Safety Data Sheet
Amiodarone Hydrochloride Tablets

Strength: 200 mg **Pack Size:** 30/60/500/1000 Tablets Per bottle
Strength: 200mg **Pack Size:** Blister pack of 100 tablets **Revision No.:** 02

EMERGENCY OVERVIEW

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

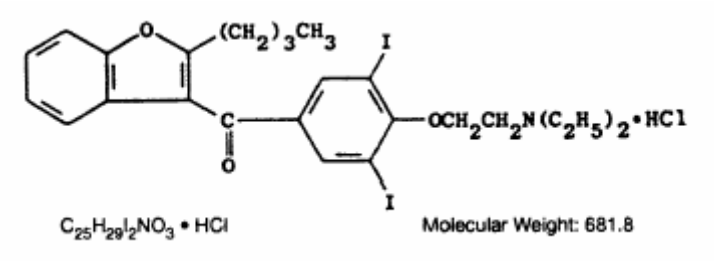
Section 1. Identification

Identification of the product

Product name: Amiodarone Hydrochloride Tablets

Formula $C_{25}H_{29}I_2NO_3 \cdot HCl$.

Chemical Name: 2-butyl-3-benzofuranyl 4-[2-(diethylamino)-ethoxy]-3,5-diiodophenyl ketone hydrochloride.



Amiodarone Hydrochloride

Manufacturer / supplier identification

Company: **Cadila Healthcare Ltd. Ahmedabad, India**

Address: Sarkhej – Bavla. N.H. 8A, Moraiya. Tal. Sanand. Dist. Ahmedabad – 382210. State: Gujarat. India

Contact for information: Tel.: +91 79 6868100 Fax: +91 79 3750319

Emergency Telephone No. Tel.: +91 79 6868100

Recommended use / Therapeutic Category A new class of antiarrhythmic drugs.

Restriction on Use / Contraindications: Amiodarone is contraindicated in patients with cardiogenic shock; severe sinus-node dysfunction, causing marked sinus bradycardia; second- or third-degree atrioventricular block; and

when episodes of bradycardia have caused syncope (except when used in conjunction with a pacemaker).

Amiodarone is contraindicated in patients with a known hypersensitivity to the drug or to any of its components, including iodine.

Section 2. Hazard(s) Information

Dose and Administration

Because of the unique pharmacokinetic properties, difficult dosing schedule, and severity of the side effects if patients are improperly monitored, amiodarone should be administered only by physicians who are experienced in the treatment of life-threatening arrhythmias who are thoroughly familiar with the risks and benefits of Amiodarone therapy, and who have access to laboratory facilities capable of adequately monitoring the effectiveness and side effects of treatment.

In order to insure that an antiarrhythmic effect will be observed without waiting several months, loading doses are required. A uniform, optimal dosage schedule for administration of amiodarone has not been determined. Because of the food effect on absorption, amiodarone should be administered consistently with regard to meals. Individual patient titration is suggested according to the following guidelines:

For life-threatening ventricular arrhythmias, such as ventricular fibrillation or hemodynamically unstable ventricular tachycardia:
Close monitoring of the patients is indicated during the loading phase, particularly until risk of recurrent ventricular tachycardia or fibrillation has abated. Because of the serious nature of the arrhythmia and the lack of predictable time course of effect, loading should be performed in a hospital setting. Loading doses of 800 to 1,600 mg/day are required for 1 to 3 weeks (occasionally longer) until initial therapeutic response occurs. (Administration of amiodarone in divided doses with meals is suggested for total daily doses of 1,000 mg or higher, or when gastrointestinal intolerance occurs.) If side effects become excessive, the dose should be reduced. Elimination of recurrence of ventricular fibrillation and tachycardia usually occurs within 1 to 3 weeks, along with reduction in complex and total ventricular ectopic beats.

Since grapefruit juice is known to inhibit CYP3A4-mediated metabolism of oral amiodarone in the intestinal mucosa, resulting in increased plasma levels of amiodarone, grapefruit juice should not be taken during treatment with oral amiodarone.

Adverse Effects

Adverse reactions have been very common in virtually all series of patients treated with amiodarone for ventricular arrhythmias with relatively large doses of drug (400 mg/day and above), occurring in about three-fourths of all patients and causing

discontinuation in 7 to 18%. The most serious reactions are pulmonary toxicity, exacerbation of arrhythmia, and rare serious liver injury, but other adverse effects constitute important problems. They are often reversible with dose reduction or cessation of amiodarone treatment. Most of the adverse effects appear to become more frequent with continued treatment beyond six months, although rates appear to remain relatively constant beyond one year. The time and dose relationships of adverse effects are under continued study.

Neurologic problems are extremely common, occurring in 20 to 40% of patients and including malaise and fatigue, tremor and involuntary movements, poor coordination and gait, and peripheral neuropathy; they are rarely a reason to stop therapy and may respond to dose reductions or discontinuation. There have been spontaneous reports of demyelinating polyneuropathy.

