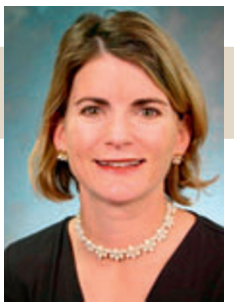
LTC Pharmacy



By Nicole Brandt, PharmD, CGP, BCPP, FASCP

Medication Monitoring in PA/LTC Always Takes a Team

"The way a team plays as a whole determines its success. You may have the greatest bunch of individual stars in the world, but if they don't play together, the club won't be worth a dime."

– Babe Ruth

In February, the Department of Health and Human Services Office of Inspector General released its report "Adverse Events in Skilled Nursing Facilities: National Incidence Among Medicare Beneficiaries" (accessible at https://oig.hhs.gov/oei/reports/oei-06-11-00370.pdf). It noted that 22% of Medicare beneficiaries experience adverse events during a short skilled nursing facility (SNF) stay and 37% of these are related to medications. It is important to note that the majority (66%) of adverse events and temporary harms that were related to medications were clearly or likely preventable, according to case reviewers. Many of these were attributed to medications that cause hypoglycemia, bleeds, falls, or changes in mental status. (See the "Public Policy" column on page 11.)

Too often, the postacute and long-term care (PA/LTC) team does not fully engage the pharmacist in educational programs, policies, and procedures regarding medication management. To illustrate the value of a pharmacist's input, consider amiodarone, frequently given to frail residents of skilled nursing facilities who have atrial fibrillation.

Amiodarone, which is on the 2012 American Geriatrics Society Beers list as a potentially inappropriate medication, is a class III antiarrhythmic that also exhibits class I, II, and IV properties. Specifically, amiodarone decreases conduction velocity by blocking potassium channels, sodium channels, beta receptors, and calcium channels.

Amiodarone has unique pharmacokinetics. Namely, it is widely distributed in the body and stored in high concentrations in fat, muscle, liver, lungs, and skin. It also can cross the blood-brain barrier due to its lipophilicity, a characteristic that also accounts for the drugs long half-life, about 52 days.

While the drug is a powerful antiarrhythmic, its use can be limited by its extensive side-effects on organs throughout the body.

The potential for serious toxicities and a multitude of drug interactions warrants careful monitoring by providers and patients. Thyroid, pulmonary, hepatic, cardiac, ophthalmologic, neurologic, and dermatologic systems are associated with amiodarone toxicity. (Am. Fam. Physician 2003;68[11]:2189–2197).

Thyroid

Amiodarone can cause either hypothyroidism or hyperthyroidism through its iodine content of up to 37.5% by weight, as well as the intrinsic effects of the drug, including reductions in triiodothyronine (T_3) and increases in reverse triiodothyronine (rT_3). Amiodarone also can directly damage thyroid cells, leading to thyrotoxicosis. Hypothyroidism or hyperthyroidism from amiodarone toxicity can affect up to 10% of patients. A thyroid-function test should be performed at baseline and at least every 6 months.

Pulmonary

A potential fatal toxicity with amiodarone is interstitial pneumonitis, which normally presents with nonspecific symptoms, and incidence may be as high as 17%. The mechanisms for this toxicity may include drug-induced phospholipidosis, indirect inflammatory process, or immune-mediated hypersensitivity. Risk factors include doses >400 mg/day, high cumulative dosage, and perhaps underlying lung disease.

To detect pulmonary toxicities, a baseline pulmonary function test and a chest x-ray are essential. These should be repeated, but as pulmonary toxicity may rapidly develop, a 3- to 6-month follow-up may not always be clinically valuable. The best approach may be for patients to self-monitor and report any change such as worsening dyspnea and cough.

Liver

Since liver toxicity is typically asymptomatic, monitoring of liver enzymes at baseline and at least every 6 months is imperative. Elevated transaminase may indicate the development of hepatitis, which may occur in up to 3% of patients on amiodarone. In such cases, amiodarone should be discontinued and supportive therapy should be initiated.

