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Please see brief summary of Prescribing Information on adjacent page.

Pharmaceuticals

BRIEF SUMMARY

# NIACIN EXTENDED-RELEASE TABLETS USP

**℞ only**

## FULL PRESCRIBING INFORMATION

### 1 INDICATIONS AND USAGE

Therapy with lipid-altering agents should be only one component of multiple risk factor intervention in individuals at significantly increased risk for atherosclerotic vascular disease due to hyperlipidemia. Niacin, USP therapy is indicated as an adjunct to diet when the response to a diet restricted in saturated fat and cholesterol and other nonpharmacologic measures alone has been inadequate.

1. Niacin Extended-Release Tablets USP are indicated to reduce elevated TC, LDL-C, Apo B and TG levels, and to increase HDL-C in patients with primary hyperlipidemia and mixed dyslipidemia.
2. Niacin Extended-Release Tablets USP in combination with simvastatin or lovastatin are indicated for the treatment of primary hyperlipidemia and mixed dyslipidemia when treatment with Niacin Extended-Release Tablets USP, simvastatin, or lovastatin monotherapy is considered inadequate.
3. In patients with a history of myocardial infarction and hyperlipidemia, niacin, USP is indicated to reduce the risk of recurrent nonfatal myocardial infarction.
4. In patients with a history of coronary artery disease (CAD) and hyperlipidemia, niacin, USP, in combination with a bile acid binding resin, is indicated to slow progression or promote regression of atherosclerotic disease.
5. Niacin Extended-Release Tablets USP in combination with a bile acid binding resin are indicated to reduce elevated TC and LDL-C levels in adult patients with primary hyperlipidemia.
6. Niacin, USP is also indicated as adjunctive therapy for treatment of adult patients with severe hypertriglyceridemia who present a risk of pancreatitis and who do not respond adequately to a determined dietary effort to control them.

**Limitations of Use**

No incremental benefit of Niacin Extended-Release Tablets USP coadministered with simvastatin or lovastatin on cardiovascular morbidity and mortality over and above that demonstrated for niacin, USP, simvastatin, or lovastatin monotherapy has been established.

Niacin Extended-Release Tablets USP, at doses of 1,500-2,000 mg/day, in combination with simvastatin, did not reduce the incidence of cardiovascular events more than simvastatin in a randomized controlled trial of patients with cardiovascular disease and mean baseline LDL-C levels of 74 mg per deciliter *[see Warnings and Precautions (5.1)]*.

### 2 DOSAGE AND ADMINISTRATION

**Table 1. Recommended Dosing**

| | Week(s) | Daily Dose | Niacin Extended-Release Tablets Dosage |
|---|---|---|---|
| INITIAL TITRATION SCHEDULE | 1 to 4 | 500 mg | 1 Niacin Extended-Release 500 mg Tablet at bedtime |
| | 5 to 8 | 1000 mg | 1 Niacin Extended-Release 1000 mg Tablet or 2 Niacin Extended-Release 500 mg Tablets at bedtime |
| | [a] | 1500 mg | 2 Niacin Extended-Release 750 mg Tablets or 3 Niacin Extended-Release 500 mg Tablets at bedtime |
| | [a] | 2000 mg | 2 Niacin Extended-Release 1000 mg Tablets or 4 Niacin Extended-Release 500 mg Tablets at bedtime |

[a] After Week 8, titrate to patient response and tolerance. If response to 1000 mg daily is inadequate, increase dose to 1500 mg daily; may subsequently increase dose to 2000 mg daily. Daily dose should not be increased more than 500 mg in a 4 week period, and doses above 2000 mg daily are not recommended. Women may respond at lower doses than men.

Maintenance Dose

Equivalent doses of Niacin Extended-Release Tablets should not be substituted for sustained-release (modified-release, timed-release) niacin preparations or immediate-release (crystalline) niacin *[see Warnings and Precautions (5)]*. Patients previously receiving other niacin products should be started with the recommended Niacin Extended-Release Tablet titration schedule (see **Table 1**), and the dose should subsequently be individualized based on patient response.

If Niacin Extended-Release Tablet therapy is discontinued for an extended period, reinstitution of therapy should include a titration phase (see **Table 1**).

### CONTRAINDICATIONS

Niacin extended-release tablets are contraindicated in the following conditions:

- Active liver disease or unexplained persistent elevations in hepatic transaminases *[see Warnings and Precautions (5.3)]*
- Patients with active peptic ulcer disease
- Patients with arterial bleeding
- Hypersensitivity to niacin or any component of this medication *[see Adverse Reactions (6.1)]*

### 5 WARNINGS AND PRECAUTIONS

**Niacin extended-release tablet preparations should not be substituted for equivalent doses of immediate-release (crystalline) niacin. For patients switching from immediate-release niacin to niacin extended-release tablets, therapy with niacin extended-release tablets should be initiated with low doses (i.e., 500 mg at bedtime) and the niacin extended-release tablet dose should then be titrated to the desired therapeutic response *[see Dosage and Administration (2)]*.**

Caution should also be used when niacin extended-release tablets are used in patients with unstable angina or in the acute phase of an MI, particularly when such patients are also receiving vasoactive drugs such as nitrates, calcium channel blockers, or adrenergic blocking agents.

Niacin is rapidly metabolized by the liver, and excreted through the kidneys. Niacin extended-release tablets are contraindicated in patients with significant or unexplained hepatic impairment *[see Contraindications (4) and Warnings and Precautions (5.3)]* and should be used with caution in patients with renal impairment. Patients with a past history of jaundice, hepatobiliary disease, or peptic ulcer should be observed closely during niacin extended-release tablet therapy.

#### 5.1 Mortality and Coronary Heart Disease Morbidity

The Atherothrombosis Intervention in Metabolic Syndrome with Low HDL/High Triglycerides: Impact on Global Health Outcomes (AIM-HIGH) trial was a randomized placebo-controlled trial of 3414 patients with stable, previously diagnosed cardiovascular disease. Mean baseline lipid levels were LDL-C 74 mg/dL, HDL-C 35 mg/dL, non-HDL-C 111 mg/dL and median triglyceride level of 163 to 177 mg/dL. Ninety-four percent of patients were on background statin therapy prior to entering the trial. All participants received simvastatin, 40 to 80 mg per day, plus ezetimibe 10 mg per day if needed, to maintain an LDL-C level of 40 to 80 mg/dL, and were randomized to receive niacin extended-release tablets 1500 to 2000 mg/day (n = 1718) or matching placebo (IR Niacin, 100 to 150 mg, n = 1696). On-treatment lipid changes at two years for LDL-C were -12% for the simvastatin plus niacin extended-release tablets group and -5.5% for the simvastatin plus placebo group. HDL-C increased by 25% to 42 mg/dL in the simvastatin plus niacin extended-release tablets group and by 9.8% to 38 mg/dL in the simvastatin plus placebo group ($P < 0.001$). Triglyceride levels decreased by 28.6% in the simvastatin plus niacin extended-release tablets group and by 8.1% in the simvastatin plus placebo group. The primary outcome was an ITT composite of the first study occurrence of coronary heart disease death, nonfatal myocardial infarction, ischemic stroke, hospitalization for acute coronary syndrome or symptom-driven coronary or cerebral revascularization procedures. The trial was stopped after a mean follow-up period of 3 years owing to a lack of efficacy. The primary outcome occurred in 282 patients in the simvastatin plus niacin extended-release tablets group (16.4%) and in 274 patients in the simvastatin plus placebo group (16.2%) (HR 1.02 [95% CI, 0.87-1.21], P = 0.79. In an ITT analysis, there were 42 cases of first occurrence of ischemic stroke reported, 27 (1.6%) in the simvastatin plus niacin extended-release tablets group and 15 (0.9%) in the simvastatin plus placebo group, a non-statistically significant result (HR 1.79, [95%CI = 0.95 to 3.36], p = 0.071). The on-treatment ischemic stroke events were 19 for the simvastatin plus niacin extended-release tablets group and 15 for the simvastatin plus placebo group *[see Adverse Reactions (6.1)]*.

#### 5.2 Skeletal Muscle

Cases of rhabdomyolysis have been associated with concomitant administration of lipid-altering doses (≥ 1 g/day) of niacin and statins. Physicians contemplating combined therapy with statins and niacin extended-release tablets should carefully weigh the potential benefits and risks and should carefully monitor patients for any signs and symptoms of muscle pain, tenderness, or weakness, particularly during the initial months of therapy and during any periods of upward dosage titration of either drug. Periodic serum creatine phosphokinase (CPK) and potassium determinations should be considered in such situations, but there is no assurance that such monitoring will prevent the occurrence of severe myopathy.

The risk for myopathy and rhabdomyolysis are increased when lovastatin or simvastatin are coadministered with niacin extended-release tablets, particularly in elderly patients and patients with diabetes, renal failure, or uncontrolled hypothyroidism.

#### 5.3 Liver Dysfunction

**Cases of severe hepatic toxicity, including fulminant hepatic necrosis, have occurred in patients who have substituted sustained-release (modified-release, timed-release) niacin products for immediate-release (crystalline) niacin at equivalent doses.**

**Niacin extended-release tablets should be used with caution in patients who consume substantial quantities of alcohol and/or have a past history of liver disease. Active liver diseases or unexplained transaminase elevations are contraindications to the use of niacin extended-release tablets.**

Niacin preparations have been associated with abnormal liver tests. In three placebo-controlled clinical trials involving titration to final daily niacin extended-release tablet doses ranging from 500 to 3000 mg, 245 patients received niacin extended-release tablets for a mean duration of 17 weeks. No patient with normal serum transaminase levels (AST, ALT) at baseline experienced elevations to more than 3 times the upper limit of normal (ULN) during treatment with niacin extended-release tablets. In these studies, fewer than 1% (2/245) of niacin extended-release tablet patients discontinued due to transaminase elevations greater than 2 times the ULN.

In three safety and efficacy studies with a combination tablet of niacin extended-release and lovastatin involving titration to final daily doses (expressed as mg of niacin/mg of lovastatin) 500 mg/10 mg to 2500 mg/40 mg, ten of 1028 patients (1%) experienced reversible elevations in AST/ALT to more than 3 times the ULN. Three of ten elevations occurred at doses outside the recommended dosing limit of 2000 mg/40 mg; no patient receiving 1000 mg/20 mg had 3 fold elevations in AST/ALT.

Niacin extended-release and simvastatin can cause abnormal liver tests. In a simvastatin-controlled, 24 week study with a fixed dose combination of niacin extended-release tablets and simvastatin in 641 patients, there were no persistent increases (more than 3x the ULN) in serum transaminases. In three placebo-controlled clinical studies of extended-release niacin there were no patients with normal serum transaminase levels at baseline who experienced elevations to more than 3x the ULN. Persistent increases (more than 3x the ULN) in serum transaminases have occurred in approximately 1% of patients who received simvastatin in clinical studies. When drug treatment was interrupted or discontinued in these patients, the transaminases levels usually fell slowly to pretreatment levels. The increases were not associated with jaundice or other clinical signs or symptoms. There was no evidence of hypersensitivity.

In the placebo-controlled clinical trials and the long-term extension study, elevations in transaminases did not appear to be related to treatment duration; elevations in AST levels did appear to be dose related. Transaminase elevations were reversible upon discontinuation of niacin extended-release tablets.

Liver function tests should be performed on all patients during therapy with niacin extended-release tablets. Serum transaminase levels, including AST and ALT (SGOT and SGPT), should be monitored before treatment begins, every 6 to 12 weeks for the first year, and periodically thereafter (e.g., at approximately 6 month intervals). Special attention should be paid to patients who develop elevated serum transaminase levels, and in these patients, measurements should be repeated promptly and then performed more frequently. If the transaminase levels show evidence of progression, particularly if they rise to 3 times ULN and are persistent, or if they are associated with symptoms of nausea, fever, and/or malaise, the drug should be discontinued.

#### 5.4 Laboratory Abnormalities

*Increase in Blood Glucose:* Niacin treatment can increase fasting blood glucose. Frequent monitoring of blood glucose should be performed to ascertain that the drug is producing no adverse effects. Diabetic patients may experience a dose-related increase in glucose intolerance. Diabetic or potentially diabetic patients should be observed closely during treatment with niacin extended-release tablets, particularly during the first few months of use or dose adjustment; adjustment of diet and/or hypoglycemic therapy may be necessary.

*Reduction in Platelet Count:* Niacin extended-release tablets have been associated with small but statistically significant dose-related reductions in platelet count (mean of -11% with 2000 mg). Caution should be observed when niacin extended-release tablets are administered concomitantly with anticoagulants; platelet counts should be monitored closely in such patients.

*Increase in Prothrombin Time (PT):* Niacin extended-release tablets have been associated with small but statistically significant increases in prothrombin time (mean of approximately +4%); accordingly, patients undergoing surgery should be carefully evaluated. Caution should be observed when niacin extended-release tablets are administered concomitantly with anticoagulants; prothrombin time should be monitored closely in such patients.

*Increase in Uric Acid:* Elevated uric acid levels have occurred with niacin therapy, therefore use with caution in patients predisposed to gout.

*Decrease in Phosphorus:* In placebo-controlled trials, niacin extended-release tablets have been associated with small but statistically significant, dose-related reductions in phosphorus levels (mean of -13% with 2000 mg).

Although these reductions were transient, phosphorus levels should be monitored periodically in patients at risk for hypophosphatemia.

## 6 ADVERSE REACTIONS

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice.

### 6.1 Clinical Studies Experience

In the placebo-controlled clinical trials database of 402 patients (age range 21 to 75 years, 33% women, 89% Caucasians, 7% Blacks, 3% Hispanics, 1% Asians) with a median treatment duration of 16 weeks, 16% of patients on niacin extended-release tablets and 4% of patients on placebo discontinued due to adverse reactions. The most common adverse reactions in the group of patients treated with niacin extended-release tablets that led to treatment discontinuation and occurred at a rate greater than placebo were flushing (6% vs. 0%), rash (2% vs. 0%), diarrhea (2% vs. 0%), nausea (1% vs. 0%), and vomiting (1% vs. 0%). The most commonly reported adverse reactions (incidence > 5% and greater than placebo) in the niacin extended-release tablets controlled clinical trial database of 402 patients were flushing, diarrhea, nausea, vomiting, increased cough and pruritus.

In the placebo-controlled clinical trials, flushing episodes (i.e., warmth, redness, itching and/or tingling) were the most common treatment-emergent adverse reactions (reported by as many as 88% of patients) for niacin extended-release tablets. Spontaneous reports suggest that flushing may also be accompanied by symptoms of dizziness, tachycardia, palpitations, shortness of breath, sweating, burning sensation/skin burning sensation, chills, and/or edema, which in rare cases may lead to syncope. In pivotal studies, 6% (14/245) of niacin extended-release tablet patients discontinued due to flushing. In comparisons of immediate-release (IR) niacin and niacin extended-release tablets, although the proportion of patients who flushed was similar, fewer flushing episodes were reported by patients who received niacin extended-release tablets. Following 4 weeks of maintenance therapy at daily doses of 1500 mg, the incidence of flushing over the 4 week period averaged 8.6 events per patient for IR niacin versus 1.9 following niacin extended-release tablets.

Other adverse reactions occurring in ≥ 5% of patients treated with niacin extended-release tablets and at an incidence greater than placebo are shown in **Table 2** below.

**Table 2. Treatment-Emergent Adverse Reactions by Dose Level in ≥ 5% of Patients and at an Incidence Greater Than Placebo; Regardless of Causality Assessment in Placebo-Controlled Clinical Trials**

| | Placebo-Controlled Studies Niacin Extended-Release Tablets Treatment[a] | | | | |
|---|---|---|---|---|---|
| | | Recommended Daily Maintenance Doses[b] | | | |
| | Placebo (n = 157) % | 500 mg[c] (n = 87) % | 1000 mg (n = 110) % | 1500 mg (n = 136) % | 2000 mg (n = 95) % |
| **Gastrointestinal Disorders** | | | | | |
| Diarrhea | 13 | 7 | 10 | 10 | 14 |
| Nausea | 7 | 5 | 6 | 4 | 11 |
| Vomiting | 4 | 0 | 2 | 4 | 9 |
| **Respiratory** | | | | | |
| Cough, Increased | 6 | 3 | 2 | < 2 | 8 |
| **Skin and Subcutaneous Tissue Disorders** | | | | | |
| Pruritus | 2 | 8 | 0 | 3 | 0 |
| Rash | 0 | 5 | 5 | 5 | 0 |
| **Vascular Disorders** | | | | | |
| Flushing[d] | 19 | 68 | 69 | 63 | 55 |

Note: Percentages are calculated from the total number of patients in each column.

[a] Pooled results from placebo-controlled studies; for niacin extended-release tablets, n = 245 and median treatment duration = 16 weeks. Number of niacin extended-release tablet patients (n) are not additive across doses.

[b] Adverse reactions are reported at the initial dose where they occur.

[c] The 500 mg/day dose is outside the recommended daily maintenance dosing range *[see Dosage and Administration* (2)*]*.

[d] 10 patients discontinued before receiving 500 mg, therefore they were not included.

In general, the incidence of adverse events was higher in women compared to men.

*Atherothrombosis Intervention in Metabolic Syndrome With Low HDL/High Triglycerides: Impact on Global Health Outcomes (AIM-HIGH)*

In AIM-HIGH involving 3414 patients (mean age of 64 years, 15% women, 92% Caucasians, 34% with diabetes mellitus) with stable, previously diagnosed cardiovascular disease, all patients received simvastatin, 40 to 80 mg per day, plus ezetimibe 10 mg per day if needed, to maintain an LDL-C level of 40 to 80 mg/dL, and were randomized to receive niacin extended-release tablets 1500 to 2000 mg/day (n = 1718) or matching placebo (IR Niacin, 100 to 150 mg, n = 1696). The incidence of the adverse reactions of "blood glucose increased" (6.4% vs. 4.5%) and "diabetes mellitus" (3.6% vs. 2.2%) was significantly higher in the simvastatin plus niacin extended-release tablets group as compared to the simvastatin plus placebo group. There were 5 cases of rhabdomyolysis reported, 4 (0.2%) in the simvastatin plus niacin extended-release tablets group and one (< 0.1%) in the simvastatin plus placebo group [see *Warnings and Precautions (5.1)*].

### 6.2 Postmarketing Experience

Because the below reactions are reported voluntarily from a population of uncertain size, it is generally not possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

The following additional adverse reactions have been identified during post-approval use of niacin extended-release tablets:

Hypersensitivity reactions, including anaphylaxis, angioedema, urticaria, flushing, dyspnea, tongue edema, larynx edema, face edema, peripheral edema, laryngismus, and vesiculobullous rash; maculopapular rash; dry skin; tachycardia; palpitations; atrial fibrillation; other cardiac arrhythmias; syncope; hypotension; postural hypotension; blurred vision; macular edema; peptic ulcers; eructation; flatulence; hepatitis; jaundice; decreased glucose tolerance; gout; myalgia; myopathy; dizziness; insomnia; asthenia; nervousness; paresthesia; dyspnea; sweating; burning sensation/skin burning sensation; skin discoloration, and migraine.

