients on hemodialysis is 200 mg every 7 days.
dose cups, packaged in trays of 10.
Store at 20° to 25°C (68° to 77°F). [See USP Controlled Room Temperature].
Dispense in original container or in a tight container as defined in USP, with a child-resistant closure (as required).

REFERENCES

Dyazide is a registered trademark of GlaxoSmithKline.

Manufactured by:
Hi-TECH PHARMACAL CO., INC.
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