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IN BRIEF

Severe Bradycardia with Sofosbuvir and Amiodarone

The FDA recently announced changes in the labeling of the hepatitis C drugs *Sovaldi* (sofosbuvir) and *Harvoni* (sofosbuvir/ledipasvir) to warn about a risk of serious and potentially fatal bradycardia when either drug is taken with the antiarrhythmic drug amiodarone (*Cordarone*, and others).¹ Symptomatic bradycardia was reported following initiation of treatment with *Harvoni* or with *Sovaldi* plus simeprevir (*Olysio*) or the investigational antiviral drug daclatasvir in 9 patients already taking amiodarone; it occurred within 24 hours of starting hepatitis C therapy in 6 patients and within 2-12 days in 3 others. One patient died of cardiac arrest and 3 required pacemaker implantation. In 3 patients who continued taking amiodarone, rechallenge with *Harvoni* or *Sovaldi* resulted in recurrence of symptomatic bradycardia. In another patient, rechallenge 8 weeks after stopping amiodarone did not result in bradycardia.

The mechanism of this effect is unknown. Factors possibly contributing to the cardiac events include

concomitant beta blocker therapy (in 7 patients) and preexisting cardiac and hepatic disease. Hepatic impairment increases the risk of cardiac conduction abnormalities and could increase adverse effects of amiodarone, which is metabolized by the liver.² Use of sofosbuvir without amiodarone has not been associated with significant bradycardia.

The new labels warn that sofosbuvir and amiodarone should not be taken concurrently. If concomitant use is necessary, cardiac monitoring in an inpatient setting is recommended for the first 48 hours. Daily monitoring of heart rate, either at home or in an outpatient setting, should continue for at least the first 2 weeks of treatment. Amiodarone has a very long half-life, and its effects may persist for weeks to months after discontinuation. ■

1. FDA. FDA Drug Safety Communication: FDA warns of serious slowing of the heart rate when antiarrhythmic drug amiodarone is used with hepatitis C treatments containing sofosbuvir Harvoni or Sovaldi in combination with another direct acting antiviral drug. Available at <http://www.fda.gov/Drugs/DrugSafety/ucm439484.htm>. Accessed April 2, 2015.
2. U Klotz. Antiarrhythmics: elimination and dosage considerations in hepatic impairment. *Clin Pharmacokinet* 2007; 46:985.

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