*Clinical Laboratory Abnormalities*

Chemistry: Elevations in serum transaminases *[see Warnings and Precautions (5.3)]*, LDH, fasting glucose, uric acid, total bilirubin, amylase and creatine kinase, and reduction in phosphorus.

Hematology: Slight reductions in platelet counts and prolongation in prothrombin time *[see Warnings and Precautions (5.4)]*.

## 7 DRUG INTERACTIONS

### 7.1 Statins

Caution should be used when prescribing niacin (≥ 1 gm/day) with statins as these drugs can increase risk of myopathy/rhabdomyolysis. Combination therapy with niacin extended-release tablets and lovastatin or niacin extended-release tablets and simvastatin should not exceed doses of 2000 mg niacin extended-release tablets and 40 mg lovastatin or simvastatin daily *[see Warnings and Precautions (5) and Clinical Pharmacology (12.3)]*.

### 7.2 Bile Acid Sequestrants

An *in vitro* study results suggest that the bile acid-binding resins have high niacin binding capacity. Therefore, 4 to 6 hours, or as great an interval as possible, should elapse between the ingestion of bile acid-binding resins and the administration of niacin extended-release tablets *[see Clinical Pharmacology (12.3)]*.

### 7.3 Aspirin

Concomitant aspirin may decrease the metabolic clearance of nicotinic acid. The clinical relevance of this finding is unclear.

### 7.4 Antihypertensive Therapy

Niacin may potentiate the effects of ganglionic blocking agents and vasoactive drugs resulting in postural hypotension.

### 7.5 Other

Vitamins or other nutritional supplements containing large doses of niacin or related compounds such as nicotinamide may potentiate the adverse effects of niacin extended-release tablets.

### 7.6 Laboratory Test Interactions

Niacin may produce false elevations in some fluorometric determinations of plasma or urinary catecholamines. Niacin may also give false-positive reactions with cupric sulfate solution (Benedict's reagent) in urine glucose tests.

## 8 USE IN SPECIFIC POPULATIONS

### 8.1 Pregnancy

*Teratogenic Effects*

Pregnancy Category C

Animal reproduction studies have not been conducted with niacin or with niacin extended-release tablets. It is also not known whether niacin at doses typically used for lipid disorders can cause fetal harm when administered to pregnant women or whether it can affect reproductive capacity. If a woman receiving niacin for primary hyperlipidemia becomes pregnant, the drug should be discontinued. If a woman being treated with niacin for hypertriglyceridemia conceives, the benefits and risks of continued therapy should be assessed on an individual basis. All statins are contraindicated in pregnant and nursing women. When niacin extended-release tablets are administered with a statin in a woman of childbearing potential, refer to the pregnancy category and product labeling for the statin.

### 8.3 Nursing Mothers

Niacin is excreted into human milk but the actual infant dose or infant dose as a percent of the maternal dose is not known. Because of the potential for serious adverse reactions in nursing infants from lipid-altering doses of nicotinic acid, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. No studies have been conducted with niacin extended-release tablets in nursing mothers.

### 8.4 Pediatric Use

Safety and effectiveness of niacin therapy in pediatric patients (≤ 16 years) have not been established.

### 8.5 Geriatric Use

Of 979 patients in clinical studies of niacin extended-release tablets, 21% of the patients were age 65 and over. No overall differences in safety and effectiveness were observed between these patients and younger patients, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

### 8.6 Renal Impairment

No studies have been performed in this population. Niacin extended-release tablets should be used with caution in patients with renal impairment *[see Warnings and Precautions (5)]*.

### 8.7 Hepatic Impairment

No studies have been performed in this population. Niacin extended-release tablets should be used with caution in patients with a past history of liver disease and/or who consume substantial quantities of alcohol. Active liver disease, unexplained transaminase elevations and significant or unexplained hepatic dysfunction are contraindications to the use of niacin extended-release tablets *[see Contraindications (4) and Warnings and Precautions (5.3)]*.

### 8.8 Gender

Data from the clinical trials suggest that women have a greater hypolipidemic response than men at equivalent doses of niacin extended-release tablets.

## 12 CLINICAL PHARMACOLOGY

### 12.3 Pharmacokinetics

**Drug Interactions**

*Lovastatin*

When niacin extended-release tablets 2000 mg and lovastatin 40 mg were coadministered, niacin extended-release tablets increased lovastatin $C_{max}$ and AUC by 2% and 14%, respectively, and decreased lovastatin acid $C_{max}$ and AUC by 22% and 2%, respectively. Lovastatin reduced niacin extended-release tablet bioavailability by 2 to 3% *[see Drug Interactions (7.1)]*.

*Simvastatin*

When niacin extended-release tablets 2000 mg and simvastatin 40 mg were coadministered, niacin extended-release tablets increased simvastatin $C_{max}$ and AUC by 1% and 9%, respectively, and simvastatin acid $C_{max}$ and AUC by 2% and 18%, respectively. Simvastatin reduced niacin extended-release tablet bioavailability by 2% *[see Drug Interactions (7.1)]*.

*Bile Acid Sequestrants*

An *in vitro* study was carried out investigating the niacin-binding capacity of colestipol and cholestyramine. About 98% of available niacin was bound to colestipol, with 10 to 30% binding to cholestyramine *[see Drug Interactions (7.2)]*.

### 14.4 Niacin Extended-Release and Lovastatin Clinical Studies

Combination Niacin Extended-Release and Lovastatin Study: In a multi-center, randomized, double-blind, parallel, 28 week study, a combination tablet of niacin extended-release and lovastatin was compared to each individual component in patients with Type IIa and IIb hyperlipidemia. Using a forced dose-escalation study design, patients received each dose for at least 4 weeks. Patients randomized to treatment with the combination tablet of niacin extended-release and lovastatin initially received 500 mg/20 mg (expressed as mg of niacin/mg of lovastatin) once daily before bedtime. The dose was increased by 500 mg at 4 week intervals (based on the niacin extended-release component) to a maximum dose of 1000 mg/20 mg in one-half of the patients and 2000 mg/40 mg in the other half. The niacin extended-release monotherapy group underwent a similar titration from 500 mg to 2000 mg. The patients randomized to lovastatin monotherapy received 20 mg for 12 weeks titrated to 40 mg for up to 16 weeks. Up to a third of the patients randomized to the combination tablet of niacin extended-release and lovastatin or niacin extended-release monotherapy discontinued prior to Week 28. Results from this study showed that combination therapy decreased LDL-C, TG and Lp(a), and increased HDL-C in a dose-dependent fashion (**Tables 8, 9, 10,** and **11**). Results from this study for LDL-C mean percent change from baseline (the primary efficacy variable) showed that:

1. LDL-lowering with the combination tablet of niacin extended-release and lovastatin was significantly greater than that achieved with lovastatin 40 mg only after 28 weeks of titration to a dose of 2000 mg/40 mg ($p < 0.0001$)
2. The combination tablet of niacin extended-release and lovastatin at doses of 1000 mg/20 mg or higher achieved greater LDL-lowering than niacin extended-release tablets ($p < 0.0001$)

The LDL-C results are summarized in **Table 8**.

**Table 8. LDL-C Mean Percent Change From Baseline**

| Week | Combination Tablet of Niacin Extended-Release and Lovastatin | | | Niacin Extended-Release Tablets | | | Lovastatin | | |
|---|---|---|---|---|---|---|---|---|---|
| | n[a] | Dose (mg/mg) | LDL | n[a] | Dose (mg) | LDL | n[a] | Dose (mg) | LDL |
| Baseline | 57 | – | 190.9 mg/dL | 61 | – | 189.7 mg/dL | 61 | – | 185.6 mg/dL |
| 12 | 47 | 1000/20 | -30% | 46 | 1000 | -3% | 56 | 20 | -29% |
| 16 | 45 | 1000/40 | -36% | 44 | 1000 | -6% | 56 | 40 | -31% |
| 20 | 42 | 1500/40 | -37% | 43 | 1500 | -12% | 54 | 40 | -34% |
| 28 | 42 | 2000/40 | -42% | 41 | 2000 | -14% | 53 | 40 | -32% |

[a] n = number of patients remaining in trial at each time point

Combination therapy achieved significantly greater HDL-raising compared to lovastatin and niacin extended-release tablet monotherapy at all doses (**Table 9**).

**Table 9. HDL-C Mean Percent Change From Baseline**

| Week | Combination Tablet of Niacin Extended-Release and Lovastatin | | | Niacin Extended-Release Tablets | | | Lovastatin | | |
|---|---|---|---|---|---|---|---|---|---|
| | n[a] | Dose (mg/mg) | HDL | n[a] | Dose (mg) | HDL | n[a] | Dose (mg) | HDL |
| Baseline | 57 | – | 45 mg/dL | 61 | – | 47 mg/dL | 61 | – | 43 mg/dL |
| 12 | 47 | 1000/20 | +20% | 46 | 1000 | +14% | 56 | 20 | +3% |
| 16 | 45 | 1000/40 | +20% | 44 | 1000 | +15% | 56 | 40 | +5% |
| 20 | 42 | 1500/40 | +27% | 43 | 1500 | +22% | 54 | 40 | +6% |
| 28 | 42 | 2000/40 | +30% | 41 | 2000 | +24% | 53 | 40 | +6% |

[a] n = number of patients remaining in trial at each time point

In addition, combination therapy achieved significantly greater TG lowering at doses of 1000 mg/20mg or greater compared to lovastatin and niacin extended-release tablet monotherapy (**Table 10**).

**Table 10. TG Median Percent Change From Baseline**

| Week | Combination Tablet of Niacin Extended-Release and Lovastatin | | | Niacin Extended-Release Tablets | | | Lovastatin | | |
|---|---|---|---|---|---|---|---|---|---|
| | n[a] | Dose (mg/mg) | TG | n[a] | Dose (mg) | TG | n[a] | Dose (mg) | TG |
| Baseline | 57 | – | 174 mg/dL | 61 | – | 186 mg/dL | 61 | – | 171 mg/dL |
| 12 | 47 | 1000/20 | -32% | 46 | 1000 | -22% | 56 | 20 | -20% |
| 16 | 45 | 1000/40 | -39% | 44 | 1000 | -23% | 56 | 40 | -17% |
| 20 | 42 | 1500/40 | -44% | 43 | 1500 | -31% | 54 | 40 | -21% |
| 28 | 42 | 2000/40 | -44% | 41 | 2000 | -31% | 53 | 40 | -20% |

[a] n = number of patients remaining in trial at each time point

The Lp(a)-lowering effects of combination therapy and niacin extended-release tablet monotherapy were similar, and both were superior to lovastatin (**Table 11**). The independent effect of lowering Lp(a) with niacin extended-release tablets or combination therapy on the risk of coronary and cardiovascular morbidity and mortality has not been determined.

**Table 11. Lp(a) Median Percent Change From Baseline**

| Week | Combination Tablet of Niacin Extended-Release and Lovastatin | | | Niacin Extended-Release Tablets | | | Lovastatin | | |
|---|---|---|---|---|---|---|---|---|---|
| | n[a] | Dose | Lp(a) (mg/mg) | n[a] | Dose (mg) | Lp(a) | n[a] | Dose (mg) | Lp(a) |
| Baseline | 57 | – | 34 mg/dL | 61 | – | 41 mg/dL | 60 | – | 42 mg/dL |
| 12 | 47 | 1000/20 | -9% | 46 | 1000 | -8% | 55 | 20 | +8% |
| 16 | 45 | 1000/40 | -9% | 44 | 1000 | -12% | 55 | 40 | +8% |
| 20 | 42 | 1500/40 | -17% | 43 | 1500 | -22% | 53 | 40 | +6% |
| 28 | 42 | 2000/40 | -22% | 41 | 2000 | -32% | 52 | 40 | 0% |

[a] n = number of patients remaining in trial at each time point

### 14.4 Niacin Extended-Release and Simvastatin Clinical Studies

In a double-blind, randomized, multicenter, multi-national, active-controlled, 24 week study, the lipid effects of a combination tablet of niacin extended-release and simvastatin were compared to simvastatin 20 mg and 80 mg in 641 patients with type II hyperlipidemia or mixed dyslipidemia. Following a lipid qualification phase, patients were eligible to enter one of two treatment groups. In Group A, patients on simvastatin 20 mg monotherapy, with elevated non-HDL levels and LDL-C levels at goal per the NCEP guidelines, were randomized to one of three treatment arms: combination tablet of niacin extended-release and simvastatin 1000/20 mg, combination tablet of niacin extended-release and simvastatin 2000/20 mg, or simvastatin 20 mg. In Group B, patients on simvastatin 40 mg monotherapy, with elevated non-HDL levels per the NCEP guidelines regardless of attainment of LDL-C goals, were randomized to one of three treatment arms: combination tablet of niacin extended-release and simvastatin 1000/40 mg, combination tablet of niacin extended-release and simvastatin 2000/40 mg, or simvastatin 80 mg. Therapy was initiated at the 500 mg dose of combination tablet of niacin extended-release and simvastatin and increased by 500 mg every four weeks. Thus patients were titrated to the 1000 mg dose of combination tablet of niacin extended-release and simvastatin after four weeks and to the 2000 mg dose of combination tablet of niacin extended-release and simvastatin after 12 weeks. All patients randomized to simvastatin monotherapy received 50 mg immediate-release niacin daily in an attempt to keep the study from becoming unblinded due to flushing in the combination tablet of niacin extended-release and simvastatin groups. Patients were instructed to take one 325 mg aspirin or 200 mg ibuprofen 30 minutes prior to taking the double-blind medication to help minimize flushing effects.

In Group A, the primary efficacy analysis was a comparison of the mean percent change in non-HDL levels between the combination tablet of niacin extended-release and simvastatin 2000/20 mg and simvastatin 20 mg groups, and if statistically significant, then a comparison was conducted between the combination tablet of niacin extended-release and simvastatin 1000/20 mg and simvastatin 20 mg groups. In Group B, the primary efficacy analysis was a determination of whether the mean percent change in non-HDL in the combination tablet of niacin extended-release and simvastatin 2000/40 mg group was non-inferior to the mean percent change in the simvastatin 80 mg group, and if so, whether the mean percent change in non-HDL in the combination tablet of niacin extended-release and simvastatin 1000/40 mg group was non-inferior to the mean percent change in the simvastatin 80 mg group.

In Group A, the non-HDL-C lowering with combination tablet of niacin extended-release and simvastatin 2000/20 and combination tablet of niacin extended-release and simvastatin 1000/20 was statistically significantly greater than that achieved with simvastatin 20 mg after 24 weeks ($p < 0.05$; **Table 12**). The completion rate after 24 weeks was 72% for the combination tablet of niacin extended-release and simvastatin arms and 88% for the simvastatin 20 mg arm. In Group B, the non-HDL-C lowering with combination tablet of niacin extended-release and simvastatin 2000/40 and combination tablet of niacin extended-release and simvastatin 1000/40 was non-inferior to that achieved with simvastatin 80 mg after 24 weeks (**Table 13**). The completion rate after 24 weeks was 78% for the combination tablet of niacin extended-release and simvastatin arms and 80% for the simvastatin 80 mg arm.

The combination tablet of niacin extended-release and simvastatin was not superior to simvastatin in lowering LDL-C in either Group A or Group B. However, the combination tablet of niacin extended-release and simvastatin was superior to simvastatin in both groups in lowering TG and raising HDL (**Tables 14** and **15**).

**Table 12. Non-HDL Treatment Response Following 24 Week Treatment Mean Percent Change From Simvastatin 20 mg Treated Baseline**

| Group A | Combination Tablet of Niacin Extended-Release and Simvastatin 2000/20 | | | | Combination Tablet of Niacin Extended-Release and Simvastatin 1000/20 | | | | Simvastatin 20 | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Week | n[a] | Dose (mg/mg) | Non-HDL[b] | | n[a] | Dose (mg/mg) | Non-HDL[b] | | n[a] | Dose (mg/mg) | Non-HDL[b] |
| Baseline | 56 | – | 163.1 mg/dL | | 108 | – | 164.8 mg/dL | | 102 | – | 163.7 mg/dL |
| 4 | 52 | 500/20 | -12.9% | | 86 | 500/20 | -12.8% | | 91 | 20 | -8.3% |
| 8 | 46 | 1000/20 | -17.5% | | 91 | 1000/20 | -15.5% | | 95 | 20 | -8.3% |
| 12 | 46 | 1500/20 | -18.9% | | 90 | 1000/20 | -14.8% | | 96 | 20 | -6.4% |
| 24 | 40 | 2000/20 | -19.5%[c] | | 78 | 1000/20 | -13.6%[c] | | 90 | 20 | -5% |
| Dropouts by Week 24: | 28.6% | | | | 27.8% | | | | 11.8% | | |

[a] n = number of subjects with values in the analysis window at each timepoint

[b] The percent change from baseline is the model-based mean from a repeated measures mixed model with no imputation for missing data from study dropouts.

[c] significant vs. simvastatin 20 mg at the primary endpoint (Week 24), $p < 0.05$

**Table 13. Non-HDL Treatment Response Following 24 Week Treatment Mean Percent Change From Simvastatin 40 mg Treated Baseline**

| Group B | Combination Tablet of Niacin Extended-Release and Simvastatin 2000/40 | | | | Combination Tablet of Niacin Extended-Release and Simvastatin 1000/40 | | | | Simvastatin 80 | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Week | n[a] | Dose (mg/mg) | Non-HDL[b] | | n[a] | Dose (mg/mg) | Non-HDL[b] | | n[a] | Dose (mg/mg) | Non-HDL[b] |
| Baseline | 98 | – | 144.4 mg/dL | | 111 | – | 141.2 mg/dL | | 113 | – | 134.5 mg/dL |
| 4 | 96 | 500/40 | -6% | | 108 | 500/40 | -5.9% | | 110 | 80 | -11.3% |
| 8 | 93 | 1000/40 | -15.5% | | 100 | 1000/40 | -16.2% | | 104 | 80 | -13.7% |
| 12 | 90 | 1500/40 | -18.4% | | 97 | 1000/40 | -12.6% | | 100 | 80 | -9.5% |
| 24 | 80 | 2000/40 | -7.6%[c] | | 82 | 1000/40 | -6.7%[d] | | 90 | 80 | -6% |
| Dropouts by week 24: | 18.4% | | | | 26.1% | | | | 20.4% | | |

[a] n = number of subjects with values in the analysis window at each timepoint

[b] The percent change from baseline is the model-based mean from a repeated measures mixed model with no imputation for missing data from study dropouts.

