

AMIODARONE

Class: Antiarrhythmic Agent, Class III

Indications: Management of life-threatening recurrent ventricular fibrillation (VF) or hemodynamically-unstable ventricular tachycardia (VT) refractory to other antiarrhythmic agents or in patients intolerant of other agents used for these conditions

Use :

Unlabeled: Atrial fibrillation (AF): Pharmacologic conversion of AF to and maintenance of normal sinus rhythm; treatment of AF in patients with heart failure [no accessory pathway] who require heart rate control (ACC/AHA/ESC Practice Guidelines) or in patients with hypertrophic cardiomyopathy (ACCF/AHA Practice Guidelines); prevention of postoperative AF associated with cardiothoracic surgery

-Paroxysmal supraventricular tachycardia (SVT) (not initial drug of choice)

-Ventricular tachyarrhythmias (ACLS/PALS guidelines): Cardiac arrest with persistent VT or VF if defibrillation, CPR, and vasopressor administration have failed; control of hemodynamically-stable monomorphic VT, polymorphic VT with a normal baseline QT interval, or wide-complex tachycardia of uncertain origin; control of rapid ventricular rate due to accessory pathway conduction in pre-excited atrial arrhythmias (ACLS guidelines) or stable narrow-complex tachycardia (ACLS guidelines)

-Adjunct to ICD therapy to suppress symptomatic ventricular tachyarrhythmias in otherwise optimally-treated patients with heart failure (ACC/AHA/ESC Practice Guidelines)

Dosage:

Note: Lower loading and maintenance doses are preferable in women and all patients with low body weight.

-Atrial fibrillation pharmacologic cardioversion (ACC/AHA/ESC Practice Guidelines) (unlabeled use):

-Oral: Inpatient: 1.2-1.8 g/day in divided doses until 10 g total, then 200-400 mg/day maintenance. Outpatient: 600-800 mg/day in divided doses until 10 g total, then 200-400 mg/day maintenance; although not supported by clinical evidence, a maintenance dose of 100 mg/day is commonly used especially for the elderly or patients with low body mass (Fuster, 2006; Zimetbaum, 2007). Note: Other regimens have been described and may be used clinically:

400 mg 3 times/day for 5-7 days, then 400 mg/day for 1 month, then 200 mg/day

Or 10 mg/kg/day for 14 days, followed by 300 mg/day for 4 weeks, followed by maintenance dosage of 200 mg/day (Roy, 2000)

-I.V.: 5-7 mg/kg over 30-60 minutes, then 1.2-1.8 g/day continuous infusion or in divided oral doses until 10 g total. Maintenance: See oral dosing.

-Atrial fibrillation prophylaxis following open heart surgery (unlabeled use): Note: A variety of regimens have been used in clinical trials, including oral and intravenous regimens:

-Oral: Starting in postop recovery, 400 mg twice daily for up to 7 days. Alternative regimen of amiodarone: 600 mg/day for 7 days prior to surgery, followed by 200 mg/day until hospital discharge, has also been shown to decrease the risk of postoperative atrial fibrillation.

-I.V.: Starting at postop recovery, 1000 mg infused over 24 hours for 2 days has been shown to reduce the risk of postoperative atrial fibrillation.

-Recurrent atrial fibrillation (unlabeled use): No standard regimen defined; examples of regimens include: Oral: Initial: 10 mg/kg/day for 14 days; followed by 300 mg/day for 4 weeks, followed by maintenance dosage of 200 mg/day (Roy, 2000). Other regimens have been described and are used clinically (ie, 400 mg 3 times/day for 5-7 days, then 400 mg/day for 1 month, then 200 mg/day).

-Ventricular arrhythmias: Oral: 800-1600 mg/day in 1-2 doses for 1-3 weeks, then when adequate arrhythmia control is achieved, decrease to 600-800 mg/day in 1-2 doses for 1 month; maintenance: 400 mg/day; lower doses are recommended for supraventricular arrhythmias.

-Pulseless VT or VF (ACLS, 2010): I.V. push, I.O.: Initial: 300 mg rapid bolus; if pulseless VT or VF continues after subsequent defibrillation attempt or recurs, administer supplemental dose of 150 mg. Note: In this setting, administering undiluted is preferred (Dager, 2006; Skrifvars, 2004). The Handbook of Emergency Cardiovascular Care (Hazinski, 2010) and the 2010 ACLS guidelines, do not make any specific recommendations regarding dilution of amiodarone in this setting. Experience limited with I.O. administration of amiodarone (ACLS, 2010).

-Upon return of spontaneous circulation, follow with an infusion of 1 mg/minute for 6 hours, then 0.5 mg/minute for 18 hours (mean daily doses >2.1 g/day have been associated with hypotension).