Cardiac

Bradycardia and heart block may occur in 1%-3% of patients receiving amiodarone. Some hospital protocols recommend holding amiodarone if heart rate falls below 60, but recommendations for patients on chronic therapy are unclear because the medication's effects on the body may linger for up to 6 months after the drug is discontinued. It is especially important to monitor for symptomatic bradycardia in older adults because they have an elevated risk of developing complete heart block. Regardless of the setting, it is recommended that patients receive a baseline electrocardiogram and follow-up at least yearly.

Ophthalmic

Corneal microdeposits may occur in up to 90% of patients receiving amiodarone. Retinopathy occurs in <2%. The American Hospital Formulary Service recommends eye examinations at baseline, at 6 months, and then every 12 months. Patients should report any changes in visual acuity and peripheral vision. Clinicians are advised to order a prompt ophthalmic examination upon any vision complaint.

Neurologic

A range of neuropsychiatric events may occur, including tremors and ataxia. The incidence ranges anywhere from 3%-35%, depending on dose and duration of therapy. Insomnia and memory impairment have also been noted. Peripheral neuropathy may also occur, although uncommonly, with an annual incidence of 0.3%. Patients should have a baseline physical examination, repeated as needed when signs and symptoms of neurological toxicity occur.

Dermatologic

Blue-gray skin discoloration may occur in 4%-9% of patients taking amiodarone, and 25%-75% can experience photosensitivity. These symptoms may be due to lysosomal alterations, as well as amiodarone and lipid accumulations. Patients on the drug should apply sunscreen and limit sun exposure as much as possible. Patients should have a baseline physical examination and be examined whenever dermatologic toxicity is suspected.

Drug Interactions

There are multiple drug interactions with amiodarone and its active metabolite, desethylamiodarone, through various metabolic enzymes, including CYP3A4, CYP2D6, and CYP2C9. Therefore, patients taking amiodarone and warfarin concomitantly should have their warfarin reduced by 50% and their INRs monitored at least weekly during the first 6 weeks of amiodarone therapy.

Digoxin also should be reduced by half, and monitoring of serum digoxin level is recommended. As amiodarone can cause atrioventricular nodal depression, patients also taking calcium channel blockers and beta-blockers can experience worsening bradycardia.

Other notable drugs that interact with amiodarone include, but are not limited to, azole antifungals, cimetidine, cholestyramine, fluoroquinolones, macrolides, statins, flecainide, and protease inhibitors.

Monitoring Challenges

Unfortunately, much of the monitoring needed to avoid amiodarone toxicities and interactions can be difficult. A retrospective review at the Medical University of South Carolina assessed adherence to monitoring for potential adverse effects of amiodarone in both outpatient and inpatient settings. Desired monitoring methods were deemed to be chest x-ray, liver function test, and thyroid function test, as systems explored by those tests are commonly associated with amiodarone toxicity.

Among the 79 patients in the study, only 11% of those initiated on the drug while hospitalized received all three tests at baseline. Among outpatients, who were on amiodarone therapy for at least 6 months, baseline chest x-rays were done in 75%, liver function was assessed in 95%, and thyroid function was measured in 75%. Only 25% and 20% of the outpatients received the liver and thyroid tests, respectively, at 6 months, and 50% got a chest x-ray yearly (J. Manag. Care Pharm. 2006;12[3]:254–59).

Most adverse events associated with amiodarone occur during the first year of therapy. But since cumulative amiodarone dose may increase toxicities, continual monitoring is all the more important.

Practitioners should hesitate before prescribing amiodarone, especially in "younger" patients with atrial fibrillation due to the greater potential for cumulative toxicities.

Implications for PA/LTC

The daunting task of medication monitoring, as illustrated by amiodarone, requires teamwork in the PA/LTC setting, where frail individuals receive elaborate combinations of medications. As there is increasing scrutiny of the monitoring of medications in this setting, all providers of care, including pharmacists, need to collaborate and document their efforts to minimize adverse events among residents.

An associate professor in the pharmacy practice department at the University of Maryland School of Pharmacy, Dr. Brandt *works as a pharmacist in multiple long-term care settings. She seeks to optimize the care of older adults through educational, clinical, and health care–policy work.* Sandy Truong, *a PharmD candidate at the University of Maryland School of Pharmacy, contributed to this article.*