[c] non-inferior to simvastatin 80 arm; 95% confidence interval of mean difference in non-HDL for the combination tablet of niacin extended-release and simvastatin 2000/40 vs. simvastatin 80 is (-7.7%, 4.5%)

[d] non-inferior to simvastatin 80 arm; 95% confidence interval of mean difference in non-HDL for combination tablet of niacin extended-release and simvastatin 1000/40 vs. combination tablet of niacin extended-release and simvastatin 80 is (-6.6%, 5.3%)

**Table 14. Mean Percent Change From Baseline to Week 24 in Lipoprotein Lipid Levels**

| | Treatment Group A | | | | | |
|---|---|---|---|---|---|---|
| TREATMENT | N | LDL-C | Total-C | HDL-C | TG[a] | Apo B |
| Baseline (mg/dL)[b] | 266 | 120 | 207 | 43 | 209 | 102 |
| Simvastatin 20 mg | 102 | -6.7% | -4.5% | 7.8% | -15.3% | -5.6% |
| Combination Tablet of Niacin Extended-Release and Simvastatin 1000/20 | 108 | -11.9% | -8.8% | 20.7% | -26.5% | -13.2% |
| Combination Tablet of Niacin Extended-Release and Simvastatin 2000/20 | 56 | -14.3% | -11.1% | 29% | -38% | -18.5% |

[a] medians are reported for TG

[b] either treatment naïve or after receiving simvastatin 20 mg

**Table 15. Mean Percent Change From Baseline to Week 24 in Lipoprotein Lipid Levels**

| | Treatment Group B | | | | | |
|---|---|---|---|---|---|---|
| TREATMENT | N | LDL-C | Total-C | HDL-C | TG[a] | Apo B |
| Baseline (mg/dL)[b] | 322 | 108 | 187 | 47 | 145 | 93 |
| Simvastatin 80 mg | 113 | -11.4% | -6.2% | 0.1% | 0.3% | -7.5% |
| Combination Tablet of Niacin Extended-Release and Simvastatin 1000/40 | 111 | -7.1% | -3.1% | 15.4% | -22.8% | -7.7% |
| Combination Tablet of Niacin Extended-Release and Simvastatin 2000/40 | 98 | -5.1 | -1.6% | 24.4% | -31.8% | -10.5% |

[a] medians are reported for TG

[b] after receiving simvastatin 40 mg

## 17 PATIENT COUNSELING INFORMATION

### 17.1 Patient Counseling

Patients should be advised to adhere to their National Cholesterol Education Program (NCEP) recommended diet, a regular exercise program, and periodic testing of a fasting lipid panel.

Patients should be advised to inform other healthcare professionals prescribing a new medication that they are taking niacin extended-release tablets.

The patient should be informed of the following:

**Dosing Time**

Niacin extended-release tablets should be taken at bedtime, after a low-fat snack. Administration on an empty stomach is not recommended.

**Tablet Integrity**

Niacin extended-release tablets should not be broken, crushed or chewed, but should be swallowed whole.

**Dosing Interruption**

If dosing is interrupted for any length of time, their physician should be contacted prior to restarting therapy; re-titration is recommended.

**Muscle Pain**

Notify their physician of any unexplained muscle pain, tenderness, or weakness promptly. They should discuss all medication, both prescription and over the counter, with their physician.

**Flushing**

Flushing (warmth, redness, itching and/or tingling of the skin) is a common side effect of niacin therapy that may subside after several weeks of consistent niacin extended-release tablet use. Flushing may vary in severity and is more likely to occur with initiation of therapy, or during dose increases. By dosing at bedtime, flushing will most likely occur during sleep. However, if awakened by flushing at night, the patient should get up slowly, especially if feeling dizzy, feeling faint, or taking blood pressure medications. Advise patients of the symptoms of flushing and how they differ from the symptoms of a myocardial infarction.

**Use of Aspirin Medication**

Taking aspirin (up to the recommended dose of 325 mg) approximately 30 minutes before dosing can minimize flushing.

**Diet**

Avoid ingestion of alcohol, hot beverages and spicy foods around the time of taking niacin extended-release tablets to minimize flushing.

**Supplements**

Notify their physician if they are taking vitamins or other nutritional supplements containing niacin or nicotinamide.

**Dizziness**

Notify their physician if symptoms of dizziness occur.

**Diabetics**

If diabetic, to notify their physician of changes in blood glucose.

**Pregnancy**

Discuss future pregnancy plans with your patients, and discuss when to stop niacin extended-release tablets if they are trying to conceive. Patients should be advised that if they become pregnant, they should stop taking niacin extended-release tablets and call their healthcare professional.

**Breastfeeding**

Women who are breastfeeding should be advised to not use niacin extended-release tablets. Patients, who have a lipid disorder and are breastfeeding, should be advised to discuss the options with their healthcare professional.

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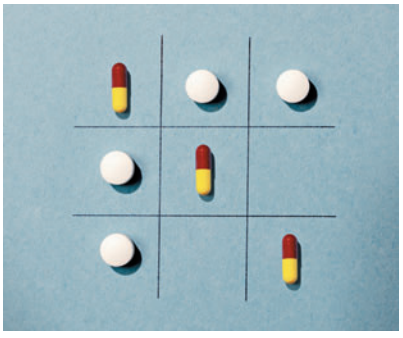

To keep their pharmacies alive and well, independent pharmacists need to plan their moves strategically. Three successful advocates for pharmacy causes tell us how it's done. PAGE 28

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Part 2 of this mini-series focuses on selection of pharmacologic treatment options in the management of osteoporosis, as well as on issues in prevention and treatment. **PAGE 36**



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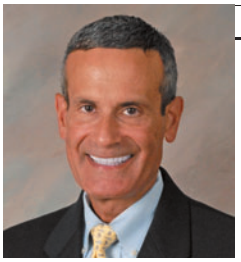

**DISPENSED AS WRITTEN**

Ernest Dole, PharmD, PhC, FASHP, BCPS; Jeffrey Fudin, BS, PharmD, DAAPM, FCCP

# Pharmacists speak out

## The AMA's "drug store intrusion" resolution and Walgreens' "good faith dispensing" policy

At its last House of Delegates meeting, the American Medical Association (AMA) introduced a resolution, "AMA response to drug store intrusion into medical practice, Resolution 218 (A-13)." Representing AMA in a public statement, Orange County delegate Dr. Melvyn Sterling had a message for pharmacists: "Don't call us, we'll call you!"

While subsequent communications with AMA members and staffers indicate disagreement with Sterling's comment, the situation set many pharmacists to gnashing their teeth and rattling their sabers against their physician colleagues.[1]

Professional pharmacy organizations, pharmacists, and physicians alike have weighed in on this issue, stating the need for collaboration between our professions to provide the best patient care possible. Professional organizations have cited the central issue precipitating this communication crisis as one of prescription drug abuse and resultant deaths.[2]

However, the title of the AMA resolution targets "drug store intrusion" and is specifically directed at Walgreens Corp. for implementation of its "good faith dispensing" (GFD) policy addressing opioid prescriptions for chronic pain.

We believe that AMA Resolution 218 (A-13) is directed *not* against pharmacists per se, but against Walgreens, which is using its pharmacists as pawns to satisfy internal requirements set forth in a deal with the Drug Enforcement Agency (DEA).[3] Walgreens, the "drug store" that lit this fuse, has emerged remarkably unscathed.

### The backstory

After a dramatic increase in the number of oxycodone doses dispensed by Walgreens pharmacies in Florida, Walgreens and the U.S. Drug Enforcement Agency (DEA) entered into a Memorandum of Agreement (MOA) in the fall of 2011.[4] It appears that as a result of this MOA, Walgreens implemented its good faith dispensing (GFD) policy.

Misinformation has accompanied the implementation of this policy. This is exemplified in a "Dear Provider" letter that attempts to explain why Walgreens pharmacists are compelled to telephone providers and ensure that "the necessary information to confirm the appropriateness of the prescription is documented to satisfy the DEA requirements."[5] However, the DEA has issued no such "requirements" for the filling of prescriptions, as Walgreens' "Dear Provider" letter claims.

To further cloud the issue, Walgreens' GFD policy is based on federal law, implying that this policy should be implemented on a consistent basis across the country. The reality is that the corporate GFD is applied inconsistently between states, and in a manner that amounts to "profiling" a state. In New York state, we have learned, Walgreens' GFD has been implemented in a manner that is not at all obstructive to patient care. However, we have discovered the opposite in states such as California, Florida, Indiana, and New Mexico.

### The consequences

The heart of the GFD policy is Title 21 of the *Code of Federal Regulations*, Section 1306.4, which states that pharmacists have a corresponding responsibility to ensure that when a prescription for a controlled substance is dispensed, the dispensing must be done for a legitimate medical purpose.[6] This is appropriate, valid, and justified; it is part of a pharmacist's responsibility.

However, Walgreens' GFD policy has compromised its pharmacists' ability to make a free-will professional interpretation and, ironically, places patient safety at risk.[7] This policy obstructs the delivery of patient medications, as it requires the gathering of medical chart information above and beyond requirements set forth by any state or federal regulations, prior to the dispensing of an opioid prescription for chronic pain.

If Walgreens honestly believed in the validity of that policy, pharmacists would also be required to obtain routine labora-

Continued on pg. 10

# Pharmacists speak out

Continued from pg. 9

tory monitoring tests prior to dispensing statins, hypoglycemic agents, and antibiotics, for example. The thought is absurd!

## Absence of accountability

The most unsettling element of Walgreens' GFD policy is that, while it promotes the concept of "corresponding responsibility," there is no advocacy for "corresponding accountability" on the part of the Walgreens pharmacist.

The question remains as to how a Walgreens pharmacist would be held accountable for "prescribing by omission" if an adverse event occurred through the withholding or delay of a patient's opioid prescription resulting from Walgreens' GFD policy.

Imagine a parallel situation, in which a patient becomes hyperglycemic because the pharmacist didn't have glucose levels and refused to fill a prescription for an oral hypoglycemic agent.

Or consider this: As a result of Walgreens' previous irresponsible dispensing behaviors, the GFD policy is stigmatizing chronic pain patients, through no fault of legitimate pain patients themselves or of the doctors and pharmacists caring for them.

## The real issue

When the above facts are elucidated, it is quite clear that behind the rhetoric of AMA Resolution 218 (A-13), the issue is not that of physicians striking out at pharmacists[1]; to the contrary, it is Walgreens Corp. itself that is being condemned.

This is not simply an issue of "prescription drug abuse." More precisely, it is the result of corporate "drug store intrusion" into patient therapy. The pharmacist's healthcare role in this instance is not being defined by our knowledge, collaboration, clinical expertise, and direct patient-care contributions, but by irresponsible and selfish corporate policy arising from an effort to satisfy previous misgivings and corporate greed, in an escalating lack of due diligence.

The issue of the necessity for advance information to be obtained before an opioid prescription can be safely dispensed is distracting from a deeper conflict.

## The business model

Walgreens' actions here are not based on the contemporary clinical role of pharmacists; they are focused on a singular business model that exudes patient neglect — not safety, as Walgreens claims.

This distinction is critically important. It speaks to a duality with which the pharmacy profession has struggled for decades.

The practice of pharmacy based on a *healthcare* model places the patient first, incorporates clinical knowledge, and enables the pharmacist to act in a fully collegial, collaborative manner with other healthcare providers in order to deliver the best patient care possible.

The pharmacy profession needs to realize the uncomfortable truth: that in this particular case, Walgreens reflects the worst that the pharmacy *business* model has to offer.

Before we see further erosion between medical and pharmacy colleagues, and further decline of the societal covenant between pharmacy and our patients, there must be careful and heartfelt examination of this crisis.

Today we call upon our professional organizations to support our colleagues who are Walgreens pharmacists on the front lines and caught in the corporate crossfire, as well as all pharmacy colleagues nationwide and, most important, the patients who heretofore confidently relied on pharmacist professionalism and integrity. DT

### References


1. AMA House of Delegates, Resolution 218 ( A-13), "AMA response to drug store intrusion into medical practice," May 17, 2013. *http://bit.ly/ama2013res*.
2. "Pharmacists feeling pain over AMA resolution. Physician group blasts profession's 'intrusion into medical practice.'" *Pharmacy Practice News*, August 2013, Vol. 40. *http://bit.ly/pharmsrespond*. Accessed August 12, 2013.
3. Houck LK. "AMA tells pharmacists: 'Don't call us, we'll call you.'" *http://bit.ly/dontcallus*. FDA Law Blog; Hyman, Phelps, & McNamara, PC. Accessed August 12, 2013.
4. U.S. DEA. "DEA serves a suspension order on Walgreens distribution center in Jupiter, Florida." *http://bit.ly/wagsuspend*. Accessed April 26, 2013.
5. Walgreens Corp. Good Faith Dispensing provider letter. *http://bit.ly/wagletter*. Received April 27, 2013.
6. *Code of Federal Regulations*, Title 21, section 1306.4. *http://bit.ly/CFR1306*. Accessed April 26, 2013.
7. Walgreens Corp. Controlled Substance Prescriptions & Good Faith Dispensing Policy. Revised June 11, 2012. *http://www.ncmedsoc.org/*.



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# Voices

**What's the message?**

Regarding Gary Einsidler's letter to the editor in the August issue of *Drug Topics* ["Pharmacy tobacco bans don't work"]:

I agree with him that people who want to purchase tobacco products will go to other vendors if they cannot buy these products in pharmacies.

However, we need to consider one of the founding principles of our profession: We are pledged to act with "conviction of conscience dedicated to the best interests of our patients."

In light of that premise, how can we justify selling tobacco products on one aisle and medications that treat the consequences of using such products on another? Is that not a conflict of interest? What message are we sending to our patients? Is the financial bottom line more important then our concern for our patients' health?

One consequence of the Affordable Care Act is that pharmacists are going to be needed to help provide healthcare services to millions of people who will now have healthcare coverage. Our profession is finally acquiring equal status with other healthcare disciplines that already have unquestioned membership on the healthcare team.

For the healthcare team approach to work, our primary concern must be the welfare of our patients. Otherwise, how can we expect to claim the respect and trust of our partners on the team?

Cancer-producing tobacco products do not belong in our pharmacies. In San Francisco and in Marin County, where I serve as president of the Marin County Pharmacists Association, pharmacy tobacco sales have been outlawed since 2008. If the only way to get tobacco products out of pharmacies in the United States is by government ban, then so be it.

*Aglaia Panos, PharmD*
MARIN, CALIFORNIA

**Fries with that?**

I'm still applauding Jim Plagakis' [June] column, "Apply sparingly to right ear until nurse stops shouting." It conjured so many specters of pharmacy's past that I had to ask, "Where did the healthcare system go wrong?" This question has so many facets and layers of context that it would make anyone's head spin, but my question specifically refers to the poor treatment other healthcare professionals give to highly educated professionals like pharmacists.

I have long equated being a pharmacist with being a manager at a fast-

Continued on pg. 24

**STUDENT CORNER** Amy Ng, PharmD Candidate 2014

# The pros and cons of OTC, Rx weight-loss products

During my public health rotation, I performed MTM at various brown-bag events, where I noticed that a few of my diabetic patients were on the heavier side. When I asked about their diet and exercise regimens, I received sheepish replies such as "Yeah, it's just hard." These patients were well aware of the need for exercise and healthy eating; what they wanted to know was whether they really could get a boost from products like Hydroxycut or Alli.

Numerous products offering quick pound-shaving results line the shelves of pharmacies nationwide. But do consumers know how these products work? And how do these products affect those among the diabetic population who struggle to lose weight?

## Is this safe?

Popular weight-loss supplements such as Hydroxycut, Zantrex-3, and Cortislim are promoted as offering "natural" alternatives to similar products. These "natural" formulations rely on a proprietary blend of herbal, root, and/or fruit extracts. Key ingredients include green tea, caffeine, guarana, and/or ginseng, which are used to stimulate the body's metabolism, in order to burn more fat.

Green tea has no harmful effects, and a systematic review has indicated that caffeine actually decreases the risk of type 2 diabetes. However, other ingredients that are included in these blends make them potentially dangerous.

For example, in the case of diabetic patients with other cardiovascular co-morbidities requiring them to take warfarin, ginseng can decrease the blood-thinner's effects, resulting in a greater risk of blood clots.

## Other considerations

FDA has discouraged the use of Hydroxycut after receiving reports of liver damage and rhabdomylosis, a condition that damages the muscles and leads to kidney injury; this is particularly hazardous for patients with diabetes who already have a heightened risk of kidney injury.

In February 2013 FDA recalled Maxiloss Weight Advanced Softgels, found to contain a hidden drug known as sibutramine, a substance that elevates blood pressure and increases risk of heart disease. Diabetic patients who are overweight or obese are already at a greater risk than the general population for cardiovascular diseases such as heart failure or stroke.

Because these products have not been tested for long-term safety and efficacy, one never knows when the next "blended solution" will be recalled.

Then there is Alli. Alli is the only prescription medication approved by FDA for long-term use in weight reduction. It works by inhibiting the absorption of dietary fat.

On the other hand, this proven product comes with a price: a whole slew of side effects, including abdominal discomfort, flatulence with discharge, fecal urgency, and oily stool. Despite those potential consequences, this drug does not require renal adjustment if the patient's kidneys are bad, and it has almost no drug-drug interactions.

In addition, a number of clinical trials have shown Alli to be effective in supporting weight reduction in obese patients with type 2 diabetes, especially when it was used as an adjunct to healthy lifestyle changes.

## Patient resource

The weight-loss product niche is a marketing gold mine. Every year we will see something new come out to take advantage of the huge demographic of potential users.

It is our duty as pharmacists to stay on top of these trending drugs to better inform and protect the public.

Providing education is one of our key roles. Since we are easily accessible healthcare providers, we are able to respond to doubts and answer queries about these weight-loss products and ultimately empower patients to take charge of their conditions. DT

**Amy Ng** *is a 2014 PharmD candidate at Touro University College of Pharmacy in Vallejo, Calif. Contact her at amy.ng@tu.edu.*


## No other BTC product relieves more cold and sinus symptoms

The only behind-the-counter (BTC) cold and sinus liquid gel that delivers pseudoephedrine with a pain reliever, cough suppressant, and antihistamine.


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**IN MY VIEW** Larry LaBenne, PharmD; Emily E. Smith, PharmD Cand.

# Acetaminophen awareness: A community survey

Martin's Pharmacy, DuBois, Penn., is a rural grocery-store pharmacy, part of a chain of stores in the New England and Mid-Atlantic states. This past summer we conducted a small, (n=50) community-pharmacy-based study to assess patient awareness of acetaminophen.

Pharmacy intern Emily Smith surveyed the randomly selected participants and created an educational brochure for participants who completed the survey. Designed to help patients identify products containing acetaminophen, the brochure emphasized the importance of pharmacist consults to ensure safe and proper use.

## The need

We created the survey because we saw an unmet need. An extensive literature search yielded no similar studies conducted at the level of community pharmacy. With acetaminophen use so extensive and related poisonings frequent, we wanted to help minimize the local potential for accidental acetaminophen overdose.

Acetaminophen is the most commonly used analgesic in the United States, with an estimated 25+ billion doses consumed annually. While it is well established that acetaminophen is safe in therapeutic doses, acetaminophen overdose remains the most common type of poisoning in the world, with significant morbidity and mortality resulting from its hepatotoxicity. Accidental overdose most often results from unknowing simultaneous use of two or more acetaminophen-containing products and/or improper dosing, as well as unsupervised ingestion by young children.