Gastrointestinal complaints, most commonly nausea, vomiting, constipation, and anorexia, occur in about 25% of patients but rarely require discontinuation of drug. These commonly occur during high-dose administration (i.e., loading dose) and usually respond to dose reduction or divided doses.

Ophthalmic abnormalities including optic neuropathy and/or optic neuritis, in some cases progressing to permanent blindness, papilledema, corneal degeneration, photosensitivity, eye discomfort, scotoma, lens opacities, and macular degeneration have been reported.

Asymptomatic corneal microdeposits are present in virtually all adult patients who have been on drug for more than 6 months. Some patients develop eye symptoms of halos, photophobia, and dry eyes. Vision is rarely affected and drug discontinuation is rarely needed.

Dermatological adverse reactions occur in about 15% of patients, with photosensitivity being most common (about 10%). Sunscreen and protection from sun exposure may be helpful, and drug discontinuation is not usually necessary. Prolonged exposure to amiodarone occasionally results in a blue-gray pigmentation. This is slowly and occasionally incompletely reversible on discontinuation of drug but is of cosmetic importance only.

Cardiovascular adverse reactions, other than exacerbation of the arrhythmias, include the uncommon occurrence of congestive heart failure (3%) and bradycardia. Bradycardia usually responds to dosage reduction but may require a pacemaker for control. CHF rarely requires drug discontinuation. Cardiac conduction abnormalities occur infrequently and are reversible on discontinuation of drug.

The following side-effect rates are based on a retrospective study of 241 patients treated for 2 to 1,515 days (mean 441.3 days).

Common Adverse effects:

Gastrointestinal: Nausea and vomiting.

Thyroid: Hypothyroidism, hyperthyroidism.

Dermatologic: Solar dermatitis/photosensitivity.

Ophthalmologic: Visual disturbances.

Neurologic: Malaise and fatigue, tremor/abnormal involuntary movements, lack of coordination, abnormal gait/ataxia, dizziness, paresthesias.

Gastrointestinal: Constipation, anorexia.

Hepatic: Abnormal liver-function tests.
Respiratory: Pulmonary inflammation or fibrosis.
Cardiovascular: Congestive heart failure, cardiac arrhythmias, SA node dysfunction.

Over Dose Effect

There have been cases, some fatal, of amiodarone overdose.

Medical Conditions

If a patient with a history of cardiac arrest does not manifest a hemodynamically unstable arrhythmia during electrocardiographic monitoring prior to treatment, assessment of the effectiveness of amiodarone requires some provocative approach, either exercise or programmed electrical stimulation (PES).

Whether provocation is also needed in patients who do manifest their life-threatening arrhythmia spontaneously is not settled, but there are reasons to consider PES or other provocation in such patients

Contraindications

Amiodarone is contraindicated in patients with cardiogenic shock; severe sinus-node dysfunction, causing marked sinus bradycardia; second- or third-degree atrioventricular block; and when episodes of bradycardia have caused syncope (except when used in conjunction with a pacemaker).

Amiodarone is contraindicated in patients with a known hypersensitivity to the drug or to any of its components, including iodine.

Pregnancy Comments

Amiodarone is cases, some fetal of Amiodarone overdose.

Labor and Delivery:
It is not known whether the use of amiodarone during labor or delivery has any immediate or delayed adverse effects. Preclinical studies in rodents have not shown any effect of amiodarone on the duration of gestation or on parturition.

Nursing Mothers:
Amiodarone and one of its major metabolites, desethylamiodarone (DEA), are excreted in human milk, suggesting that breast-feeding could expose the nursing infant to a significant dose of the drug. Nursing offspring of lactating rats administered amiodarone have been shown to be less viable and have reduced body-weight gains. Therefore, when amiodarone therapy is indicated, the mother should be advised to discontinue nursing.

Pediatric Use:
The safety and effectiveness of amiodarone hydrochloride tablets in pediatric patients have not been established.
Geriatric Use:
Clinical studies of amiodarone hydrochloride tablets did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently

from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

Pregnancy Category D

Section 3. Composition / information on ingredients

Component	Exposure Limit	CAS No.
Principle Component:		
Amiodarone Hydrochloride	Not Found	1977-82-4
Inactive Ingredients :		
Colloidal silicon dioxide	Not Found	7621-86-9
Corn starch	Not Found	9005-25-8
Lactose monohydrate	Not Found	63-42-3
Magnesium stearate	Not Found	557-04-0
Povidone	Not Found	9003-39-8
Sodium starch glycolate	Not Found	9063-38-1

Section 4. First -aid measures

General

Inhalation: Remove to fresh air. If not breathing give artificial respiration. If breathing is difficult, give oxygen. Seek medical attention.

Contact with skin: Immediately wash skin with soap and copious amounts of water for at least 15 minutes. If irritation persists, seek medical attention.

Contact with eyes:
Immediately flush eyes with copious amounts of water for at least 15 minutes. Seek medical advice

Ingestion: If swallowed, wash out mouth with water, provided person is concious. Seek medical advice

Remove and wash/dispose of contaminated clothing promptly.