-Stable VT or SVT (unlabeled use): First 24 hours: 1050 mg according to following regimen :Step 1: 150 mg (100 mL) over first 10 minutes (mix 3 mL in 100 mL D₅W)

Step 2: 360 mg (200 mL) over next 6 hours (mix 18 mL in 500 mL D₅W): 1 mg/minute

Step 3: 540 mg (300 mL) over next 18 hours: 0.5 mg/minute

Note: After the first 24 hours: 0.5 mg/minute utilizing concentration of 1-6 mg/mL Breakthrough stable VT or SVT: 150 mg supplemental doses in 100 mL D₅W or NS over 10 minutes (mean daily doses >2.1 g/day have been associated with hypotension)

-I.V. to oral therapy conversion: Use the following as a guide:

<1-week I.V. infusion: 800-1600 mg/day

1- to 3-week I.V. infusion: 600-800 mg/day

>3-week I.V. infusion: 400 mg

Note: Conversion from I.V. to oral therapy has not been formally evaluated. Some experts recommend a 1-2 day overlap when converting from I.V. to oral therapy especially when treating ventricular arrhythmias.

Recommendations for conversion to intravenous amiodarone after oral administration: During long-term amiodarone therapy (ie, ≥ 4 months), the mean plasma-elimination half-life of the active metabolite of amiodarone is 61 days. Replacement therapy may not be necessary in such patients if oral therapy is discontinued for a period < 2 weeks, since any changes in serum amiodarone concentrations during this period may not be clinically significant.

Renal Impairment:

No dosage adjustment necessary. Hemodialysis: Not dialyzable (0% to 5%); supplemental dose is not necessary

Peritoneal dialysis: Not dialyzable (0% to 5%); supplemental dose is not necessary

Hepatic Impairment:

Dosage adjustment is probably necessary in substantial hepatic impairment. No specific guidelines available. If hepatic enzymes exceed 3 times normal or double in a patient with an elevated baseline, consider decreasing the dose or discontinuing amiodarone

Available dosage form in the hospital: 150MG/ 3ML AMP , 200MG TAB.

Common side effect: In a recent meta-analysis, adult patients taking lower doses of amiodarone (152-330 mg daily for at least 12 months) were more likely to develop thyroid, neurologic, skin, ocular, and bradycardic abnormalities than those taking placebo (Vorperian, 1997). Pulmonary toxicity was similar in both the low-dose amiodarone group and in the placebo group, but there was a trend towards increased toxicity in the amiodarone group. Gastrointestinal and hepatic events were seen to a similar extent in both the low-dose amiodarone group and placebo group. As the frequency of adverse events varies considerably across studies as a function of route and dose, a consolidation of adverse event rates is provided by Goldschlager, 2000.

>10%: Cardiovascular: Hypotension (I.V. 16%, refractory in rare cases)

Central nervous system (3% to 40%): Abnormal gait/ataxia, dizziness, fatigue, headache, malaise, impaired memory, involuntary movement, insomnia, poor coordination, peripheral neuropathy, sleep disturbances, tremor

Dermatologic: Photosensitivity (10% to 75%)

Endocrine & Metabolic: Hypothyroidism (1% to 22%) . Gastrointestinal: Nausea, vomiting, anorexia, and constipation (10% to 33%)

Hepatic: AST or ALT level $> 2x$ normal (15% to 50%)

Ocular: Corneal microdeposits ($> 90\%$; causes visual disturbance in $< 10\%$)

1% to 10%: Cardiovascular: CHF (3%), bradycardia (3% to 5%), AV block (5%), conduction abnormalities, SA node dysfunction (1% to 3%), cardiac arrhythmia, flushing, edema. Additional effects associated with I.V. administration include asystole, atrial fibrillation, cardiac arrest, electromechanical dissociation, pulseless electrical activity (PEA), ventricular tachycardia, and cardiogenic shock. Dermatologic: Slate blue skin discoloration ($< 10\%$)

Endocrine & metabolic: Hyperthyroidism (3% to 10%; more common in iodine-deficient regions of the world), libido decreased

Gastrointestinal: Abdominal pain, abnormal salivation, abnormal taste (oral), diarrhea, nausea (I.V.)

Hematologic: Coagulation abnormalities. Hepatic: Hepatitis and cirrhosis ($< 3\%$)

local: Phlebitis (I.V., with concentrations > 3 mg/mL)

Ocular: Visual disturbances (2% to 9%), halo vision ($< 5\%$ occurring especially at night), optic neuritis (1%)

Respiratory: Pulmonary toxicity has been estimated to occur at a frequency between 2% and 7% of patients (some reports indicate a frequency as high as 17%). Toxicity may present as hypersensitivity pneumonitis; pulmonary fibrosis (cough, fever, malaise); pulmonary inflammation; interstitial pneumonitis; or alveolar pneumonitis. ARDS has been reported in up to 2% of patients receiving amiodarone, and postoperatively in patients receiving oral amiodarone.

Miscellaneous: Abnormal smell (oral)

Pregnancy Risk Factor: D