## The study

Participants were randomly selected at the pharmacy counter. The 12-question survey sought to assess patients' ability to identify acetaminophen on OTC and prescription labels, to follow conventional dosing instructions, to identify products that have the same active ingredient as Tylenol, and to determine when acetaminophen use is or is not appropriate.

The results of the survey raised significant concerns. Only 42% of the respondents could name the active ingredient in the OTC medication(s) they took regularly, and 34% failed to recognize acetaminophen as synonymous with Tylenol, while 24% mistakenly identified other common OTC active ingredients as synonymous with Tylenol. Alarmingly, only 42% of respondents correctly identified the maximum daily dose as 4,000 mg. Most alarmingly, 70% failed to recognize the widely used APAP abbreviation as synonymous with Tylenol and/or acetaminophen on images of actual pharmacy labels.

## The takeaway

Although the study size was limited, it reflects similar results found by many other studies, indicating that significant potential exists for accidental acetaminophen overdose by patients who are insufficiently aware and informed. Patients must be more aware of which products contain acetaminophen as well as how to use them safely and appropriately.

Significant opportunities exist for pharmacists to educate patients on how to avoid acetaminophen toxicity. Patients who receive Rx products containing acetaminophen should be screened for concurrent use of OTC products, and vice versa. Possible concurrent administration should be kept firmly in mind when a prescription product bearing the APAP abbreviation on the label is dispensed.

In our pharmacy, we are more vigilant than ever about counseling on every Rx acetaminophen product we dispense. Just saying, "This product contains Tylenol, also know as acetaminophen. Do not take with any other products that contain the same active ingredient," can help prevent overdose. And we are making signs for the OTC aisle that urge patients not to guess when it comes to Tylenol/acetaminophen products, but to ask the pharmacist for advice.

The circumstances surrounding accidental acetaminophen overdose are many, and therefore prevention strategies need to be equally diverse. However, data on the circumstances surrounding accidental overdose are limited, which could make prevention strategies difficult.

For the next phase of this study, we want to make our survey available to pharmacists throughout the country in a form that can be submitted to us electronically. Data generated by the ongoing study will help us to better identify the circumstances surrounding accidental acetaminophen overdose. DT

**Larry LaBenne, PharmD,** *is staff pharmacist with Martin's Pharmacy in DuBois, Penn. For links to the survey and brochure, contact him at larrylabenne.rx@gmail.com.*

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# Drug Topics

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**VIEW FROM THE ZOO** David Stanley, RPh

# The small-business owner's BFF

When I was a child, I had an imaginary friend. Now that I'm an adult, I have an artificial one … I'm starting off this month's column with that statement not to spark an inquiry into the state of my mental health, but to answer the most common question I've received since I took over my drugstore, namely, "Where do you start?"

## Get hooked up

Remember my column from a few months back, the one that pointed out how the corporate structures of the giant chains made it possible for them to put massive amounts of controlled substances onto the streets with ease *and* escape with a penalty far less than the one an actual human being would have incurred for doing the exact same thing?

Well, it may surprise you to learn that the first thing I did when I went into business for myself was to set up a corporation, an "artificial person," as it were, which legally owns my store.

My corporation won't be issuing shares on the New York Stock Exchange anytime soon, and I doubt that it will ever be able to employ an army of lobbyists to roam the halls of Capitol Hill advocating for its interests, but having an artificial self does offer some advantages for the small business owner. For starters, I can pay myself less than I made toiling for the chains.

You read that right. Before you are tempted again to question my mental health, let me explain that as the sole shareholder, as well as president, CEO, treasurer, and secretary of my little S-corp (not to mention chief janitor and lightbulb-changer), I'll be compensated in two different ways.

First, I'll make a salary that was negotiated with my head of human resources, who also happens to be me. Second, as holder of all my corporation's shares, I'll be entitled to whatever profits come rolling in. Take a look at what you pay in taxes on your salary vs. how federal and state government treats corporate profits, and chances are you'll see why it might not always pay to be a really hard-nosed negotiator when it comes to setting a salary rate.

## The front

There may also be times when it comes in handy for an artificial person to be legally responsible for your business affairs.

When I was deciding how I wanted to structure my business, my lawyer told me about a case he was familiar with, that of a pharmacist who had set up his store as a sole proprietorship.

This pharmacist was subject to a routine third-party audit, which found some claims that were disallowed. The pharmacist didn't dispute the claims, and he had every intention of paying the amount in question, but for whatever reason, he was negligent in sending in the money.

Interest accumulated, and then interest on top on interest, until the pharmacist was looking at losing his house, as well as every other asset he owned, because he was personally responsible for everything the business did.

Of course I'll be making every effort to stay on top of my bills, but hearing that story made me glad that my car is registered under my name and not that of the business.

I love my car so much I gave it a name, which I guess means maybe I still do have an imaginary friend.

## This pal hangs in

So if you're at the point where I was a year ago, looking to cut your link to the chains that weigh down your ability to practice the profession the way you were trained, your first step just might be to create an artificial friend to stand beside you as you start your journey.

Don't expect any politicians to fall over themselves granting you favors, the way so many do when a big-box retailer comes to town. Nonetheless, there are advantages, not the least of them that a stock certificate from your own company, which looks pretty good in a frame on your office wall.

What to do, though, with any imaginary friends you still have, may be something to discuss with your doctor. DT

**David Stanley** *is a pharmacy owner, blogger, and professional writer in northern California. Contact him at drugmonkeyrph@gmail.com.*

*While all albuterol may be the same*

# ONE QUICK-RELIEF INHALER IS DIFFERENT


## ProAir® HFA (albuterol sulfate) offers a complete package of helpful features including a built-in dose counter[1]

- Patients know how many puffs are left[1] and when to refill
- A longer-duration, less forceful, warmer plume[2] may give patients more time to inhale
- Storage flexibility and portability[1,3,4] means no need to reprime if dropped

ProAir HFA (albuterol sulfate) Inhalation Aerosol is indicated in patients 4 years of age and older for the treatment or prevention of bronchospasm with reversible obstructive airway disease and for the prevention of exercise-induced bronchospasm.

## Important Safety Information

- Inhaled albuterol sulfate can produce paradoxical bronchospasm that may be life-threatening. It should be recognized that paradoxical bronchospasm, when associated with inhaled formulations, frequently occurs with the first use of a new canister
- Fatalities have been reported in association with excessive use of inhaled sympathomimetic drugs in patients with asthma
- ProAir HFA, as with all sympathomimetic amines, should be used with caution in patients with cardiovascular disorders (especially coronary insufficiency, cardiac arrhythmias, and hypertension), convulsive disorders, hyperthyroidism, and diabetes
- Potential drug interactions can occur with beta-blockers, diuretics, digoxin, or monoamine oxidase inhibitors, and tricyclic antidepressants
- Do not exceed the recommended dose
- Adverse events, which occurred at an incidence rate of at least 3% with ProAir HFA, include headache, tachycardia, pain, dizziness, pharyngitis, and rhinitis

**Please see Brief Summary of Prescribing Information on next 2 pages.**

To learn more about ProAir HFA, visit
**ProAirHFA.com/hcp**

PROAIR® HFA
(albuterol sulfate) Inhalation Aerosol

***The difference is in the design***

**References: 1.** ProAir HFA Prescribing Information. Horsham, PA: Teva Respiratory, LLC; May 2012. **2.** McCabe JC, Koppenhagen F, Blair J, Zeng X-M. ProAir HFA delivers warmer, lower-impact, longer-duration plumes containing higher fine particle dose than Ventolin® HFA. *J Aerosol Med Pulm Drug Deliv.* 2012;25(2):104-109. **3.** Everard ML, Devadason SG, Summers QA, Le Souëf PN. Factors affecting total and "respirable" dose delivered by a salbutamol metered dose inhaler. *Thorax.* 1995;50(7):746-749. **4.** Graham SJ, Ormsby ED, Lovering EG. Single spray drug content in a metered-dose aerosol formulation and a collection scheme for content uniformity. *Pharm Forum.* 1992;18(6):4400-4403.

TEVA Respiratory

**BRIEF SUMMARY OF PRESCRIBING INFORMATION FOR PROAIR® HFA (ALBUTEROL SULFATE) INHALATION AEROSOL**
For Oral Inhalation Only

**SEE PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION**

## 1 INDICATIONS AND USAGE

### 1.1 Bronchospasm

PROAIR HFA Inhalation Aerosol is indicated for the treatment or prevention of bronchospasm in patients 4 years of age and older with reversible obstructive airway disease.

### 1.2 Exercise-Induced Bronchospasm

PROAIR HFA Inhalation Aerosol is indicated for the prevention of exercise-induced bronchospasm in patients 4 years of age and older.

## 4 CONTRAINDICATIONS

PROAIR HFA Inhalation Aerosol is contraindicated in patients with a history of hypersensitivity to albuterol and any other PROAIR HFA Inhalation Aerosol components. Rare cases of hypersensitivity reactions, including urticaria, angioedema, and rash have been reported after the use of albuterol sulfate *[see **Warnings and Precautions (5.6)**]*.

## 5 WARNINGS & PRECAUTIONS

### 5.1 Paradoxical Bronchospasm

PROAIR HFA Inhalation Aerosol can produce paradoxical bronchospasm that may be life threatening. If paradoxical bronchospasm occurs, PROAIR HFA Inhalation Aerosol should be discontinued immediately and alternative therapy instituted. It should be recognized that paradoxical bronchospasm, when associated with inhaled formulations, frequently occurs with the first use of a new canister.

### 5.2 Deterioration of Asthma

Asthma may deteriorate acutely over a period of hours or chronically over several days or longer. If the patient needs more doses of PROAIR HFA Inhalation Aerosol than usual, this may be a marker of destabilization of asthma and requires re-evaluation of the patient and treatment regimen, giving special consideration to the possible need for anti-inflammatory treatment, e.g., corticosteroids.

### 5.3 Use of Anti-inflammatory Agents

The use of beta-adrenergic-agonist bronchodilators alone may not be adequate to control asthma in many patients. Early consideration should be given to adding anti-inflammatory agents, e.g., corticosteroids, to the therapeutic regimen.

### 5.4 Cardiovascular Effects

PROAIR HFA Inhalation Aerosol, like other beta-adrenergic agonists, can produce clinically significant cardiovascular effects in some patients as measured by pulse rate, blood pressure, and/or symptoms. Although such effects are uncommon after administration of PROAIR HFA Inhalation Aerosol at recommended doses, if they occur, the drug may need to be discontinued. In addition, beta-agonists have been reported to produce ECG changes, such as flattening of the T wave, prolongation of the QTc interval, and ST segment depression. The clinical significance of these findings is unknown. Therefore, PROAIR HFA Inhalation Aerosol, like all sympathomimetic amines, should be used with caution in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias, and hypertension.

### 5.5 Do Not Exceed Recommended Dose

Fatalities have been reported in association with excessive use of inhaled sympathomimetic drugs in patients with asthma. The exact cause of death is unknown, but cardiac arrest following an unexpected development of a severe acute asthmatic crisis and subsequent hypoxia is suspected.

### 5.6 Immediate Hypersensitivity Reactions

Immediate hypersensitivity reactions may occur after administration of albuterol sulfate, as demonstrated by rare cases of urticaria, angioedema, rash, bronchospasm, anaphylaxis, and oropharyngeal edema. The potential for hypersensitivity must be considered in the clinical evaluation of patients who experience immediate hypersensitivity reactions while receiving PROAIR HFA Inhalation Aerosol.

### 5.7 Coexisting Conditions

PROAIR HFA Inhalation Aerosol, like all sympathomimetic amines, should be used with caution in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias, and hypertension; in patients with convulsive disorders, hyperthyroidism, or diabetes mellitus; and in patients who are unusually responsive to sympathomimetic amines. Clinically significant changes in systolic and diastolic blood pressure have been seen in individual patients and could be expected to occur in some patients after use of any beta-adrenergic bronchodilator. Large doses of intravenous albuterol have been reported to aggravate preexisting diabetes mellitus and ketoacidosis.

### 5.8 Hypokalemia

As with other beta-agonists, PROAIR HFA Inhalation Aerosol may produce significant hypokalemia in some patients, possibly through intracellular shunting, which has the potential to produce adverse cardiovascular effects. The decrease is usually transient, not requiring supplementation.

## 6 ADVERSE REACTIONS

Use of PROAIR HFA may be associated with the following:

- Paradoxical bronchospasm *[see **Warnings and Precautions (5.1)**]*
- Cardiovascular Effects *[see **Warnings and Precautions (5.4)**]*
- Immediate hypersensitivity reactions *[see **Warnings and Precautions (5.6)**]*
- Hypokalemia *[see **Warnings and Precautions (5.8)**]*

### 6.1 Clinical Trials Experience

A total of 1090 subjects were treated with PROAIR HFA Inhalation Aerosol, or with the same formulation of albuterol as in PROAIR HFA Inhalation Aerosol, during the worldwide clinical development program.

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

**Adult and Adolescents 12 Years of Age and Older:** The adverse reaction information presented in the table below concerning PROAIR HFA Inhalation Aerosol is derived from a 6-week, blinded study which compared PROAIR HFA Inhalation Aerosol (180 mcg four times daily) with a double-blinded matched placebo HFA-Inhalation Aerosol and an evaluator-blinded marketed active comparator HFA-134a albuterol inhaler in 172 asthmatic patients 12 to 76 years of age. The table lists the incidence of all adverse events (whether considered by the investigator drug related or unrelated to drug) from this study which occurred at a rate of 3% or greater in the PROAIR HFA Inhalation Aerosol treatment group and more frequently in the PROAIR HFA Inhalation Aerosol treatment group than in the matched placebo group. Overall, the incidence and nature of the adverse events reported for PROAIR HFA Inhalation Aerosol and the marketed active comparator HFA-134a albuterol inhaler were comparable.

**Adverse Experience Incidences (% of Patients) in a Six-Week Clinical Trial***

| Body System/Adverse Event (as Preferred Term) | | PROAIR HFA Inhalation Aerosol (N = 58) | Marketed active comparator HFA-134a albuterol inhaler (N = 56) | Matched Placebo HFA-134a Inhalation Aerosol (N = 58) |
|---|---|---|---|---|
| Body as a Whole | Headache | 7 | 5 | 2 |
| Cardiovascular | Tachycardia | 3 | 2 | 0 |
| Musculoskeletal | Pain | 3 | 0 | 0 |
| Nervous System | Dizziness | 3 | 0 | 0 |
| Respiratory System | Pharyngitis | 14 | 7 | 9 |
| | Rhinitis | 5 | 4 | 2 |

* This table includes all adverse events (whether considered by the investigator drug related or unrelated to drug) which occurred at an incidence rate of at least 3.0% in the PROAIR HFA Inhalation Aerosol group and more frequently in the PROAIR HFA Inhalation Aerosol group than in the placebo HFA Inhalation Aerosol group.

Adverse events reported by less than 3% of the patients receiving PROAIR HFA Inhalation Aerosol but by a greater proportion of PROAIR HFA Inhalation Aerosol patients than the matched placebo patients, which have the potential to be related to PROAIR HFA Inhalation Aerosol, included chest pain, infection, diarrhea, glossitis, accidental injury (nervous system), anxiety, dyspnea, ear disorder, ear pain, and urinary tract infection.

In small cumulative dose studies, tremor, nervousness, and headache were the most frequently occurring adverse events.

**Pediatric Patients 4 to 11 Years of Age:** Adverse events reported in a 3-week pediatric clinical trial comparing the same formulation of albuterol as in PROAIR HFA Inhalation Aerosol (180 mcg albuterol four times daily) to a matching placebo HFA inhalation aerosol occurred at a low incidence rate (no greater than 2% in the active treatment group) and were similar to those seen in adult and adolescent trials.

### 6.2 Postmarketing Experience

The following adverse reactions have been identified during postapproval use of PROAIR HFA. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. Reports have included rare cases of aggravated bronchospasm, lack of efficacy, asthma exacerbation (reported fatal in one case), muscle cramps, and various oropharyngeal side-effects such as throat irritation, altered taste, glossitis, tongue ulceration, and gagging.

The following adverse events have been observed in postapproval use of inhaled albuterol: urticaria, angioedema, rash, bronchospasm, hoarseness, oropharyngeal edema, and arrhythmias (including atrial fibrillation, supraventricular tachycardia, extrasystoles). In addition, albuterol, like other sympathomimetic agents, can cause adverse reactions such as: angina, hypertension or hypotension, palpitations, central nervous system stimulation, insomnia, headache, nervousness, tremor, muscle cramps, drying or irritation of the oropharynx, hypokalemia, hyperglycemia, and metabolic acidosis.

## 7 DRUG INTERACTIONS

Other short-acting sympathomimetic aerosol bronchodilators should not be used concomitantly with PROAIR HFA Inhalation Aerosol. If additional adrenergic drugs are to be administered by any route, they should be used with caution to avoid deleterious cardiovascular effects.

**7.1 Beta-Blockers**

Beta-adrenergic-receptor blocking agents not only block the pulmonary effect of beta-agonists, such as PROAIR HFA Inhalation Aerosol, but may produce severe bronchospasm in asthmatic patients. Therefore, patients with asthma should not normally be treated with beta-blockers. However, under certain circumstances, e.g., as prophylaxis after myocardial infarction, there may be no acceptable alternatives to the use of beta-adrenergic-blocking agents in patients with asthma. In this setting, consider cardioselective beta-blockers, although they should be administered with caution.

**7.2 Diuretics**

The ECG changes and/or hypokalemia which may result from the administration of non-potassium sparing diuretics (such as loop or thiazide diuretics) can be acutely worsened by beta-agonists, especially when the recommended dose of the beta-agonist is exceeded. Although the clinical significance of these effects is not known, caution is advised in the coadministration of beta-agonists with non-potassium sparing diuretics. Consider monitoring potassium levels.

**7.3 Digoxin**

Mean decreases of 16% and 22% in serum digoxin levels were demonstrated after single dose intravenous and oral administration of albuterol, respectively, to normal volunteers who had received digoxin for 10 days. The clinical significance of these findings for patients with obstructive airway disease who are receiving albuterol and digoxin on a chronic basis is unclear. Nevertheless, it would be prudent to carefully evaluate the serum digoxin levels in patients who are currently receiving digoxin and PROAIR HFA Inhalation Aerosol.

**7.4 Monoamine Oxidase Inhibitors or Tricyclic Antidepressants**

PROAIR HFA Inhalation Aerosol should be administered with extreme caution to patients being treated with monoamine oxidase inhibitors or tricyclic antidepressants, or within 2 weeks of discontinuation of such agents, because the action of albuterol on the cardiovascular system may be potentiated. Consider alternative therapy in patients taking MAO inhibitors or tricyclic antidepressants.

