Safety Data Sheet
Amantadine Hydrochloride Capsules, USP

Strength: 100 mg **Pack Size:** 30/100/500 Capsules per bottle **Revision No.:** 00
Unit-dose blister cartons of 100 Capsules (10 X 10 Unit-dose)

EMERGENCY OVERVIEW

Each Amantadine Hydrochloride Capsules intended for oral administration contains Amantadine Hydrochloride and excipients generally considered to be non- toxic and non-hazardous in small quantities and under conditions of normal occupational exposure.

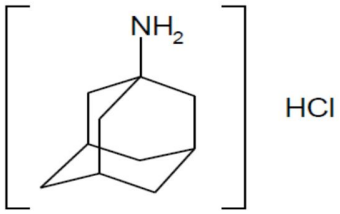
Section 1. Identification

Identification of the product

Product Name: Amantadine Hydrochloride Capsules, USP

Formula: $C_{10}H_{17}N.HCl$

Chemical Name: 1-adamantanamine hydrochloride



Manufacturer / supplier identification

Company: **Cadila Healthcare Ltd., Metoda**

Address: Plot No - 1/1A & 2, Zydus-Pharma-SEZ
Sarkhej - Bavla N.H.NO - 8 Vill.- Matoda
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Recommended use / Therapeutic Category An anti-Parkinson and an antiviral drug

Restriction on Use / Contraindications: Amantadine hydrochloride capsules USP are contraindicated in patients with known hypersensitivity to amantadine hydrochloride or any of the other ingredients in amantadine hydrochloride capsules, USP.

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Section 2. Hazard(s) Identification

Dose and Administration

Amantadine Hydrochloride Capsules, USP is available as Conventional Capsules - each containing 100 mg Amantadine Hydrochloride.

The dose of amantadine hydrochloride capsules may need reduction in patients with congestive heart failure, peripheral edema, orthostatic hypotension, or impaired renal Function.

Adult
The adult daily dosage of amantadine hydrochloride capsules is 200 mg; two 100 mg capsules as a single daily dose. The daily dosage may be split into one capsule of 100 mg twice a day. If central nervous system effects develop in 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 capsules 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 illness. In recent clinical trials, 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 to 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/lb/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 one capsule of 100 mg 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.

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Adverse Effects

The adverse reactions reported most frequently at the recommended dose of amantadine (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, livedoreticularis, 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, dyspnea, skin rash, vomiting, weakness, slurred speech, euphoria, thinking abnormality, amnesia, hyperkinesia, hypertension, decreased libido and visual disturbance, including punctate subepithelial or other corneal opacity, 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, eczematoid dermatitis, oculogyric episodes, suicidal attempt, suicide, and suicidal ideation.

Over Dose Effect

Deaths have been reported from overdose with amantadine. 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 (including adult respiratory distress syndrome – ARDS) have been reported; renal dysfunction including increased BUN, decreased creatinine clearance and renal insufficiency can occur. Central nervous system effects that have been reported 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 in cases where a drug overdose has occurred.

Contraindications	Amantadine hydrochloride capsules USP are contraindicated in patients with known hypersensitivity to amantadine hydrochloride or to any of the other ingredients in amantadine hydrochloride capsules, USP.
Pregnancy Comments	The effect of amantadine on embryofetal and peri-postnatal development has not been adequately tested, that is, in studies conducted under Good Laboratory Practice (GLP) and according to current recommended methodology. However, in two non-GLP studies in rats in which females were dosed from 5 days prior to mating to Day 6 of gestation or on Days 7 to 14 of gestation, amantadine produced increases in embryonic death at an oral dose of 100 mg/kg (or 3 times the maximum recommended human dose on a mg/m^2 basis). In the non-GLP rat study in which females were dosed on Days 7 to 14 of gestation, there was a marked increase in severe visceral and skeletal malformations at oral doses of 50 and 100 mg/kg (or 1.5 and 3 times, respectively, the maximum recommended human dose on a mg/m^2 basis). The no-effect dose for teratogenicity was 37 mg/kg (equal to the maximum recommended human dose on a mg/m^2 basis). The safety margins reported may not accurately reflect the risk considering the questionable quality of the study on which they are based. There are no adequate and well-controlled studies in pregnant women. Human data regarding teratogenicity after maternal use of amantadine is scarce. Tetralogy of Fallot and tibial hemimelia (normal karyotype) occurred in an infant exposed to amantadine during the first trimester of pregnancy (100 mg P.O. for 7 days during the 6th and 7th week of gestation). Cardiovascular maldevelopment (single ventricle with pulmonary atresia) was associated with maternal exposure to amantadine (100 mg/d) administered during the first 2 weeks of pregnancy. Amantadine should be used during pregnancy only if the potential benefit justifies the potential risk to the embryo or fetus.
Pregnancy Category	Pregnancy Category C

