**Amantadine Hydrochloride Capsules, USP**

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

**Pharmacodynamics**

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

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**Pharmacokinetics**

Amantadine pharmacokinetics are described in normal adult volunteers for oral administration of a single amantadine hydrochloride 200 mg capsule, with a mean oral plasma clearance of 0.10 ± 0.04 L/hr/kg (range 0.06 to 0.17 L/hr/kg) and half-life was 29 ± 7 hours (range 20 to 41 hours). Whether these changes are due to decline in renal function or in the apparent volume of distribution in the elderly is not understood. Amantadine plasma clearance is reduced in elderly patients, and clearance is reduced in patients with renal disease. In all age groups, amantadine clearance is inversely related to body weight.

**Pharmacodynamics**

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 levels of 0.49 ± 0.30 mcg/mL and 0.27 ± 0.12 mcg/mL, respectively. Across studies, the administration of amantadine tablets as a 200 mg single dose to 6 healthy volunteers. The administration of amantadine tablets as a 200 mg single dose to 6 healthy subjects resulted in a Cmax of 0.51 ± 0.14 mcg/mL. Across studies, 14-25% of an administered oral dose of amantadine is absorbed systemically.

**Viral Resistance**

Amantadine-resistant influenza A viruses can develop during the treatment of influenza with capsules or tablets. The resistance is generally associated with a mutation at position 52 of the M2 gene of the virus and is detectable in cell cultures by 48 hours after treatment begins. The amantadine-resistant strains have reduced activity in tissue cultures and are less virulent in animal models than are the sensitive strains of influenza A virus. However, these resistant strains have been shown to be capable of causing significant disease in unusual circumstances. Although the resistance to amantadine varies with different isolates and different test systems, resistance is usually less than or equal to 8 mcg/mL. Cross-resistance occurs with rimantadine (Flumadine) in test systems similar to those used for amantadine. It is not known if clinically significant resistance to rimantadine will occur in strains with lower concentrations of amantadine resistance.

**Postmarketing Surveillance**

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Pediatric Use: The safety and efficacy of amantadine hydrochloride have not been established in pediatric patients 10 yrs. to 12 yrs. of age. The maximum recommended dose is 150 mg per day. For children 6 to 10 yrs. of age, the usual dose is 100 mg per day. The total daily dose is 200 mg given as one capsule of 100 mg twice a day. The 100 mg daily dose has not been studied in this pediatric population to assess safety and efficacy for treatment of uncomplicated influenza A virus illness. One clinical study demonstrated that younger children (2 to 5 yrs. of age) may benefit from a dosage of 10 mg/kg per day of amantadine hydrochloride (or 1.5 mg/kg per day on a mg/m² basis) in the treatment of uncomplicated influenza A virus illness.

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

- Nervous System/Psychiatric: Hallucinations, paranoid reaction, stupor, anxiety, depression and slurred speech; Parkinson's disease, psychosis, psychoses (including delusional, hallucinatory, disorienting, dysphoric, and manic reactions); manic or hypomanic episodes; panic attack; suicidal attempt, suicide, and suicidal ideation (see Warnings).

- Special Senses: Corneal opacity, corneal edema, decreased visual acuity, sensitivity to light, and optic nerve palsy.

- Skin and Appendages: Livedo reticularis, peripheral edema, orthostatic hypotension, headache, somnolence, nervousness, dream abnormality, agitation, dry nose, diarrhea and fatigue.

- Other: Dizziness, fatigue, headache, depression, convulsions, muscle cramps, mydriasis, rhinorrhea, tachycardia, urticaria, fever, and worsening of pre-existing parkinsonism.

Usage in the Elderly: In elderly patients with Parkinson's disease, the age-related risk of dementia has been observed in controlled and non-controlled trials. Postmarketing experience suggests that amantadine hydrochloride may be less effective in terminating this risk in the elderly. Elderly patients treated for uncomplicated influenza A virus illness should be treated with the recommended dose and dosage adjustments should be made according to the severity of disease. Elderly patients treated for Parkinson's disease should be treated with the total daily dose of 200 mg. This dosage has been found to be effective in preventing the dopaminergic effects of levodopa in elderly patients with Parkinson's disease.

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OVERDOSAGE

Amantadine hydrochloride overdosage is rarely treated, because amantadine is considered to be self-limited in humans. Overdosage symptoms include nausea, vomiting, drowsiness, headache, mental confusion, insomnia, and peripheral neuritis. There have been no reported fatalities due to amantadine hydrochloride overdosage. The treatment of an amantadine hydrochloride overdose consists of supportive therapy for symptoms, and should be provided by medical personnel familiar with the effects and treatment of overdosage.