## 8 USE IN SPECIFIC POPULATIONS

**8.1 Pregnancy**

Teratogenic Effects: Pregnancy Category C:

There are no adequate and well-controlled studies of PROAIR HFA Inhalation Aerosol or albuterol sulfate in pregnant women. During worldwide marketing experience, various congenital anomalies, including cleft palate and limb defects, have been reported in the offspring of patients treated with albuterol. Some of the mothers were taking multiple medications during their pregnancies. No consistent pattern of defects can be discerned, and a relationship between albuterol use and congenital anomalies has not been established. Animal reproduction studies in mice and rabbits revealed evidence of teratogenicity. PROAIR HFA Inhalation Aerosol should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

In a mouse reproduction study, subcutaneously administered albuterol sulfate produced cleft palate formation in 5 of 111 (4.5%) fetuses at an exposure approximately eight-tenths of the maximum recommended human dose (MRHD) for adults on a $mg/m^2$ basis and in 10 of 108 (9.3%) fetuses at approximately 8 times the MRHD. Similar effects were not observed at approximately one-thirteenth of the MRHD. Cleft palate also occurred in 22 of 72 (30.5%) fetuses from females treated subcutaneously with isoproterenol (positive control).

In a rabbit reproduction study, orally administered albuterol sulfate induced cranioschisis in 7 of 19 fetuses (37%) at approximately 630 times the MRHD.

In a rat reproduction study, an albuterol sulfate/HFA-134a formulation administered by inhalation did not produce any teratogenic effects at exposures approximately 65 times the MRHD *[see **Nonclinical Toxicology (13.2)**]*.

**8.2 Labor and Delivery**

Because of the potential for beta-agonist interference with uterine contractility, use of PROAIR HFA Inhalation Aerosol for relief of bronchospasm during labor should be restricted to those patients in whom the benefits clearly outweigh the risk. PROAIR HFA Inhalation Aerosol has not been approved for the management of pre-term labor. The benefit:risk ratio when albuterol is administered for tocolysis has not been established. Serious adverse reactions, including pulmonary edema, have been reported during or following treatment of premature labor with $beta_2$-agonists, including albuterol.

**8.3 Nursing Mothers**

Plasma levels of albuterol sulfate and HFA-134a after inhaled therapeutic doses are very low in humans, but it is not known whether the components of PROAIR HFA Inhalation Aerosol are excreted in human milk.

Caution should be exercised when PROAIR HFA Inhalation Aerosol is administered to a nursing woman. Because of the potential for tumorigenicity shown for albuterol in animal studies and lack of experience with the use of PROAIR HFA Inhalation Aerosol by nursing mothers, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

**8.4 Pediatric Use**

The safety and effectiveness of PROAIR HFA Inhalation Aerosol for the treatment or prevention of bronchospasm in children 12 years of age and older with reversible obstructive airway disease is based on one 6-week clinical trial in 116 patients 12 years of age and older with asthma comparing doses of 180 mcg four times daily with placebo, and one single-dose crossover study comparing doses of 90, 180, and 270 mcg with placebo in 58 patients *[see **Clinical Studies (14.1)**]*. The safety and effectiveness of PROAIR HFA Inhalation Aerosol for treatment of exercise-induced bronchospasm in children 12 years of age and older is based on one single-dose crossover study in 24 adults and adolescents with exercise-induced bronchospasm comparing doses of 180 mcg with placebo *[see **Clinical Studies (14.2)**]*.

The safety of PROAIR HFA Inhalation Aerosol in children 4 to 11 years of age is based on one 3-week clinical trial in 50 patients 4 to 11 years of age with asthma using the same formulation of albuterol as in PROAIR HFA Inhalation Aerosol comparing doses of 180 mcg four times daily with placebo. The effectiveness of PROAIR HFA Inhalation Aerosol in children 4 to 11 years of age is extrapolated from clinical trials in patients 12 years of age and older with asthma and exercise-induced bronchospasm, based on data from a single-dose study comparing the bronchodilatory effect of PROAIR HFA 90 mcg and 180 mcg with placebo in 55 patients with asthma and a 3-week clinical trial using the same formulation of albuterol as in PROAIR HFA Inhalation Aerosol in 95 asthmatic children 4 to 11 years of age comparing a dose of 180 mcg albuterol four times daily with placebo *[see **Clinical Studies (14.1)**]*.

The safety and effectiveness of PROAIR HFA Inhalation Aerosol in pediatric patients below the age of 4 years have not been established.

**8.5 Geriatric Use**

Clinical studies of PROAIR HFA Inhalation Aerosol did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently from younger patients. Other reported clinical experience has not identified differences in responses between elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy *[see **Warnings and Precautions (5.4, 5.7)**]*.

All $beta_2$-adrenergic agonists, including albuterol, are known to be substantially excreted by the kidney, and the risk of toxic reactions may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

## 10 OVERDOSAGE

The expected symptoms with overdosage are those of excessive beta-adrenergic stimulation and/or occurrence or exaggeration of any of the symptoms listed under ADVERSE REACTIONS, e.g., seizures, angina, hypertension or hypotension, tachycardia with rates up to 200 beats per minute, arrhythmias, nervousness, headache, tremor, dry mouth, palpitation, nausea, dizziness, fatigue, malaise, and insomnia.

Hypokalemia may also occur. As with all sympathomimetic medications, cardiac arrest and even death may be associated with abuse of PROAIR HFA Inhalation Aerosol.

Treatment consists of discontinuation of PROAIR HFA Inhalation Aerosol together with appropriate symptomatic therapy. The judicious use of a cardioselective beta-receptor blocker may be considered, bearing in mind that such medication can produce bronchospasm. There is insufficient evidence to determine if dialysis is beneficial for overdosage of PROAIR HFA Inhalation Aerosol.

The oral median lethal dose of albuterol sulfate in mice is greater than 2,000 mg/kg (approximately 6,800 times the maximum recommended daily inhalation dose for adults on a $mg/m^2$ basis and approximately 3,200 times the maximum recommended daily inhalation dose for children on a $mg/m^2$ basis). In mature rats, the subcutaneous median lethal dose of albuterol sulfate is approximately 450 mg/kg (approximately 3,000 times the maximum recommended daily inhalation dose for adults on a $mg/m^2$ basis and approximately 1,400 times the maximum recommended daily inhalation dose for children on a $mg/m^2$ basis). In young rats, the subcutaneous median lethal dose is approximately 2,000 mg/kg (approximately 14,000 times the maximum recommended daily inhalation dose for adults on a $mg/m^2$ basis and approximately 6,400 times the maximum recommended daily inhalation dose for children on a $mg/m^2$ basis). The inhalation median lethal dose has not been determined in animals.

Mktd by: Teva Respiratory, LLC
Horsham, PA 19044

Mfd by: IVAX Pharmaceuticals Ireland
Waterford, Ireland



Manufactured In Ireland Rev 05/12

PA0512BS-A

# Walgreens acquires Kerr Drug chain

Walgreens has reached agreement with privately held Kerr Drug to acquire its retail drugstores and specialty pharmacy business, which last year had sales of about $381 million.

Financial terms of the deal were not disclosed. The deal will include Kerr's 76 retail stores and a distribution center. It does not include Kerr's long-term-care pharmacy business.

According to Walgreens, the Kerr acquisition would help it expand throughout North Carolina, where Kerr is based.

"The Kerr Drug retail drugstores and specialty pharmacy business are an exceptional addition to the Walgreens family of companies," said Greg Wasson, Walgreens' president and CEO. "We are closely aligned on the important task of expanding the healthcare role that community pharmacists can have with their patients, and we share the common goal of stepping out of the traditional drugstore format to create a new experience for our customers."

Anthony Civello, president, CEO, and chairman of Kerr Drug, called the Walgreens deal a good fit for his company. "Kerr Drug's strategy and core principles have always been focused on its unique ability to provide patients access to the most comprehensive and convenient health and wellness offering in the industry," Civello said. "Walgreens is the perfect partner to continue this journey as a patient-oriented company dedicated to expanding the role of the pharmacist as an integral part of health care."

Kerr Drug will continue to operate separately until federal regulators approve the deal, which is expected to happen later this year. Founded in 1951, Kerr Drug has gained a reputation for innovative community pharmacy. It was among the first chains to offer resource centers within its locations that were staffed with pharmacy doctors and pharmacy students from local colleges.

Kerr pharmacies offered programs for many treatment areas, including diabetes, cholesterol control, osteoporosis, thyroid disease, and smoking cessation. It was also a participant in the groundbreaking 1996 Asheville Project, which has become the model for medication therapy management programs throughout the country.

*– Mark Lowery, Content Editor*

**"The perfect partner": Kerr Drug's visionary policies paved the way.**

NEW POWERS

## California pharmacists nearing provider status

Pharmacists throughout California are a signature away from being able to administer a full range of immunizations, as well as dispensing birth control pills and certain medications for international travel.

On September 17, a pharmacist provider-status bill passed both houses of the California State Assembly. As of press time, the bill had been delivered to California Governor Jerry Brown, who had until October 13 to act. If signed by the governor, the law would take effect in January.

"The California Pharmacists Association (CPHA) is pleased that the California State legislature has recognized the added value that pharmacists can play in providing expanded access to care to patients in California communities," said Jon Roth, CPHA CEO. "This legislation, SB 493, is an acknowledgment that the education, training, and skills of pharmacists go far beyond providing medications to patients."

Under present law, pharmacists in California can provide only flu shots and emergency contraception. The new law would authorize pharmacists to administer drugs and biological products. It would also expand the duties pharmacists in California can legally perform, including furnishing self-administered hormonal contraceptives, prescribing smoking cessation drugs, and prescribing medications not requiring a diagnosis that are recommended for international travelers.

### Vastly underused

"Pharmacists are vastly underutilized for the amount of training and education they receive," said Sen. Ed Hernandez (D-West Covina), who sponsored the bill. "The pharmacy profession can play and will play an important role in this expansion mode, and they'll need an expansion of their scope of service to enable them to do so."

The new law also establishes board recognition and training requirements for an advanced practice pharmacist with expanded functions. Pharmacists would also gain the authority to order and interpret tests to monitor and manage efficacy and toxicity of drug therapies.

*–Mark Lowery, Content Editor*

THUMBS DOWN

## Seniors oppose mandatory mail order, survey finds

A majority of Medicare beneficiaries said they would oppose mandatory mail order if it would lead to closure of their local community pharmacies, a new study has found.

In the September, 2013, issue of the *Journal of Managed Care Pharmacy*, study author Michael T. Rupp, PhD, BPharm, stated that 83.7% of the 669 Medicare-eligible individuals 65 and older surveyed were opposed to mandated mail order if it meant that the pharmacies they used would close as a result.

### Aversion to risk and loss of choice

"Seniors are relatively risk adverse when it comes to the loss of their local community pharmacies, indicating that, on average, they would oppose a mandatory mail order provision if there were greater than about a 4-in-10 chance that it would lead to the closure of their local pharmacies," wrote Rupp, who is professor of pharmacy administration at Midwestern University's College of Pharmacy in Glendale, Ariz.

In the event that they were required to use a mail-order pharmacy, 62.9% of seniors said, they would be concerned about losing their freedom to use the pharmacy of their choice.

Approximately 55% agreed they would be concerned about not having a pharmacist who knows them and the medications they take if they were required to use mail order.

However, 34.1% of the seniors receive the majority of their medications via mail order, while 47.7% get their medications from chain pharmacies, and 13.1% receive them from independent pharmacies.

In addition, 51.6% of those surveyed said they believe that using a mail-order pharmacy is less expensive than using a local pharmacy.

### Preference for face-to-face, quick turnaround

To the benefit of community pharmacies, more than half (51.1%) of seniors said they would be concerned about whether they fully understood their medications if they used a mail-order pharmacy and 41.2% said they would be concerned about not being able to speak face-to-face with a pharmacist.

In addition, nearly 60% of respondents agreed they would be concerned about getting their medications when they needed them right away if they used a mail-order pharmacy. Around 40% of seniors are concerned that their medications might be lost or stolen if they use a mail-order pharmacy.

Seniors in rural areas are especially concerned about mail-order pharmacy deliveries.

"This study found that seniors living in rural areas have significantly greater concerns than their counterparts in non-rural areas about lost or stolen medications, receiving the exact medication the physician prescribed, and the effects of exposure to heat, cold, or moisture," Rupp wrote.

*–Christine Blank, Contributing Editor*

THUMBS UP

## TRICARE's mail-order program earns high marks in federal audit

An audit by the Department of Defense's Office of the Inspector General (OIG) has found the TRICARE mail-order pharmacy program to be "more efficient and effective than retail programs," as well as less prone to errors.

### NACDS objects

TRICARE is the healthcare plan that serves 10 million active and retired military personnel and their families.

In May, the National Association of Chain Drug Stores (NACDS) urged a congressional panel to reject proposals that would force military families to use mail-order services to fill prescriptions. The proposed changes were part of discussions regarding the 2014 Defense Budget.

According to NACDS, mandating the use of TRICARE would limit choices for service members, retirees, and their families. NACDS also asserted that in the case of generics, mail-order prices are more expensive than those of retail pharmacy.

**"Despite repeated claims by the retail pharmacy lobby, TRICARE could not identify information that quantified waste resulting from delivered and unneeded prescriptions."**

***— Report No. DODIG-2013-108***
***Office of the Inspector General***
***Department of Defense***

### Audit findings

However, the OIG audit concluded that the TRICARE mail-order program saved taxpayers 16.7% over the costs incurred through use of retail pharmacy. In addition, 96% of the TRICARE beneficiaries responding to the survey said that they were either "somewhat," "very," or "completely satisfied" with the program.

The audit also revealed that TRICARE's rate of prescription errors was lower than that of retail pharmacy, including when shipment of the wrong drugs was factored in. According to the audit, TRICARE dispensations were 99.997% error free vs. a 98.5% error-free rate for retail pharmacy.

### The bottom line

"Despite repeated claims by the retail pharmacy lobby, TRICARE could not identify information that quantified waste resulting from delivered and unneeded prescriptions," the audit declared, adding, "What OIG did find was that TRICARE has imposed strong operational controls, including auto refill programs, to ensure beneficiaries receive only necessary pharmaceuticals."

*–Mark Lowery, Content Editor*

Up front

EXPANDED ROLE

## Canadian Medical Association calls increased pharmacist functions beneficial

Pharmacists in Canada were recently given broader responsibilities including, in certain provinces, prescribing privileges, vaccination ability, and the authority to order and interpret laboratory tests.

According to an article published in the *Canadian Medical Association Journal,* this newly expanded role for Canadian pharmacists can benefit both patients and physicians.

Written by Cara Tannenbaum, MD, associate professor of medicine and pharmacy at the University of Montreal, and Ross Tsuyuki, PharmD, professor of medicine at the University of Alberta, the article was based on a review of evolving pharmacist activities and responsibilities observed around the world. It appeared in the August 19, 2013 issue of the journal.

### Medication therapy management

The authors said that expanded functions for pharmacists can be especially helpful to physicians managing patients who are using several medications simultaneously.

"Because more than 10% of visits to emergency departments are for drug-related problems, collaboration can help reduce the number of drug-drug interactions and avoid visits to the emergency department," Tannenbaum and Tsuyuki wrote. "Pharmacists, who have specialized expertise in drug dosing, drug interactions, pharmacology and related areas, can help physicians manage safe prescribing in complex (often elderly) patients taking five or more drugs."

**"The expanding scope of pharmacists' practice offers many opportunities to improve patient care. Once established, collaborative care with pharmacists will likely yield tremendous benefits to both patients and physicians."**

### Accountability

The authors added, "As pharmacists more actively participate in medication management, physicians should be aware that in interprofessional models of care, every member of the team is accountable for the care he or she provides and is not to be held directly liable for the acts of others."

The authors concluded, "Once established, collaborative care with pharmacists will likely yield tremendous benefits to both patients and physicians. The expanding scope of pharmacists' practice offers many opportunities to improve patient care. However, it is also an ongoing process that must be evaluated as regulated activities change, new pharmacists enter practice and scopes of activities continue to expand."

*–Christine Blank, Contributing Editor*

# Voices

Continued from pg. 13

food restaurant. I often feel like asking an inconsiderate nurse or a belligerent patient, "Would you like fries with that?" Getting 15 minutes to prepare a medication and check for potentially lethal drug interactions seems to be way too much to ask for these days.

Then there are the "clerical" errors of doctors and nurses. Exactly when did the arrogance that seems to come with having the two letters MD or DO after your name transfer over to nurses, MAs, and receptionists? These menial employees seem to think that because pharmacists are at the end of the medication delivery industry (essentially), they can talk to us like we're about to serve them their Big Macs. It is a shame that highly trained professionals have to endure such verbal assaults from people who are, in most cases, less educated — yet seemingly more entitled to respect.

I think that the take-home message is that we are ALL busy individuals, all striving for the same outcome: to ensure the health and wellbeing of our patients.

Do mistakes happen? Yes, of course they do. But there needs to be less "we don't do things that way" and more "let me see what I can do to help you."

***Ryan Racino, PharmD, AAHIVP***
SAN DIEGO, CALIFORNIA

### Seen on Facebook/DrugTopics

Commenting on the article "Seniors oppose mandatory mail order, survey finds," [*Drug Topics*, September 6, *http://bit.ly/srmailorder*], reader Sharon Beust Sanchez writes:

"When we had the pharmacy, one day Dr. O'Bryant's nurse came in with a vial of injectable gold shot. She thought something was funny about it. I told her it was MAIL ORDER. She asked how could I tell, since she was still holding it. I told her that the vial had cooked in someone's mailbox. The injectable should have been lemon yellow, but it was peanut-color brown. Now, do you want mail order?"

### We want to hear from you

Printed and e-mailed letters should be brief and include the writer's name, address, daytime phone number, and date of the issue you are referencing: Editor, ***Drug Topics***, 24950 Country Club Blvd., Suite 200, North Olmsted, OH 44070-5351. E-mail address: drugtopics@advanstar.com. Letters may be edited for length, style, content, and clarity at our discretion.

Up front » In Depth

Jonathan Sin, PharmD candidate 2014; Nissa Mazzola, PharmD, CGP, CDE

# Educating patients in drug disposal

Unused medications pose a public safety issue, especially when not handled or disposed of properly. Prescription drugs, taken without physician supervision or authorization, can lead to accidental poisoning, overdose, and/or abuse. In recent years, hospitalizations and deaths from use of opioid analgesics and psychoactive medications have increased.

## Education

Those who do not dispose of medications may hoard them in their homes or give them to friends or family. These actions directly contribute to drug diversion. Medications are commonly stored in household bathrooms and kitchens, without locks or security measures. This is a concern in the case of adolescents and young adults, who may have unsupervised access.

According to the Centers for Disease Control and Prevention, between 2000 and 2009, fatal poisonings in 15- to 19-year-old patients increased 91%, partly because of a jump in opioid overdoses. Also, college students claim to obtain medications from their peers. Drug-sharing is equivalent to self-medicating and is dangerous, since the identity and purity of the medication cannot be ensured.

Education is crucial if society is to address this issue. According to the Office of National Drug Control Policy and the Food and Drug Administration (FDA), if patients discard medications with their trash, they should follow these steps:

- Take drugs out of their original containers.
- Mix drugs with undesirable substances, such as cat litter or coffee grounds.
- Put the mixture into disposable containers with lids, such as margarine tubs, or sealable bags.
- Conceal personal information on the original containers with permanent marker/duct tape or remove by scratching it off.
- Place the sealed container with the mixture, along with the empty drug containers, in the trash.