Overdose Treatment

In addition to general supportive measures, the patient's cardiac rhythm and blood pressure should be monitored, and if bradycardia ensues, a β-adrenergic agonist or a pacemaker may be used. Hypotension with inadequate tissue perfusion should be treated with positive inotropic and/or vasopressor agents. Neither amiodarone nor its metabolite is dialyzable.

The acute oral LD_{50} of amiodarone hydrochloride in mice and rats is greater than 3,000 mg/kg.

The difficulty of using amiodarone effectively and safely itself poses a significant risk to patients. Patients with the indicated arrhythmias must be hospitalized while the loading dose of amiodarone is given, and a response generally requires at least one week, usually two or more. Because absorption and elimination are variable, maintenance-dose selection is difficult, and it is not unusual to require dosage decrease or discontinuation of treatment. In a retrospective survey of 192 patients with ventricular tachyarrhythmias, 84 required dose reduction and 18 required at least temporary discontinuation because of adverse effects, and several series have reported 15 to 20% overall frequencies of discontinuation due to adverse reactions. The time at which a previously controlled life-threatening arrhythmia will recur after discontinuation or dose adjustment is unpredictable, ranging from weeks to months. The patient is obviously at great risk during this time and may need prolonged hospitalization. Attempts to substitute other antiarrhythmic agents when amiodarone must be stopped will be made difficult by the gradually, but unpredictably, changing amiodarone body burden. A similar problem exists when amiodarone is not effective; it still poses the risk of an interaction with whatever subsequent treatment is tried.

Section 5. Fire -fighting measures

Flash point	Not Found	**Upper Flammable Limit:**	Not Found
Auto-Ignition Temperature:	Not Found	**Lower Flammable Limit:**	Not Found
Extinguishing Media	Water Spray, dry chemical, carbon dioxide or foam as appropriate for	**Fire and Explosion Hazard**	This material is assumed to be combustible. As with all dry powders it is advisable to ground

surrounding fire and material.

mechanical equipment in contact with the dry material to dissipate the potential build up of static electricity.

Fire Fighting Procedure As with all fires, evacuate personnel to a safe area. Fire fighter should use self-contained breathing equipment and protective clothing.

Section 6. Accidental Release Measures

Spill Response Wear approved respiratory protection, chemically compatible gloves and protective clothing. Wipe up spillage or collect spillage using high efficiency vacuum cleaner. Avoid breathing dust. Place spillage in appropriately labelled container for disposal. Wash spill site.

Section 7. Handling and Storage

Storage Store at 20° to 25°C (68° to 77°F). Protect from light**.**
Dispense in a tight, light-resistant container.

Incompability No data available.

Section 8. Exposure controls / personal protection

Respiratory protectio Protection from inhalation is not normally necessary. If ventilation is inadequate or dust is likely to generate, use of suitable dust mask would be appropriate.

Skin Protection Skin protection is not normally necessary, however it is good practice to avoid contact with chemical to use suitable gloves when handling.

Eye protection Eye protection is not normally necessary. If concerned wear protective goggles or glasses. Wash hands prior to touching eye and in particular handling contact lenses.

Protective Clothing Protective clothing is not normally necessary, however it is good practice to use apron.

Section 9. Physical and chemical properties

Appearance Amiodarone Hydrochloride Tablets, 200 mg are white to off-white, round-shaped, flat beveled-edge, uncoated tablets with bisect on one side and other side is plain; one side of bisect is debossed with ‘ZE’ and other side is debossed with ‘65’.

Solubility Slightly soluble in water, soluble in alcohol and freely soluble in chloroform. **Odour** Odorless

Boiling point	No Data Available	**Melting Point**	No Data Available
Evaporation rate	No Data Available	**Vapour density**	No Data Available
Reactivity in water	No Data Available	**Evaporation rate**	No Data Available
Percentage Volatile by volume	No Data Available	**Specific gravity**	No Data Available
Vapour pressure	No Data Available	**Other information**	Not Applicable

Section 10. Stability and Reactivity

Condition to avoid	Avoid exposure to extreme heat, light and moisture.	**Stable**	Stable under predefined storage and handling conditions.
Decomposition Products	No Data Available	**Hazardous Reaction**	No data available.
Incompatibilities	No data 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 tablet.
Other	In pregnant rats and rabbits, Amiodarone hydrochloride in doses of 25mg/kg/day had no adverse effects on the fetus. In the rabit, 75mg/kg/day caused abortions in greater than 90% of the animals. In the rat, dosage of 50 mg/kg/day or more were associated with slight displacement of the tests and an increased incident of incomplete ossification of some skull and digital bones; at 100 mg/kg/day or more, fetal body weights were reduced; at 200 mg/kg/day, there was an increased incident of fetal resorption.

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. Approved by USFDA & the ANDA Number is 079029

Section 16. Other information

None

Date of issue: 28/05/2015 **Supersedes edition of:** 01

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