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Section 3. Composition / information on ingredients

Component	Exposure Limit	CAS No.
Principle Component:		
Amantadine Hydrochloride	Not Found	665-66-7
Inactive Ingredients:		
Cross carmellose Sodium (ACDISOL)	Not Found	74811-65-7
Microcrystalline Cellulose 101 (Comprecel M 101D+)	Not Found	9004-34-6
Ethyl Cellulose 4CPS (Ethocel Std 4 premium) (Dow)	Not Found	9004-57-3
Isopropyl alcohol	Not Found	67-63-0
Microcrystalline Cellulose 102 (Comprecel M 102D+)	Not Found	9004-34-6
Pregelatinised Starch (Starch 1500)	Not Found	9057-07-2
Megnesium Stearate (FERRO)	Not Found	557-04-0

Section 4. First -aid measures

General

Inhalation:
Move to fresh air. If breathing is difficult, trained personnel should give oxygen. Call a physician if symptoms develop or persist. Under normal conditions of intended use, this material is not expected to be an inhalation hazard.

Skin contact:
Immediately flush skin with plenty of water. Take off contaminated clothing and wash before reuse. Get medical attention if symptoms occur.

Eye contact:
Rinse thoroughly with plenty of water for at least 15 minutes and consult a physician.

Ingestion:
If swallowed, rinse mouth with water (only if the person is conscious). If ingestion of a large amount does occur, call a poison control center immediately. Do not induce vomiting without advice from poison control center.

Overdose Treatment

There is no specific antidote for an overdose of amantadine. However, slowly administered intravenous physostigmine in 1 and 2 mg doses in an adult[2] at 1- to 2-hour intervals and 0.5 mg doses in a child[3] at 5- to 10-minute intervals up to a maximum of 2mg/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 mantadine. Since the excretion rate of amantadine 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 antihypertensive 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 overdose, since the dopaminergic activity of amantadine 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.

Section 5. Fire -fighting measures

Flash point	Not Found	**Upper Flammable Limit:**	Not Found
Auto-Ignition Temperature	Not Found	**Lower Flammable Limit:**	Not Found

Suitable extinguishing media	Water. Foam. Dry chemical powder. Carbon dioxide (CO2).
Specific hazards arising from the chemical	During fire, gases hazardous to health may be formed.
Special protective equipment and precautions for firefighters	Self-contained breathing apparatus and full protective clothing must be worn in case of fire
Fire fighting equipment/instructions	Move containers from fire area if you can do so without risk.
Specific methods	Use standard firefighting procedures and consider the hazards of other involved materials.
General fire hazards	No unusual fire or explosion hazards noted

Section 6. Accidental Release Measures

Spill Response	Keep unnecessary personnel away. Keep people away from and upwind of spill/leak. Keep out of low areas. Wear appropriate protective equipment and clothing during clean-up. Do not touch damaged containers or spilled material unless wearing appropriate protective clothing. Ensure adequate ventilation. Local authorities should be advised if significant spillages cannot be contained.

Section 7. Handling and Storage

Storage:	Store at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature]. Dispense in a tight container as defined in the USP.
	Precautions for safe handling Do not get this material in contact with eyes. Avoid contact with eyes, skin, and clothing. Avoid prolonged exposure. Do not taste or swallow. When using, do not eat, drink or smoke. Should be handled in closed systems, if possible. Provide adequate ventilation. Wear appropriate personal protective equipment. Wash hands thoroughly after handling. Avoid release to the environment. Observe good industrial hygiene practices.