These tactics discourage others from rummaging through trash. However, determined individuals will go to great lengths to obtain a drug. FDA has compiled a list of especially harmful medications that should be flushed to reduce the risk of unintentional use. Opioids compose the bulk of the list.

Questions about these practices may arise, particularly in relation to contamination of the water supply. Drug take-back programs remain the gold standard for proper disposal.

## Take-back programs

Increasingly popular over the last several years, drug take-back programs staffed by pharmacy and other healthcare professionals, or law-enforcement officials, have sprung up in many communities, often at police precincts or local pharmacies. In 2010, the Drug Enforcement Administration (DEA) started a take-back initiative, designating certain days as "National Prescription Drug Take-Back Days."

Currently, the Controlled Substances Act does not allow community-based programs to accept controlled substances, unless the DEA has granted permission and law enforcement officers are present to receive them. Therefore, community-based programs must advertise the exclusion of controlled substances or employ law enforcement, which may be inconvenient and costly. Although the programs are beneficial, this restriction prevents communities from protecting residents from the drugs most likely to be diverted.

Fortunately, the Secure and Responsible Drug Disposal Act of 2010 was designed to amend the Controlled Substances Act, allowing the DEA to develop methods to transfer controlled medications for responsible disposal. The proposed regulations will allow drug take-back events, mail-back programs, and collection-box receptacles to accept non-controlled and controlled medications.

Manufacturers, distributors, reverse distributors, and pharmacies may also voluntarily participate in mail-back programs and implement collection-boxes. Until these provisions are permanently adopted, the DEA will continue holding National Prescription Drug Take-Back Days. For information about the initiative and upcoming events, visit the official website at *http://www.deadiversion.usdoj.gov/drug_disposal*.

## Pharmacist responsibility

Pharmacists are in a unique position to inform patients about disposal, as they are the most accessible healthcare professionals. They are at the forefront of medication information, and that includes knowledge of proper handling of drugs. Student pharmacists also can volunteer and educate.

To prevent overprescribing of medications, it is most important to ensure that patients receive well-targeted doses and optimal therapies with the fewest adverse effects. Compliance counseling is also crucial in reducing nonadherence. These best practices can help minimize drug diversion, abuse, and waste. DT

**Jonathan Sin is** *a 2014 PharmD candidate at St. John's University College of Pharmacy and Health Sciences, Queens, N.Y.*

**Nissa Mazzola** *is assistant clinical professor, St. John's University College of Pharmacy and Health Sciences, and an ambulatory care clinical pharmacist for North Shore University Hospital Division of General Internal Medicine.*

Up front
In Depth

Joel Claycomb, PharmD

# Keys to caring for complex patients

The issue of providing proper pharmaceutical care to individuals with multiple disease states is one that continues to grow. As the population of the United States continues to age, as diagnostic screening methods improve, and as more individuals have better access to healthcare, pharmacists will encounter an increasing number of patients who require a more comprehensive approach to their treatment management.

In September, I attended the annual International Pharmaceutical Federation (FIP) Congress. While there, I had the opportunity to attend a session titled "Complex patients and obstacles to quality use of medicines: A patient's perspective." This particular session addressed some of the challenges that arise in connection with these multifaceted individuals. Tara Hehir, a consultant pharmacist from Sydney, Australia, and Parisa Aslana from the University of Sydney led the presentation.

## Complex patients

For the purposes of this discussion, a complex patient was defined as someone with any of the following characteristics: multiple medications or disease states, comprehension difficulties, physical or mental disabilities, or psychological issues. Patients with multiple disease states can have highly complicated regimens that may be difficult to manage. These patients often require a more individualized approach, one that is tailored to their needs.

Aside from the challenges of handling the various health issues of complex individuals, we may also face communication barriers in dealing with them. Complex patients are more likely to have issues with vision, hearing, or cognition. In addition, they may have psychological issues that need to be acknowledged.

Often when their physicians assess them, patients receive only the basic details about their conditions and disease progression. When they are given information, it may be too complicated or technical for them to grasp fully.

Perhaps their healthcare providers will suggest only one or two options for treatment, when there may be as many as half a dozen options available. Sometimes the providers who deal with such patients may be overwhelmed and find themselves "too busy" to fully address their patients' concerns.

## Communication factors

This is where we as pharmacists have the ability to step in and help fill some of the communication gaps.

Here's the payoff: When we deliver accurate information to our patients in a manner they can use, good things happen. Increased interventions mean increased medication adherence. This in turn results in better health outcomes, leading to a reduction in healthcare costs.

When we take the time to present information to a patient, it is critical that we be aware of the manner in which we present it. It is also important to understand that we may not be the first healthcare provider the patient has spoken with on any given day. And in delivering information, we need to assess the patient's current level of understanding about the condition in question. Depending on the patient, the language should not be overly technical.

We should convey important information in a manner that is not rushed. When we hurry the message, it can often make our patients feel as though they, or their conditions, are not important to us. Take the time to answer any questions and respond to concerns.

Last, the counseling environment should be free of distractions and comfortable for the patient. A good rule of thumb is to treat your patients as you would treat your own grandmother.

## An active role

The take-home message from this is that we as pharmacists need to take an active role in communicating with our patients and their other healthcare providers.

We do this by explaining the specific purpose of each medication. We inform the patient of any adverse side effects that may occur in connection with a particular treatment. And we need to communicate effectively with the various providers involved in order to gather all the information needed to complete the patient picture.

All this may seem like common sense. It may seem as if these are all parts of our job description. Even so, sometimes it's necessary to take a closer look at our process.

When it comes to dealing with complex patients, there is no "one size fits all" approach. Each case needs to be examined on an individual basis. Every situation and patient is different, and what may work for one person may fail miserably for another. By keeping an open mind and an open dialogue, we can often make a very real difference to our patients and their outcomes.

Most important is to always be mindful, to use common sense, and to show sensitivity toward the patients: If you were in their shoes, how would you like to be cared for? DT

**Joel Claycomb** *reported on last year's FIP Congress in the December 2012 and February 2013 issues of* Drug Topics. *Contact him at jcclaycomb@gmail.com.*

# LIVE EVENT

# *Medication Therapy Management for Patients with Diabetes CPE Series*

## SATURDAY, NOVEMBER 9, 2013

**The University of Connecticut School of Pharmacy and *Drug Topics* present a 7–hour innovative program to reinforce the knowledge-based and application-based activities of this CPE series.**

**The event will held at Lincoln Medical and Mental Health Center in Bronx, NY.**

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***Prerequisite:** Completion prior to the event of all knowledge-based and application-based activities in this CPE Series.*

**Successful completion of all activities earns you a certificate of achievement entitled "Medication Therapy Management (MTM) for Patients with Diabetes."**

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**For more information and to register, go to**
http://pharmacy.uconn.edu/academics/ce/mtm-for-patients-with-dm/

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Julia Talsma
Content Channel Director

# Fight for survival

## How three independents advocate to win provider status, fairer audits

Crimes against U.S. pharmacies have been rampant in recent years, with almost 700 armed robberies occurring in 2010 alone. From 2006 to 2010, armed robberies of pharmacies rose 81%, jumping from 380 to 686. Since 2010, more than 1,800 pharmacy thefts and a number of pharmacy murders have resulted from acts committed by drug-seeking individuals.

Small independent pharmacies are particularly vulnerable, because they may lack the resources to fund the services of a security guard or to install and maintain a security system, said Joe Harmison, RPh, owner of two pharmacies in Arlington, Texas, and past president of the National Community Pharmacists Association (NCPA) from 2009 to 2010.

Joe Harmison

"About five to six years ago, the street value of prescription drugs climbed, and more and more [people] were abusing," said Harmison, who has been advocating for 15 years for legislation to make pharmacy burglary and robbery federal crimes with longer sentences for pharmacy criminals.

Harmison testified on behalf of NCPA in July 2012 before the U.S. Senate Caucus on International Narcotics Control about legislative efforts to combat pharmacy crime. NCPA also supported the Safe Doses Act (S. 1002), which increased the penalties for theft and diversion of prescription drugs. In October 2012, President Barack Obama signed the legislation into law, increasing the maximum sentence of pharmacy thefts from 10 to 20 years in prison.

Harmison is proud that after his years of advocacy, tougher penalties for these criminals are now a reality.

"Now there is a price to pay for harming people," he said. His own pharmacy has been burglarized three times.

### How to advocate for pharmacy

Drawing upon his years of experience in championing a cause, Harmison had this advice for his colleagues. Pharmacists who want to become advocates for their profession can start with their state pharmacy associations. First,

contact the state government affairs department and get to know individuals within the association. It is important to be interested and willing to listen and learn, he said.

"Go out and start building relationships with the legislators within the government who write the policies," Harmison told *Drug Topics*. "It is not really all that difficult. It is building personal relationships with individuals, as you do with patients and neighbors."

Pharmacists can advocate at any level — local, state, or federal — by letting community groups, state associations, or the national associations know that they are willing and able to participate, Harmison said.

"Do your homework. Know who are your state and federal representatives and senators, and how to get ahold of them," he said. "You can start by writing a letter to your state representative and going to fundraisers. Then they will be able to associate a name and a face, and your profession."

## Get involved

Beverly Schaefer, RPh, co-owner of Katterman's Sand Point Pharmacy, Seattle, Wash., believes that one good way for independents to learn about pharmacy issues is to join NCPA. The association has developed a strong, collegial network of pharmacists who understand what the issues are, and it can help pharmacists and future pharmacists convey this information to state or federal legislators, as well as to employer groups.


Beverly Schaefer


Keith Hodges

"It is important that we educate individuals within our communities about the benefits of community pharmacy," Schaefer said.

M. Keith Hodges, RPh, owner of Gloucester Pharmacy, Gloucester, Va., believes that community pharmacists should get involved at the community, state, and national levels, because knowledge of wider issues pertaining to pharmacy helps with running a pharmacy business more effectively.

"If you just stay in the pharmacy, you only see what is going on in the pharmacy," Hodges said. "When you network with others and you advocate for your profession, you learn what is going on within the industry, which helps you with your business."

Hodges, who was elected to the Virginia House of Delegates in 2011, said that, speaking as a state legislator, he values the time he spends with individuals who are working within their profession over time spent with paid lobbyists.

"We need to hear from experts who give us good information," he said.

For a number of years, Hodges has been an active advocate within the profession at both the state and national levels. He has been involved with the state association in Virginia, has chaired the national legislative committee for NCPA and served on NCPA's board of directors, and is a board member for Epic Pharmacy.

In his current elected position, Hodges serves as an advisor to other legislators on matters connected with pharmacy.

"When pharmacy bills come up in the state legislature, other legislators look to me for guidance. You [the pharmacy owner and pharmacist] can't introduce legislation for pharmacy, because it can be self-serving, but you can offer advice to other legislators."

More pharmacists need to run for political office, Hodges said. While there are no pharmacists serving in Congress, a number of pharmacists have been elected to state legislatures, including Hodges and another pharmacist in Virginia.

Pharmacists who run for political office have a good chance of winning.

"Typically pharmacists are apolitical. People don't see me as a Republican or a Democrat. They see me as Keith Hodges," he said. "They trust you, as you are considered one of the most trusted health professionals, and they trust you to make the decisions in government as well."

## Represent pharmacy

Schaefer, who started out making deliveries for Katterman's Pharmacy and worked her way up to pharmacy store manager before purchasing the drugstore with a partner in 1996, has been a strong, successful advocate for independents as a spokesperson for the profession.

Pharmacists who want to get involved, she said, should try to tap specific groups to speak to about legislative issues that are important to independents, including legislators, payers, employer organizations, public service groups, local colleges of pharmacy, their students, and the media.

"Prepare your message ahead of time, before you talk to the media. I figure out the message that I want to deliver to them, not the other way around," said Schaefer, who is active with Seattle media.

For pharmacists who want to connect with legislators, Schaefer suggested attending any local events, such as town-hall meetings or coffee hours, where they can introduce themselves and present their business cards.

TABLE 1

## Advocacy tips for pharmacists

| |
|---|
| · Join your state pharmacy association. |
| · Join the National Community Pharmacists Association. |
| · Attend functions to meet with your state and federal legislators. |
| · Learn about pharmacy issues that affect your business. |
| · Serve on committees for your state and national pharmacy associations. |
| · Speak to groups interested in pharmacy issues, such as legislators, payers, employer organizations, public service groups, local colleges of pharmacy, pharmacy students, and the media. |
| · Prepare your message before meeting with interested stakeholders. |
| · Educate community members about the benefits of community pharmacy. |
| · Advocate to practice at the top of your license. |

*Source: Joe Harmison, Beverly Schaefer, M. Keith Hodges*

"Offer to be a resource on any pharmacy issues that your legislators encounter. Sometimes they don't understand pharmacy issues," Schaefer said. "Explain that you would be willing to talk with their assistants."

### Campaign for provider status

In the state of Washington, Schaefer said, pharmacists have been able to make some inroads into the issue of provider status, but it is important to keep advocating for the profession.

"It is a constant battle — a constant vigilance on the part of pharmacy — to be recognized as providers and let people know that we are performing a valuable service for the community," Schaefer said.

With the development of accountable care organizations (ACOs), it is important for pharmacists to be recognized as providers as these healthcare models take shape. Pharmacists were not specifically mentioned in the ACO accreditation standards developed by the National Committee for Quality Assurance. However, "pharmacy could be a big help in meeting some of their goals, in serving more patients and lowering costs. We want to be at the table," Schaefer said. "Without provider status, it marginalizes us."

In connection with ACOs, pharmacists need to advocate for patient choice, which would allow patients to continue to use their own community pharmacies. At this point it is unknown whether ACO pharmacy networks will be open or closed, Schaefer said.

In her state, Schaefer has been on the cutting edge of progress for years. In 1996, Schaefer's pharmacy became one of the first pharmacies in the country to offer mass immunizations administered by a pharmacist. Before that, patients received their flu shots only in doctors' offices.

"We did over 1,200 flu shots that year. This was a major change for pharmacists," she said.

### Create collaborative agreements

In March 2012, Schaefer testified before FDA on behalf of NCPA, advocating for a third class of drugs. FDA had invited comments on implementation from all interested stakeholders, including pharmacists, doctors, and nurses. The turf battles were evident, with pharmacists favoring a third class of drugs and doctors and nurses against it.

When Schaefer returned to the state of Washington, she realized that establishing collaborative practice agreements with physicians would be the best approach to becoming a pharmacist prescriber of specific prescription drugs. Collaborative practice agreements with physicians have been part of the state's pharmacy practice acts since the 1970s.

"So if you write up a protocol with specific parameters about what would fall under this protocol, and you find a physician who agrees to let you follow this protocol, then you — the pharmacist — become the prescriber of the drug," said Schaefer.

Schaefer worked through the summer of 2012, writing 30 protocols for the prescription of specific drugs on a one-time basis or in an emergency situation. In the fall she developed patient assessments and forms to accompany the protocols. Then, after four months of negotiation with a physician, she obtained prescriptive authority for 30 prescription drugs in the state of Washington.

"There are a lot of ailments that need acute care, like a bee sting, a dog bite, an outdated EpiPen renewal, a urinary tract infection, a cold sore, the start of shingles. These are things that people come to the pharmacy for anyway, so if we had a little bit of prescriptive authority, we could help these people. It would prevent a trip to the ER and prevent them from getting worse," she said.

What really convinced the physician and the state board of pharmacy to accept this collaborative agreement was the stipulation concerning when to refer a patient to a physician or emergency department (ED), Schaefer said. In the case of a dog bite, for a pharmacist to prescribe, the wound must be new; the skin cannot be torn so that it would leave a scar upon healing; and the wound cannot be red or filled with pus. Otherwise, the pharmacist must refer to a physician or the ED, she said.

Schaefer said that she has made a gift of the protocols, patient assessments, and forms to the Washington State Pharmacy Foundation. The foundation is working on a toolkit and a 10- to 12-hour CE program, which will include all the protocols and written material, to share with interested pharmacists.

"I'm advocating to practice at the top of my license. Pharmacists are so well trained in clinical skills. We really don't get to use those clinical skills and be recognized and paid for them. This would change how people would access pharmacies," Schaefer said.

**"I'm advocating to practice at the top of my license. This would change how people would access pharmacies."**

## Push for fair PBM audits

NCPA has been at the forefront of those advocating at the state and federal levels for fairer standards for pharmacy audits. Hodges, who has been active with NCPA for more than nine years, knows firsthand how important these standards are, having been through a PBM audit just 6 months ago.

Despite the institution of some fair business practices for PBMs in Virginia, the auditor came on a Monday, the busiest day of the week for pharmacies, and complained that Hodges wasn't pulling and copying the 100 prescriptions and 50 signatures fast enough. A few weeks later, he received the results, a payback of $17,000.

"We jumped through hoops to bring the amount down to zero. We shouldn't have to jump through hoops over clerical issues. These are valid prescriptions. The average prescription price was over $700," he said. "So clearly it is a predatory audit, where they are looking for clerical errors. These audits should be random samplings of your business that you are doing with them, unless there is suspected fraud."

In January 2014, Hodges will present his comments on Virginia's PBM issues to his legislative colleagues. He said he isn't sure whether his colleagues will introduce legislation or try to work out problems administratively.

## Support compounding issues

Both Hodges and Harmison advocated against Senate bill 959, the Pharmaceutical Quality, Security, and Accountability Act, which calls for greater FDA oversight of compounding pharmacies.

In addition to mandating FDA supervision of compounding manufacturers who compound sterile drug products without a prescription and offer or sell them across state lines, the legislation required traditional compounding pharmacies to report to FDA when they compound medications in response to a drug shortage. This could cause delay for patients who may need to receive medications quickly.

The act also allowed FDA to create a "do not compound" list, which could give FDA authority to "impede patient access to vital medications," said Hodges, who wrote a commentary about his opposition that was published in the *Roanoke Times*.

Along with Harmison, Hodges gave his support to House bill 3089, the Compounding Clarity Act, introduced in September by Congressman Morgan Griffith (R-VA), Congressman Gene Green (D-TX), and Congresswoman Diana DeGette (D-CO). This legislation would give FDA authority over compounding manufacturers such as the New England Compounding Center (NECC), which was responsible for the multistate fungal meningitis outbreak last year. However, state boards of pharmacy would continue to have oversight of traditional compounding pharmacies. The Compounding Clarity Act also preserves the right of traditional pharmacies to compound for multiple patients who are receiving the same medications at hospitals, doctors' offices, and other health facilities.

Harmison said he thinks it is reasonable for FDA to have some power, specifically over operations that masquerade as pharmacies when they are really manufacturers.

At press time, congressional leaders introduced The Drug Quality and Security Act to address compounding drug safety and security issues. NCPA endorsed the legislation, which provides FDA oversight of compounders who decide to register as "outsourcing facilities" and practice outside the scope of traditional pharmacy practice. DT

# Innovation. Independence. Cooperation.

**American Associated Pharmacies (AAP)** is an independent-owned and independent-directed pharmacy cooperative. And it's been steadily growing throughout the past few years to become today's ninth-largest national retail pharmacy chain.* Backed by more than 35 years of combined independent pharmacy experience and expertise, AAP is the result of the 2009 merger of two respected pharmacy-buying and store-support organizations: Scottsboro, Ala.-based **Associated Pharmacies, Inc. (API)** and Phoenix-based **United Drugs**.

