Amantril®

Amantadine Hydrochloride

Description

Amantril® is the preparation of Amantadine Hydrochloride, which has direct and indirect effects on dopamine neurons. It acts on the pre-synaptic membrane, enhancing the release of dopamine and inhibiting its reuptake. Post-synaptically, Amantadine acts directly on the dopamine receptor, and up regulates D2 receptors. This may be due to Amantadine-induced hypersensitivity of dopamine receptors. It has antimuscarinic properties. Amantadine also has antiglutamatergic properties, via non-competitive antagonism of NMDA receptors. Furthermore, potent, competitive, non-subunit selective NMDA receptor antagonists reduce the severity of levodopa-induced dyskinesias. NMDA receptor sensitization may be a key event in the genesis of levodopa-induced dyskinesias. It also has immunomodulatory properties. It restores the production of interleukin-2 (IL-2), which is defective in Parkinson's disease patients. 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. 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.

Indication & usage

Amantril® is indicated for-

- treatment of parkinsonism
- treatment of drug-induced extrapyramidal reactions
- prophylaxis and treatment of signs and symptoms of infection caused by various strains of influenza A virus

Dosage and administration

Parkinson's disease

Adults: The usual dose is 100 mg twice a day when used alone.

The initial dose of **Amantril®** 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 **Amantril®** at 200 mg daily may benefit from an increase up to 400 mg daily in divided doses.

Dosage for Concomitant Therapy

Some patients who do not respond to anticholinergic antiparkinson drugs may respond to **Amantril®**. When **Amantril®** or anticholinergic antiparkinson drugs are each used with marginal benefit, concomitant use may produce additional benefit.

When **Amantril®** and levodopa therapy are initiated concurrently, the patient can exhibit rapid therapeutic benefits. **Amantril®** dose, should be held constant at 100 mg daily or twice daily while the daily dose of levodopa is gradually increased to optimal benefit.

When **Amantril®** 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 **Amantril®**.

Drug-induced extrapyramidal reactions

Adults: The usual dose is 100 mg twice a day.

Occasionally, patients whose responses are not optimal with **Amantril®** at 200 mg daily may benefit from an increase up to 300 mg daily in divided doses.

Prophylaxis and treatment of Influenza A virus illness

Adults: 200 mg/day as single dose or 100 mg twice daily. If CNS effects develop on a once-daily dosage, split dosage schedule may reduce complaints.

Elderly over 65 years of age: 100 mg every day.

Children:
1 to 9 years of age: 4.4 to 8.8 mg/kg/day; not to exceed 150 mg/day.
9 to 12 years of age: 100 mg twice daily

Method of administration: Each capsule is to be taken orally either with or without food.

Patients with renal impairment

The dose should be reduced. This can be achieved by either reducing the total daily dose, or by increasing the dosage interval in accordance with the creatinine clearance. For example:

Creatinine clearance (ml/min)	**Dose**
< 15	Amantadine Hydrochloride capsules contra-indicated
15 – 35	100mg every 2 to 3 days
> 35	100mg every day

The above recommendations are for guidance only and physicians should continue to monitor their patients for signs of unwanted effects.

Patients with hepatic impairment: Use with caution

Use in pregnancy and lactation
Pregnancy category C. No well-controlled studies have been done in pregnant women to evaluate Amantadine's safety. Amantadine may be used during pregnancy when the potential benefits outweigh the potential but unknown risks to the fetus.
Amantadine is excreted into breast milk in low concentrations. As no information is available on the effects in infants, therefore amantadine should be used cautiously in women who are breastfeeding.

Side Effects
The adverse effects of Amantadine are generally mild and, when they occur, may diminish or cease after a week or more on the medication. The most commonly reported side effects include nausea, dizziness/lightheadedness, and insomnia.

Other side effects may include edema of ankles, livedo reticularis; anxiety, elevation of mood, headache, lethargy, hallucinations, ataxia, slurred speech, blurred vision, loss of concentration, nervousness, depression, myalgia, palpitations, orthostatic hypotension, dry mouth, anorexia, constipation and diaphoresis.

Precautions
Amantadine 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 atropine-like effects appear when these drugs are used concurrently. Abrupt discontinuation may also precipitate delirium, agitation, delusions, hallucinations, paranoid reaction, stupor, anxiety, depression and slurred speech.

Drug interactions
Concurrent administration of Amantadine and anticholinergic agents or levodopa may increase confusion, hallucinations, nightmares, gastro-intestinal disturbances, or other atropine-like side effects. Psychotic reactions have been observed in patients receiving Amantadine and Levodopa.
Concurrent administration of Amantadine and drugs or substances (e.g. alcohol) acting on the CNS may result in additive CNS toxicity. Close observation is recommended.

Contraindications
Amantadine is contraindicated in patients with known hypersensitivity to the active substances or to any of the excipients.

Overdose
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 overdosing 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 have been reported; renal dysfunction including increased BUN, decreased creatinine clearance and renal insufficiency can occur. Central nervous system effects include insomnia, anxiety, agitation, aggressive behavior, hypertonia, hyperkinesia, 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.

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 at 1- to 2-hour intervals and 0.5 mg doses in a child at 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 antiarrhythmic and antihypotensive therapy should be given. Electrocardiographic monitoring may be required after ingestion, since malignant tachyarrhythmias can appear after overdose.

Pharmaceutical precautions
Keep away from the reach of children. Store in a cool & dry place. Protect from light.

Presentation
Amantril® capsule: Each capsule contains Amantadine Hydrochloride USP 100 mg.

Package quantities
Amantril® capsule: Carton of 30 capsules in blister pack.

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Narayanganj, Bangladesh