



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 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 pink tablet, or 100, 200 and 400 mg generics) or an intravenous (IV) preparation, each mL containing amiodarone 50 mg, benzyl alcohol 20.2 mg, polysorbate-80 (surfactant) 100 mg & water.
- ✓ Amiodarone is primarily classified as a [Vaughan Williams](#) Class-III antiarrhythmic (K⁺ channel antagonist), however its superior antiarrhythmic effects result from action in all four classes. (Na⁺ channel antagonism, Beta-blockade, K⁺ channel antagonism and Ca⁺² channel antagonism)

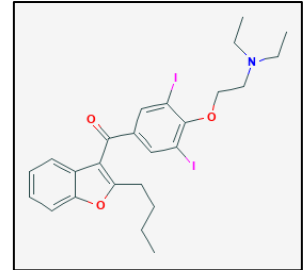


Table 1: The Pharmacokinetic Profile of Amiodarone

Absorption	- Highly variable oral absorption (20-80%)
Distribution	- Very lipophilic with extensive tissue distribution (Vd = 40-80 L/kg, T _{1/2 (dist)} = 17 h) - Distribution from blood to tissue means serum concentrations fall rapidly until the peripheral tissue compartment is saturated. IV bolus always needs to be followed by infusion to maintain activity in acute administration. - It has a very long elimination half-life of approximately 8 weeks (56 days)
Metabolism	- Large first-pass effect through the liver with extensive enterohepatic recirculation - Major metabolism is via liver CYP3A4 enzymes - Active metabolite: N-Desethylamiodarone (DEA), which possesses Class-II antiarrhythmic & vasodilatory properties
Excretion	- Predominantly biliary excretion with near-absent renal excretion

- ✓ IV amiodarone does not truly “load” a patient, rather it maintains effective plasma concentrations until such a time as an oral loading protocol can be initiated or the drug is no longer required.
- ✓ Oral administration requires a loading dose of 10 - 16 grams over 1-2 weeks, followed by daily maintenance dosing. Despite an appropriate loading protocol, steady-state plasma concentration is not achieved for several months following initiation of amiodarone.
- ✓ Patients on amiodarone should have access to a physician with expertise in its monitoring and use.



The Calgary Clinical Pharmacology physician consultation service is available Mon-Fri, 8am-5pm. The on-call physician is listed in ROCA. Click [HERE](#) for more details.



The Poison and Drug Information Service (PADIS) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414, and select option 1.