Independent pharmacy owners join this member-owned, national cooperative group to gain common purchasing power as well as access to merchandising, distribution, managed-care contracting and back-end business services that help them to more powerfully compete with big-box chains.

**'Compliance GUARDIAN helps enhance regulatory protection for individual pharmacies and for our membership as a whole.'**

## AAP membership benefits include:

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- **Compliance GUARDIAN:** New in 2013, the program was specifically designed to help independent pharmacies comply with federally-mandated sanction checks and monitoring.
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- **Industry updates:** Regular communication keeps members informed about key industry news such as the impact of the Affordable Care Act (ACA) and dynamic compliance trends and mandates.

"Our new Compliance GUARDIAN suite of services was created as a result of new laws that require pharmacists to perform a variety of tasks to meet federal requirements," said AAP President and CEO Jon Copeland, R.Ph. "For example, pharmacists must now check the OIG (Office of Inspector General/U.S. Department of Health and Human Services) and GSA (General Services Administration) databases each month and validate whether or not their employees can provide services to beneficiaries of federally-funded programs. If a pharmacy employs an individual on one or both of these sanctioned lists, they may be forced to pay back all federal funds received via these programs going back to the date their employee was hired. Compliance GUARDIAN helps enhance regulatory protection for individual pharmacies and for our membership as a whole."

And in 2012, AAP's subsidiary API purchased and modernized a second distribution center in Memphis, Tenn., which more than doubled its distribution capacity. The result has been more efficient and improved delivery service to Mountain and Pacific time zone customers.

** Source: Drug Store News, June 2013*

## AAP At A Glance

| | |
|---|---|
| **Headquarters**<br>Scottsboro, Ala. | **No. of stores with Rx**<br>2,012 |
| **2012 sales**<br>$4.53 billion | **Avg. store size**<br>2,000 sq. ft. |
| **No. of stores 2012**<br>2,012 | **Avg. sales per store**<br>$2.2 million |

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*Drug Store News*, June 3, 2013

**NEW DRUG REVIEW** Diana M. Sobieraj, PharmD

# FDA approves acyclovir buccal tablets for recurrent herpes labialis

In April 2013, the Food and Drug Administration approved acyclovir (Sitavig, BioAlliance Pharma) mucoadhesive buccal tablets (MBT) for the treatment of recurrent herpes labialis in immunocompetent adults. Acyclovir is a synthetic purine nucleoside that is converted into a triphosphate form through enzymatic reactions. Acyclovir triphosphate inhibits replication of herpes viral DNA through insertion into the viral DNA chain and subsequent termination. Each tablet contains 50 mg of acyclovir. Acyclovir MBT is contraindicated in patients with hypersensitivity to acyclovir, milk protein concentrate, or any other components of the product.

## Efficacy

In a randomized, double-blind, placebo-controlled trial, 378 patients were treated with acyclovir MBT and 397 were treated with placebo. A single dose of acyclovir MBT 50 mg was given to patients with recurrent herpes labialis, of which the majority (68.4%) had five or more episodes in the previous year. Patients' average age was 41 years of age; most were Caucasian (94.9%) and female (68.6%). Patients were instructed to apply acyclovir MBT within one hour of appearance of prodromal symptoms, with the same instructions as for the approved dosing.

Duration of the herpes labialis episode for patients in the acyclovir MBT group was approximately one-half day less than that for patients taking placebo. Additional outcomes showed that patients randomized to acyclovir MBT experienced less time from prodromal symptoms to healing, more patients had abortive episodes that did not progress to vesicular lesions, and duration of abortive episodes was briefer. For patients who agreed to follow up at nine months, the time to recurrence of a herpes labialis episode was significantly delayed — by 37 days — for those treated with acyclovir MBT, compared to recurrence time for those treated with placebo.

## Safety

The same randomized trial evaluated patients for safety outcomes. Treatment of emergent adverse events occurring in 1% or more of the patients included headache (1% acyclovir MBT and 2% placebo) and application site pain (1% in both groups). No one discontinued drug therapy due to adverse events. In each group, one report of headache was classified as severe. Other adverse events reported by 1% or more of the patients included dizziness, lethargy, gingival pain, aphthous stomatitis, application site pain, application site irritation, erythema, and rash (all 1% in the acyclovir MBT group), and headache (3% in the acyclovir MBT group).

Although no studies of drug-interactions have been performed, they are not expected to be significant as there is minimal systemic absorption with acyclovir MBT. Acyclovir is primarily excreted unchanged in the urine through active tubular secretion. Therefore, drugs that compete for tubular secretion, theoretically, may increase acyclovir levels.

## Dosing

Acyclovir MBT should be used within one hour of emergence of prodromal symptoms prior to the appearance of signs of herpes labialis. One MBT should be applied to the canine fossa, the area of the upper gum right above the incisor tooth, on the side of the mouth exhibiting symptoms. The MBT should be held in place with slight pressure over the upper lip for 30 seconds to ensure proper adhesion. The MBT has a flat side and a rounded side; the manufacturer suggests that the rounded side be applied facing the gum for comfort. Over the course of the day, the MBT will slowly dissolve. Should the MBT fall out of place or fail to adhere within the first 6 hours, the MBT should be repositioned immediately. If the patient swallows the MBT within the first 6 hours, she should drink a glass of water and apply a new MBT to the same area. If the MBT falls out of place or is swallowed after 6 hours, nothing further need be done. Patients should be instructed not to chew, crush, swallow, or suck on the MBT. While the MBT is in place, patients can eat and drink as usual. Actions such as chewing gum, touching or pressing the MBT after it is attached, wearing upper dentures or brushing teeth should be avoided. Patients with dry mouth should drink plenty of water. No dosing recommendations are available for patients with renal dysfunction. DT

**Diana M. Sobieraj** *is assistant professor of pharmacy practice, University of Connecticut School of Pharmacy, Storrs, Conn.*

**ANTICOAGULATION THERAPIES** Anna D. Garrett, PharmD, BCPS

# Many patients with AF lack indication for aspirin use

In recently published findings, investigators with the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF) have indicated that the benefit of adding aspirin therapy to oral anticoagulation (OAC) in patients with atrial fibrillation (AF) is unclear.

The registry enrolled 10,126 AF patients from 176 U.S. practices from June 2010 through August 2011. The study was limited to patients taking OAC (n=7,347).

Primary outcomes were 6-month bleeding, hospitalization, ischemic events, and mortality. Overall, 35% of AF patients on OAC also received aspirin (OAC+ASA). Patients receiving OAC+ASA were more frequently male and had more comorbid illness than those on OAC alone. Over one-third (39%) of OAC+ASA had no history of atherosclerotic disease, yet 17% had elevated ATRIA bleeding risk scores (≥5). Major bleeding and bleeding hospitalizations were significantly higher in those on OAC+ASA vs. those taking OAC alone. Rates of ischemic events were low.

The authors could find no explanation for the variation in aspirin use based on concomitant illnesses or bleeding risk. They suggested that, in light of the risks of OAC+ASA, physicians carefully assess the presence of an indication for combination therapy.

*Source: Steinberg BA, Kim S, Piccini JP, et al. Use and associated risks of concomitant aspirin therapy with oral anticoagulation in patients with atrial fibrillation: Insights from the ORBIT-AF registry.* Circulation. *Available at* http://bit.ly/AFoacASA. *Accessed July 27, 2013.*

## Dabigatran and MI risk questioned again

Dabigatran is in the news again. Two new analyses have raised questions once again about the risk of MI in dabigatran treatment. Both studies showed an increased risk of MI, ranging from 38% to 70%, compared to treatment with comparator drugs and placebo.

In the first study, researchers looked at all randomized, controlled studies, including data from the RE-LY trial, on the use of dabigatran in patients with venous thromboembolism and acute coronary syndrome, as well as data presented to the Food and Drug Administration. The review showed a statistically significant 48% increased risk of MI compared with controls.

The risk of MI with dabigatran also was highlighted at the recent 2013 Congress of the International Society on Thrombosis and Haemostasis meeting in Amsterdam, the Netherlands. A meta-analysis of 10 studies that included 23,839 dabigatran-treated patients showed an overall 32% increase in the risk of MI. Compared with warfarin, the risk of MI was increased 38%, while the risk of MI was 70% higher among dabigatran-treated patients compared with placebo-treated patients.

The data connected with this issue have been conflicting and consensus is lacking in the cardiology community. Other studies have found no increased risk, so the debate is likely to continue. The newer target-specific agents, rivaroxaban and apixaban, have not been reported to have an association with increased risk of coronary events and thus offer an alternative to dabigatran if physicians so choose.

*Source: O'Riordan M. Two new analyses link dabigatran to MI. Posted at www.the heart.org July 10, 2013. Available at* http://bit.ly/MIdabig. *Accessed July 27, 2013.*

## Aspirin shows benefit for extended VTE prophylaxis after total hip arthroplasty

The role of aspirin in thromboprophylaxis after total hip arthroplasty (THA) is controversial. A recent study compared aspirin with dalteparin for prevention of venous thromboembolism after hip replacement surgery. The study included 778 patients who had elective unilateral THA between 2007 and 2010.

After an initial 10 days of dalteparin prophylaxis following elective THA, patients were randomly assigned to receive 28 days of dalteparin or aspirin. The primary efficacy outcome was symptomatic VTE confirmed by objective testing and bleeding.

Five of 398 patients (1.3%) assigned to dalteparin and one of 380 (0.3%) assigned to aspirin developed VTE. Aspirin was noninferior but not superior to dalteparin. Clinically significant bleeding occurred in five patients (1.3%) receiving dalteparin and two (0.5%) receiving aspirin.

The authors concluded that considering the low cost and greater convenience, aspirin may be considered a reasonable alternative for extended thromboprophylaxis after THA.

*Source: Anderson DR, Dunbar MJ, Bohm ER et al. Aspirin versus low-molecular-weight heparin for extended venous thromboembolism prophylaxis after total hip arthroplasty: A randomized trial.* Ann Intern Med. *2013;158(11):800–806.* DT

**Anna D. Garrett** *is a clinical pharmacist and president of Dr. Anna Garrett (www.drannagarrett.com). Her mission is to help women in midlife maximize their mojo! Contact her at info@drannagarrett.com.*

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## EDUCATIONAL OBJECTIVES

**Goal:** To understand the role and limitations of available drug therapy for osteoporosis prevention and treatment and to improve osteoporosis management by pharmacists.

**After participating in this activity, pharmacists will be able to:**

- **Review the indications and efficacy of antiresorptive agents and anabolic therapy used in the treatment of low bone density or osteoporosis.**
- **Discuss potential limitations and contraindications of current agents.**
- **Identify how to counsel patients on the appropriate use and potential side effects of these agents.**
- **Identify patient self-care measures for osteoporosis prevention and management.**

The University of Connecticut School of Pharmacy is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.

Pharmacists are eligible to participate in the knowledge-based activity, and will receive up to 0.2 CEUs (2 contact hours) for completing the activity, passing the quiz with a grade of 70% or better, and completing an online evaluation. Statements of credit are available via the online system.

**ACPE #0009-9999-13-073-H01-P**

**Grant Funding:** This activity is supported by an educational donation provided by Amgen.

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**Initial release date: 10/10/2013**

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IMAGE: THINKSTOCK / ISTOCK

# MTM considerations in osteoporosis care: Current issues for prevention and treatment

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## Abstract

*Several FDA-approved pharmacologic agents are used in the management of osteoporosis. This second article in our continuing education series on osteoporosis provides an overview of considerations in selecting existing treatment options for the prevention and treatment of this chronic disease with an emphasis on current issues and how a pharmacist can provide pharmaceutical care in osteoporosis management.*

**Faculty: Fei Wang, MSc, PharmD, BCPS, FASHP; Audrey Corman, BS, PharmD Candidate; Cindi Sounthonevat, PharmD Candidate; Joshua Baldino, PharmD Candidate**
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**Faculty Disclosure:** Dr. Wang, Ms. Corman, Ms. Sounthonevat, and Mr. Baldino have no actual or potential conflict of interest associated with this article.

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**Editor's note:** This is the second article in a two-part series. Last month, we covered pathophysiology, screening, and prevention strategies for osteoporosis.

Osteoporosis has a huge public health impact through the increased morbidity, mortality, and economic costs associated with resultant fractures. Hip fractures account for 94% of costs and 73% of fractures and are associated with greater increases in morbidity and mortality than other types of fractures.[1-4] Because osteoporosis is a silent condition, prevention and early detection of low bone mass and osteoporosis, together with treatment when indicated, can reduce the debilitation and costs associated with fractures. Guidelines on screening and when to initiate pharmacologic therapy in persons with osteopenia and osteoporosis have been previously discussed in the September 2013 issue of *Drug Topics*.

Despite available guideline recommendations, osteoporosis screening rates remain low so most patients who are at high risk of developing fractures and treatments are not identified.[5-8] It is also well documented that adherence to osteoporosis pharmacotherapy is suboptimal.[9-11] Pharmacists can play an important role in reducing gaps in osteoporosis management through screening initiatives to identify high-risk patients (eg, those on chronic glucocorticoid therapy or with a fracture history not on drug therapy).[12] Medication adherence can be optimized through pharmacist interventions that can include patient counseling and education on the purpose and proper use and storage of osteoporosis medications, potential adverse effects, and risk reduction of potential drug interactions and rare adverse effects. Patients who are candidates for a bisphosphonate drug holiday can also be identified. Pharmacists should engage all patients on calcium and vitamin D dietary requirements and supplementation and other nonpharmacologic methods to reduce the risk of osteoporosis. Pharmacy care services could be targeted towards assessments of calcium intake, review of risk factors, calculating a FRAX score, initiating osteoporosis therapy, performing medication reconciliation, smoking cessation, and fall risk reduction counseling. Pharmacy-run services for osteoporosis in various practice settings have demonstrated improvements in care of this patient population.[13-16]

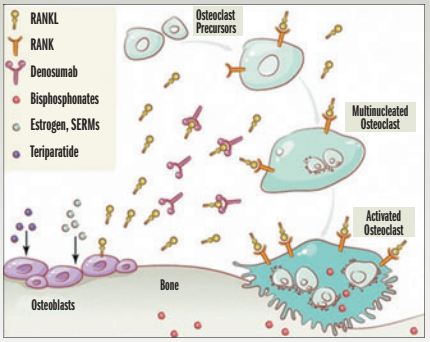
## Drug targets

Postmenopausal osteoporosis is characterized by accelerated bone turnover, with resorption exceeding formation leading to declines in bone mass and strength. Therapies for osteoporosis are broadly classified into either antiresorptive (anticatabolic) or anabolic (bone-forming) depending on their primary mechanism of action (**Figure 1**). Antiresorptive agents do not build new bone but stabilize the osteoporotic skeleton by reducing bone loss through inhibition of osteoclast resorption of bone, whereas anabolic agents add new bone to the existing skeleton. Antiresorptive agents do not lead to net accrual of bone in the skeleton, despite the fact that BMD is increased. These drugs reduce the remodeling space and increase the degree by which bone matrix is mineralized, which leads to a modest increase in BMD by 2% to 10%.[17] Several FDA-approved pharmacologic options are available for prevention or treatment of osteoporosis. All of these treatments are antiresorptive agents with the exception of teriparatide (**Table 1**).

In clinical trials of osteoporosis therapies, reduction of fracture risk is used as a clinical endpoint to demonstrate treatment efficacy; therefore selection of treatment options is based on their antifracture efficacy. To date, no head-to-head studies have prospectively compared any of the available therapies for antifracture risk.[18] In practice, agents demonstrating a reduction in spine, hip, and other nonvertebral fractures should be used preferentially over agents that demonstrate antifracture efficacy in the spine alone.[18-20] By this criteria, only alendronate, risedronate, zoledronic acid, and denosumab are first-line agents, ibandronate a second-line agent, raloxifene a second- or third-line agent, and calcitonin is the last-line agent. Teriparatide should be reserved for patients at very high fracture risk or in whom bisphosphonate therapy has failed (ie, no significant change in BMD after an adequate course of therapy or prior fractures and intolerance while on other anti-osteoporotic agents) (**Table 2**).[19]

FIGURE 1

**SITES OF ACTION FOR FIRST-LINE OSTEOPOROSIS TREATMENTS**




Mechanism of action: antiresorptives reduce bone turnover by targeting osteoclasts. Teriparatide stimulates bone formation by increasing osteoblast activity. Raloxifene and estrogen replacement therapy interfere with osteoblast-derived factors that stimulate osteoclasts. Denosumab binds the cytokine RANKL, preventing it from binding its receptor, RANK. Bisphosphonates bind to bone mineral and are taken up by osteoclasts, causing them to undergo apoptosis or have reduced resorptive capacity. When osteoclast number and activity decline, bone formation slows to maintain a balance of bone resorption and formation.

*Source: Ref 83. Reprinted with permission*

BMD is an important determinant of fracture risk, especially in women age 65 and older. Lower BMDs are associated with a higher risk of fracture.[18] BMD and bone turnover markers are intermediate endpoints that can be used to determine treatment response. A positive response to therapy results in an increase in BMD and a reduction in markers of bone turnover.[21] Treatment-induced changes in BMD, however, do not always correlate with reductions in vertebral fracture risk.[21,22] The antifracture benefits of FDA-approved drugs have mostly been studied in women with postmenopausal osteoporosis. There are limited fracture data in glucocorticoid-induced osteoporosis and in men. Pharmacotherapy options may also reduce fractures in patients with low bone mass without fractures, but the evidence is less compelling.[20] Individual therapeutic decisions must carefully balance the benefits versus risks of treatment.

