



Clinical Pharmacology & Toxicology Pearl of the Week

~Amiodarone - Part 1 - Facts & Pharmacology~

- ✓ Amiodarone was developed in 1962 as an anti-anginal vasodilator akin to “a long-acting version of nitroglycerine”. It was soon noted to have antiarrhythmic properties in ischemic patients and decades later is still recognized as the most effective antiarrhythmic medication for both supraventricular and ventricular arrhythmias.
- ✓ Each molecule contains 2 iodine atoms, such that ~6 mg of iodine is freed from each 200 mg tablet, ~20-fold the normal North American dietary intake (0.3 mg/day).
- ✓ Amiodarone comes in oral form (200 mg original and generic round, pink tablet, or 100, 200 and 400 mg forms) or an intravenous (IV) preparation, amiodarone 50 mg/mL, containing benzyl alcohol 20.2 mg, polysorbate-80 (surfactant) 100 mg & water.
- ✓ Amiodarone is noted for its Vaughan Williams Class-III antiarrhythmic (K⁺ channel antagonist) activity; however, its superior antiarrhythmic effects result from combination the other 3 classes. (Na⁺ channel antagonism, Beta-blockade, Ca⁺² channel antagonism) and its very limited daily decline in concentration.

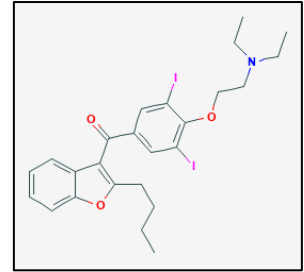


Table 1: The Pharmacokinetic Profile of Amiodarone

Absorption	- Widely variable oral absorption (20-80%)
Distribution	- Highly lipophilic with extensive tissue distribution (Vd = 40-80 L/kg, T _{1/2} (distribution) = 17 h) - Initial distribution from blood to tissue causes serum concentrations to fall rapidly until the peripheral tissue compartment is saturated. IV bolus always needs to be followed by infusion to maintain activity in acute administration to amiodarone-naïve patient.
Metabolism	- Important hepatic first-pass effect with extensive enterohepatic recirculation - Major metabolism is via liver CYP3A4 enzymes is slowed halogenation with iodine - Active metabolite: N-Desethylamiodarone (DEA), similar structure and antiarrhythmic and toxic activities
Excretion	- Predominantly biliary excretion with near-absent renal excretion being water insoluble - In contrast to distribution, elimination half-life is typically 80 times longer at 56 days.

- ✓ IV amiodarone does not truly “load” a patient, rather it maintains effective plasma concentrations until such a time as an oral dosing protocol can be initiated for sufficiently long to saturate the peripheral compartment.
- ✓ Oral administration requires a loading dose to provide the first 10 - 16 grams over 1-2 weeks, followed by daily maintenance dosing that takes 6-12 months to reach true steady-state serum concentrations, i.e. the full effect of a dose choice is not reached until 6 months after it is initiated.
- ✓ Patients taking amiodarone should have access to a physician with familiarity in its monitoring and use.

The Clinical Pharmacology (CP) physician consultation service is available Mon-Fri, 8am-5pm. The on-call physician is listed in ROCA on the AHS Insite page. CP consultations are also available through Netcare e-referral, Specialist Link and through RAAPID. You can also find us in the [Alberta Referral Directory](#) (ARD) by searching "Pharmacology" from the ARD home page. Click [HERE](#) for more details about the service.

The Poison and Drug Information Service (PADIS) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414 (AB and NWT) or 1-866-454-1212 (SK). Information about our outpatient Medical Toxicology Clinic can be found in [Alberta Referral Directory](#) (ARD) by searching "Toxicology" from the ARD home page.

More CPT Pearls of the Week can be found [HERE](#).

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