

Amiodarone (eg, Cordarone) **2**

## Simvastatin (Zocor)

**SUMMARY:** Amiodarone appears likely to increase the risk of simvastatin toxicity.

**RISK FACTORS:** No specific risk factors are known.

**MECHANISM:** Amiodarone is known to inhibit both CYP3A4 and CYP2D6. The first-pass metabolism of simvastatin is primarily via CYP3A4 while both enzymes contribute to the systemic metabolism of simvastatin.

**CLINICAL EVALUATION:** A patient with hypertension, hyperlipidemia, and diabetes mellitus was taking amiodarone 200 mg for 6 weeks and simvastatin 80 mg for nearly 4 weeks before being admitted with weakness, muscle pain, and dark urine.<sup>1</sup> Serum creatine kinase and myoglobin were elevated. Following discontinuation of simvastatin and amiodarone, the patient slowly improved over the next few weeks. Several other cases of rhabdomyolysis have been reported in patients taking simvastatin and amiodarone.<sup>2,3</sup>

**RELATED DRUGS:** The metabolism of lovastatin (eg, *Mevacor*) and, to a lesser extent, atorvastatin (*Lipitor*) may be reduced by amiodarone. Fluvastatin (*Lescol*) is metabolized by CYP2C9, an enzyme that also is inhibited by amiodarone.

**REFERENCES:**

1. Ricaurte B, et al. Simvastatin-amiodarone interaction resulting in rhabdomyolysis, azotemia, and possible hepatotoxicity. *Ann Pharmacother.* 2006;40:753-757.
2. Roten L, et al. Rhabdomyolysis in association with simvastatin and amiodarone. *Ann Pharmacother.* 2004;38:978-981.
3. de Denus S, et al. Amiodarone's role in simvastatin-associated rhabdomyolysis. *Am J Health Syst Pharm.* 2003;60:1791-1792.

**MANAGEMENT OPTIONS:**

➔ **Use Alternative.** Avoid the concurrent use of amiodarone and simvastatin. If amiodarone must be administered, select a statin that is not a CYP3A4 substrate. Pravastatin (*Pravachol*) and rosuvastatin (*Crestor*) are less likely to be affected by amiodarone.

Amiodarone (eg, Cordarone) **3**

## Sotalol (eg, Betapace)

**SUMMARY:** A patient given amiodarone following chronic sotalol therapy developed hypotension and bradycardia, but a causal relationship for an interaction between the drugs was not established.

**RISK FACTORS:** No specific risk factors are known.

**MECHANISM:** Not established. Sotalol may inhibit the normal compensatory response to amiodarone-induced vasodilation, resulting in enhanced hypotensive effects. Both drugs may slow the heart rate.

**CLINICAL EVALUATION:** A 59-year-old patient with nonsustained ventricular tachycardia was treated with sotalol 160 mg twice daily.<sup>1</sup> Because of increasing episodes of arrhythmia, sotalol was discontinued and, 4 hours later, an infusion of amiodarone 50 mg/hr was started. After 5 hours of the infusion, the patient became profoundly hypotensive, and her heart rate decreased to 60 beats/min. The amiodarone infusion was discontinued and inotropic agents were required for the next 18 hours. Oral amiodarone therapy was initiated 24 hours later without further hemodynamic instability. Rechallenge with sotalol and amiodarone was not attempted. Because amiodarone may produce hypotension, causation was not clearly established.

**RELATED DRUGS:** Beta-blockers, including metoprolol (eg, *Lopressor*) and propranolol (eg, *Inderal*), have been noted to produce bradycardia when administered with amiodarone.

**REFERENCES:**

1. Warren R, et al. Serious interaction of sotalol with amiodarone and flecainide. *Med J Aust.* 1990;152:277.

**MANAGEMENT OPTIONS:**

➔ **Circumvent/Minimize.** Avoid the administration of amiodarone for several days in patients previously receiving drugs that depress myocardial conduction and contractility.

➔ **Monitor.** Until further information is available, carefully monitor patients receiving sotalol (and perhaps other beta-blockers) and amiodarone for hemodynamic depression.