Section 8. Exposure controls / personal protection

Respiratory Protection	Use a NIOSH/MSHA approved respirator if there is a risk of exposure to dust/fume at levels exceeding the exposure limits. No personal respiratory protective equipment normally required.
Skin protection	For prolonged or repeated skin contact use suitable protective gloves.
Eye/face protection	If contact is likely, safety glasses with side shields are recommended.
Protective Clothing	Protective clothing is not normally necessary, however it is good practice to use apron.
Biological limit values	No biological exposure limits noted for the ingredient(s).
Exposure guidelines	General ventilation normally adequate.
Thermal hazards	Wear appropriate thermal protective clothing, when necessary.
General hygiene considerations	Always observe good personal hygiene measures, such as washing after handling the material and before eating, drinking, and/or smoking. Routinely wash work clothing and protective equipment to remove contaminants. For advice on suitable monitoring methods, seek guidance from a qualified environment, health and safety professional.
Engineering controls	Engineering controls should be used as the primary means to control exposures. General room ventilation is adequate unless the process generates dust, mist or fumes. Keep airborne contamination levels below the exposure limits listed above in this section.

Section 9. Physical and chemical properties

Appearance	Amantadine Hydrochloride Capsules, USP, 100 mg are white to off-white powder filled in size “2” empty hard gelatin capsule having red opaque colored cap imprinted with “652” in white ink and red opaque colored body.
Solubility	Freely soluble in water, ethanol and

	methanol; soluble in chloroform; sparingly soluble in methylene chloride; practically insoluble in ether.	**Odour**	Not available.
Boiling point	Not available.	**Melting Point**	Not available.
Evaporation rate	Not available.	**Vapour density**	Not available.
Reactivity in water	Not available.	**Vapour pressure**	Not available.
% Volatile by volume	Not available.	**Specific gravity**	Not available.

Other information Amantadine hydrochloride, USP is a white or almost white, crystalline powder.

Section 10. Stability and Reactivity

Conditions to avoid Contact with incompatible materials.

Stable

Reactivity
The product is stable and non-reactive under normal conditions of use, storage and transport.

Hazardous reactions No dangerous reaction known under conditions of normal use.

Decomposition products None known. Irritating and/or toxic fumes and gases may be emitted upon the product's decomposition.

Incompatible materials Not available.

Section 11. Toxicological information

General Handling of formulated product is not expected to cause any toxicological affects. The data pertains to the ingredient in formulations, rather than this specie formulation.

Target Organ Eye contact, Skin contact and inhalation is not great risk as this product is Capsules.

Ingestion	Slightly hazardous in case of skin contact (irritant), of ingestion, of inhalation.
Other	Acute Potential Health Effects: Skin Contact: May cause skin irritation. Eye Contact: May cause eye irritation. Inhalation: May cause respiratory tract irritation. Ingestion: May cause nausea, constipation or diarrhea, dry mouth, and loss of appetite. May affect behavior/central nervous system, cardiovascular system, respiration, skin. Other symptoms may include: Skin rash, confusion, seizures, hallucinations, disorientation, depression, personality changes, agitation, somnolence, insomnia, dizziness, irritability, distractability, thinking abnormality, slurred speech, amnesia, difficulty sleeping, weakness, depression, fatigue, anxiety, headache, lightheadedness, euphoria, excitement, coma, increased pulse rate, hypotension or hypertension, difficulty breathing (dyspnea), visual disturbances, sensitivity to light, optic nerve palsy, swollen feet, corneal opacity, corneal edema, swelling of the eyes, loss of libido, urinary retention. The effects of Amantadine can be altered by alcohol, amphetamines, diet pills, asthma, and medicines, methylphenidate, nabilone, and pemoline. Anticholinergic drugs can increase the side effects of Amantadine.

Section 12. Ecological information

Do not allow product to enter drinking water supplies, waste water or soil.

Section 13. Disposal Consideration

Dispose the waste in accordance with all applicable Federal, State and local laws.

Section 14. Transport Information

The product is not hazardous when shipping via air (IATA), ground (DOT), or sea (IMDG).

Section 15. Regulatory Information

Generic Medicine. ANDA Number is 208278

Section 16. Other information

None

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Date of issue: 05/08/2016 **Supersedes edition:** New Edition

The information contained herein is based on the state of our knowledge. It characterizes the product with regard to the appropriate safety precautions. It does not represent a guarantee of the properties of the product.