## Bisphosphonates

Bisphosphonates are indicated for the treatment and prevention of postmenopausal osteoporosis, treatment in men with osteoporosis, treatment in glucocorticoid-induced

TABLE 1

## FDA-APPROVED MEDICATIONS FOR THE PREVENTION AND TREATMENT OF POSTMENOPAUSAL OSTEOPOROSIS

| Generic | Generic formulation | Available as | Dosage forms | Strengths | Indications | | Contraindications and comments |
|---|---|---|---|---|---|---|---|
| | | | | | Prevention | Treatment | |
| Alendronate | Yes | Alendronate sodium | Tablet | 5, 10, 35, 40, 70 mg | 5 mg/d<br>35 mg wk | 10 mg/d<br>70 mg/wk | • ClCr <35 mL/min (alendronate, zoledronic acid)<br>• ClCr <30 mL/min (ibandronate, risedronate)<br>• Inability to stand or sit upright for at least 30 min (alendronate, risedronate)<br>• Inability to stand or sit upright for at least 60 min (ibandronate)<br>• Hypocalcemia<br>• Esophageal abnormalities<br>• Increased risk of aspiration (effervescent tablet, oral solution) |
| | | | Oral solution | 70 mg/75 mL | | | |
| | | Fosamax | Tablet | 70 mg | --- | | |
| | | Binosto | Effervescent tablet | | | | |
| Alendronate and vitamin D3 | No | Fosamax Plus D | Tablet | 70-2800 mg/U<br>70-5600 mg/U | --- | 70-2800 mg/U wk<br>70-5600 mg/U wk | |
| Ibandronate | Yes | Ibandronate sodium | Tablet | 150 mg | 150 mg mo | 150 mg mo | |
| | | Boniva | IV solution | 3 mg/3 mL | --- | 3 mg every 3 mo | |
| Risedronate | No | Actonel | Tablet | 5, 35, 150 mg | 5 mg/d<br>35 mg wk<br>150 mg mo | 5 mg/d<br>35 mg wk<br>150 mg mo | |
| | | Atelvia | Delayed-release tablet | 35 mg | | 35 mg wk | |
| Zoledronic acid | Yes | Zoledronic acid | IV solution | 5 mg/5 mL | 5 mg every 2 yr | 5 mg yr | |
| | | Reclast | | | | | |
| Denosumab | No | Prolia | SQ injection | 60 mg/mL single-use prefilled syringe or vial | --- | 60 mg every 6 mo | • Hypocalcemia must be corrected prior to therapy (may worsen if ClCr <30 mL/min)<br>• Must be refrigerated prior to use or stored at room temperature and used within 14 days. |
| Raloxifene | No | Evista | Tablet | 60 mg | 60 mg/d | 60 mg/d | • History of VTE, stroke, or TIA |
| Calcitonin* | Yes | Calcitonin (salmon) generics | Nasal spray | 200 IU/ACT | --- | 200 IU 1 nostril daily | • Salmon allergy |
| | | Fortical | | | | | |
| | | Miacalcin | IM, SQ injection | 200 IU/mL | --- | 100 IU every other day | |
| Teriparatide | No | Forteo | SQ injection | 600 µg/2.4 mL prefilled multidose pen | --- | 20 µg/d | • Patients at increased baseline risk for osteosarcoma |

Abbreviations: ClCr, creatinine clearance; IM, intramuscular; SQ, subcutaneous; TIA, transient ischemic attack; VTE, venous thromboembolic events
Note: Prescribing information is summarized from the respective medication package inserts.
*FDA Advisory Committee recommends removal of calcitonin salmon nasal spray from the United States market (March 2013).

*Source: Refs. 23-29, 61, 95, 111, 121-122, 127, 134*

osteoporosis, and treatment of Paget disease of bone. Refer to individual package inserts for indications.[23-29] Bisphosphonates reduce bone resorption by reducing the recruitment and activity of osteoclasts and increasing premature osteoclast cell death via apoptosis.[30,31] The 4 bisphosphonates available in the United States for the prevention and treatment of osteoporosis differ in their route of administration, dose frequency, binding affinity for bone hydroxyapatite, and availability of a generic equivalent (**Table 1**). The rank order for binding affinity is zoledronate, alendronate, ibandronate, risedronate.[32,33] Higher-affinity bisphosphonates remain in the bone matrix for many years.[33] The terminal half-life of alendronate is similar to that of bone mineral, approximately 10.5 years; thus some of the advantageous skeletal effects of alendronate and other bisphosphonates may last for years after treatment stops.[34]

TABLE **2**

**SUMMARY OF EVIDENCE OF FRACTURE RISK REDUCTION OF FDA-APPROVED AGENTS**

| Drug | Fracture risk reduction | | |
|---|---|---|---|
| | Spine | Hip | Nonvertebral |
| Calcitonin | Yes | No effect demonstrated* | No effect demonstrated* |
| Raloxifene | Yes | No effect demonstrated* | No effect demonstrated* |
| Ibandronate | Yes | No effect demonstrated* | No effect demonstrated* |
| Alendronate | Yes | Yes | Yes |
| Risedronate | Yes | Yes | Yes |
| Zoledronic acid | Yes | Yes | Yes |
| Denosumab | Yes | Yes | Yes |
| Teriparatide | Yes | Yes | No effect demonstrated* |

* Lack of demonstrable effect at these sites should be considered in the context that studies may not have been adequately powered.

*Source: Ref 19*

## Effects on fracture risk

Pivotal randomized controlled trials (RCTs) in postmenopausal women (with low BMD and/or previous vertebral fracture) of bisphosphonates were powered for demonstration of fracture efficacy over a 3- to 4-year period. Alendronate, risedronate, and zoledronic acid reduced fracture risk at the spine, hip, and nonvertebral sites by 40% to 70%, 30% to 50%, and 25% to 39%, respectively.[35-42] Treatment for up to 3 years was also associated with a reduction in mortality.[42-44] Owing to the absence of data demonstrating risk reduction of hip and nonvertebral fractures with ibandronate, it is not considered a first-line agent, although daily oral ibandronate therapy reduced the risk of developing new vertebral fractures by 50% to 60%.[45,46]

In the pivotal studies with bisphosphonates, antifracture efficacy was demonstrated primarily with once-a-day oral or once-a-year intravenous formulations. There are no fracture risk reduction data with prolonged oral dosage formulations and intravenous ibandronate therapy. Approval of these dosage forms used BMD and bone turnover as parameters of efficacy. Based on these parameters, alendronate 70 mg per week was seen to be similar to 10 mg per day, leading to the approval of the weekly dosage form.[47]

## Duration of use

The optimal duration of treatment in postmenopausal osteoporosis is uncertain. The long residence time of bisphosphonates in bone matrix suggests that stopping treatment after 3 to 5 years might result in residual clinical efficacy.[48] In response to postmarketing reports of long-term safety concerns, FDA reviewed long-term data from 3 extension studies ranging from 6 to 10 years.

All 3 studies were extensions of initial pivotal fracture trials in postmenopausal women of alendronate, zoledronic acid, and risedronate that included comparison of a placebo arm with active extension.[34,49,50] Most of the evidence on which FDA based their recommendations are derived from the 10-year alendronate (FLEX) and 6-year zoledronic acid (HORIZON-PFT) extension studies with a combined sample size of 2342 women.[34,49] Changes in BMD was the primary endpoint; they were all underpowered to detect fracture risk (a more meaningful endpoint for osteoporosis therapies).

Overall, findings for all 3 bisphosphonates were similar. Continuation of treatment beyond 5 years resulted in maintenance of femoral neck BMD and further increases in BMD at the lumbar spine. In patients who were switched to placebo, BMD in the femoral neck decreased modestly during the first 2 years and then stabilized, whereas BMD in the lumbar spine continued to increase despite discontinuation of bisphosphonate therapy.[51] The benefit in terms of fracture protection from continued bisphosphonate therapy was consistent in showing significant reductions in the risk of vertebral fracture; however, there was no overall reduction in nonvertebral fractures. This long persistence of effect is not true for all bisphosphonates. The FLEX and HORIZON trials showed that bone loss after discontinuation of therapy was only modest as compared with that during continued therapy, suggesting a similarly persistent effect of alendronate (5 years) and zoledronic acid (3 years). One observational study found that there is greater bone loss after discontinuation of risedronate therapy.[52] There are no data on effects after discontinuation of ibandronate therapy; thus recommendations regarding discontinuation should be limited to alendronate and zoledronic acid.[53]

In sum, although the evidence of long-

**Pause&Ponder**

**Due to recent long-term safety concerns, when should bisphosphonate therapy be stopped?**

term efficacy with bisphosphonate therapy is most robust for decreasing vertebral fractures, consistent evidence of a statistically significant reduction in nonvertebral fractures with the continuation of bisphosphonates is lacking. When considering the pooled composite endpoint of all osteoporotic fractures, both vertebral and nonvertebral, across the 3 extension trials (2496 patients), fracture rates were similar in patients who received continuous bisphosphonate treatment compared to patients switched to placebo. The available data suggest little benefit of continued bisphosphonate treatment beyond 5 years. No adequate clinical trials, however, have yet delineated how long the drugs' benefits are maintained after cessation.[51]

## "Drug holiday"

The decision about whether to stop therapy with bisphosphonates after 5 years of therapy is subject to debate. The long skeletal residence time of bisphosphonates and concern about the risks of rare adverse events with long-term therapy raise the possibility that bisphosphonate therapy may be interrupted for a drug holiday. Patients at low risk for fractures (women with femoral neck BMD T-score above -2.0 and without fracture history) are unlikely to benefit from continued treatment and are therefore good candidates for discontinuation of bisphosphonate therapy after 3 to 5 years of treatment, whereas patients at high risk for fracture may benefit from continued bisphosphonate therapy. Post-hoc analysis shows this high-risk group to include patients with a femoral neck BMD T-score below -2.5 or pre-existing vertebral fracture (with femoral neck T-score not higher than -2.0) after 5 years of treatment.[53,54] These recommendations may change as additional data about long-term risks of bisphosphonate therapy become available. For patients who discontinue treatment, there are currently no data to guide clinicians in determining when and whether to resume treatment.[53]

## Dosing, side effects, safety issues

Bisphosphonates are available for both oral (daily, weekly, monthly) and intravenous administration (**Table 2**). The bioavailability of oral bisphosphonates is poor and absorption is less than 1% even under ideal conditions. Absorption is further reduced when a bisphosphonate is taken with food, beverages (other than plain water), and medications. In addition, supplements containing divalent cations (calcium, magnesium, aluminum, iron) form complexes with bisphosphonates rendering them completely unavailable.[48]

The most common adverse effect associated with oral bisphosphonates is upper gastrointestinal (GI) intolerance (nausea, dyspepsia, abdominal pain, gastritis) secondary to mucosal irritation of the upper GI tract. There are additional postmarketing reports of esophagitis with esophageal erosions and ulcerations, especially when oral bisphosphonates are taken incorrectly. Proper patient instructions reduce the risk of esophagitis and facilitate adequate absorption.

[The effervescent 70-mg alendronate tablet] contains a very high sodium content, equivalent to 1650 mg NaCl.

**Patient counseling.** Instruct patients to take oral bisphosphonates in the morning on arising, at least 30 minutes (60 minutes with ibandronate) before eating, drinking, or taking other medications. Oral bisphosphonates should be swallowed with a full glass (180-240 mL) of plain water. Patients must remain in an upright position during that interval to avoid reflux of the drug into the esophagus and minimize GI irritation.[55-57] Oral bisphosphonates should not be given to patients who cannot remain upright for 30 to 60 minutes, who have active GI symptoms, or have delayed esophageal emptying (strictures or achalasia).[33]

Recent innovative formulations to facilitate ease of administration include a delayed-release formulation of risedronate, which can be taken immediately after breakfast with at least 4 ounces (half a glass) of plain water. The potential advantage of this delayed-release dosage form is improved bioavailability. Patients should remain upright for 30 to 60 minutes after administration to minimize esophageal irritation. This dosage form has an enteric coating to deliver risedronate beyond the stomach in the small intestine, with active drug released at a pH level above 5.5. It also contains a chelating agent—edetate disodium—which binds free divalent cations. This delayed-release regimen had similar efficacy and safety compared to the daily immediate-release regimen.[58-60] In March 2012 FDA approved a strawberry-flavored, buffered effervescent 70-mg alendronate tablet, which is dissolved over 5 minutes in 4 ounces of water and stirred for 10 seconds before drinking. The 70-mg effervescent tablet is bioequivalent to the usual 70-mg tablet formulations of alendronate, but no comparative studies are available. It also contains a very high sodium content, equivalent to 1650 mg NaCl, and must therefore be used with caution in patients on sodium-restricted diets.[28,61]

Intravenous bisphosphonates are not associated with upper GI events. Acute phase reactions with transient mild-to-moderate influenza-like symptoms occur with monthly oral or intravenous bisphosphonate therapy.[41,42,62,63] Symptoms usually start within 24 to 48 hours after administration and may last up to 3 days. Treatment with antipyretic agents generally improves the symptoms, and these rarely recur with subsequent infusions.

## Contraindications and precautions

Renal excretion is the only route of elimination for bisphosphonates.[48] Postmarketing cases of renal impairment and acute renal failure after rapid administration of intravenous zoledronic acid have been reported.[64] FDA product labeling states that bisphosphonates are not recommended for use in patients with creatinine clearance below 30 to 35 mL/min.[23-29] In addition, zoledronic acid should be infused over no less than 15 minutes. Pharmacists can recommend that patients' creatinine clearance and glomerular filtration rate be assessed before initiating therapy.[65]

By inhibiting bone resorption, bisphosphonates reduce calcium efflux from bone,

resulting in a small transient decrease in calcium. Symptomatic hypocalcemia is a rare complication to bisphosphonate use and risk factors include vitamin D deficiency, hypoparathyroidism, and impaired renal function.[66,67] Pre-existing hypocalcemia is a contraindication and should be corrected before beginning therapy.

An increased incidence of atrial fibrillation (AF) was reported in the pivotal phase 3 trial with zoledronic acid (1.3% in treated groups vs 0.5% in placebo groups; $P<.001$).[41] Subsequent analysis of post-hoc trials linking use of bisphosphonates with an increased risk of AF are discordant, however, and the available information does not reveal a consistent association.[33] At present, FDA does not recommend that healthcare providers or patients should change either their prescribing practices or their use of bisphosphonates.[68]

## Long-term safety

Although 3- to 4-year trials of bisphosphonates have not identified any consistent safety concerns, long-term safety concerns focus on osteonecrosis of the jaw (ONJ), esophageal cancer, and atypical femur fractures. Much of the long-term safety data are derived from case reports or epidemiology studies, and causality is uncertain, not established, or inconsistent.

ONJ was first identified in 2003, with over 94% of cases observed after invasive dental procedures in patients with malignancy receiving high doses of intravenous bisphosphonates.[69] The overall risk of ONJ in the treatment of osteoporosis seems very low, and the benefit of bisphosphonates in reducing fracture risk far outweighs the potential risk of ONJ.[70,71]

In 2009 there was a case series report of esophageal cancer occurring in patients with a history of oral bisphosphonate use.[72] Two case-control studies using the same United Kingdom general practice database reported opposite results.[73,74] Another report found no significant increases of esophageal cancer with long-term oral bisphosphonate use.[75] FDA has determined that the available evidence is inconsistent and there is not enough information to make definitive conclusions about a possible association between oral bisphosphonates and esophageal cancer.[76]

Bisphosphonates are associated with sporadic cases of atypical femoral fracture. Atypical femoral fractures are usually atraumatic, may be bilateral, are occasionally preceded by prodromal thigh pain (weeks to months), have unique radiologic features, and may have delayed fracture healing.[77,78] Since 2005 numerous case reports, case reviews, and small retrospective studies suggested a link between long-term bisphosphonate use and atypical femoral fractures.[79-85] This association was not supported by a reanalysis of randomized trials; however, this study was underpowered for definitive conclusions.[86] Recent large epidemiologic studies show conflicting evidence.[87-89] In 2010 the FDA required labeling changes to acknowledge that no causality was established but issued a safety notification and recommendation that new-onset groin or thigh pain must be ruled out for atypical fractures.[90] Thus nonhealing femoral fractures are considered to be unusual adverse effects associated with prolonged bisphosphonate use.[78,91,92]

## Denosumab

Denosumab is the newest antiresorptive agent approved in 2010 with a novel mechanism of action. It is a fully human monoclonal antibody that inhibits bone resorption by blocking endogenous RANK ligand (RANKL; receptor activator of nuclear factor kappa B ligand), which is essential for the formation, function, and survival of osteoclasts. RANKL is produced and released by osteoblasts and binds with its receptor RANK on the osteoclast. Denosumab, by binding to RANKL, prevents its interaction with RANK on osteoclasts, thus inhibiting its action. Osteoclast recruitment, maturation, and action are inhibited, and bone resorption slows.[93,94]

Label indications for denosumab include treatment of postmenopausal women with osteoporosis at high risk of fracture or who have failed or are intolerant to other available osteoporosis therapies. Denosumab is also approved for use in men with osteoporosis for increasing bone mass or who are receiving androgen deprivation therapy for prostate cancer and in women who are receiving adjuvant aromatase inhibitor therapy for breast cancer.[95-97] In clinical trials subcutaneous denosumab 60 mg every 6 months was shown to reduce bone turnover and increase BMD.[98-102] It also has been shown to reduce fracture risk in the FREEDOM study, a randomized, double-blinded, 3-year trial in postmenopausal women with osteoporosis. Vertebral fractures were reduced by 68%, hip fractures by 40%, and all nonvertebral fractures by 20%.[103] In a head-to-head trial comparing denosumab with alendronate, denosumab was associated with significantly greater increases in BMD and greater reduction in bone turnover markers.[101] When women treated with alendronate were switched to denosumab, continued improvement in BMD was greater than that seen in those continuing alendronate.[104] Neither trial, however, was powered to evaluate fracture as an endpoint. This phenomenon was also observed in an open-label study with ibandronate.[105]

Studies of up to 6 years' indicate a good safety profile.[102,103,106,107] The product information lists several common adverse effects that were not significantly different in rate compared to placebo.[95] Denosumab can exacerbate hypocalcemia (especially when creatinine clearance is <30 mL/min); therefore hypocalcemia must be corrected before beginning therapy. ONJ has been reported in a small number of cases.[102,108,109] Because RANKL is a member of the tumor necrosis factor family, there is concern of potential increased risk of serious adverse events including infections and malignancy. FDA is further assessing this through REMS (Risk Evaluation and Mitigation Strategies).[110]

**Patient counseling.** Pharmacists should

**Pause&Ponder**

**Mrs. X. is refilling her alendronate prescription and has heard of atypical fractures associated with bisphosphonate use. She wants to know if she should stop her therapy.**

encourage patients to report symptoms of hypocalcemia (paresthesias or muscle stiffness, twitching, spasms, cramps). In addition, because denosumab must be administered by healthcare professionals only, patients picking up denosumab from the pharmacy must be instructed on proper storage conditions for the single-use prefilled syringe prior to administration.[95] Pharmacists should also monitor for potential therapy with other denosumab products used in the treatment of bone metastases from solid tumors, multiple myeloma, and giant cell tumor of the bone.

## Partial estrogen agonists/antagonists

These agents, also known as selective estrogen receptor modulators, are nonsteroidal partial estrogen agonists that have the ability to bind to estrogen receptors and act preferentially as agonists in bone and as antagonists in breast and endometrial tissue. Raloxifene is the first and only agent of this class that is currently licensed for both the treatment and prevention of osteoporosis and for reduction in risk of invasive breast cancer in postmenopausal women.[111]

As an estrogen agonist in bone, raloxifene decreases bone resorption and bone turnover, and increases BMD. The approved dosage of raloxifene for all indications is 60 mg by mouth daily. It can be taken any time of the day without regard to meals. Administered at this dose raloxifene demonstrated beneficial effects on BMD and decreased bone turnover.[112-114] In the pivotal 3-year RCT Multiple Outcomes of Raloxifene Evaluation (MORE) trial, raloxifene therapy reduced the risk of fractures of the spine by 30% and 55% in patients with and without a prevalent fracture, respectively.[113] A study up to 4 years' duration suggests continued efficacy.[114] Continued treatment is necessary to maintain BMD.[115,116] Fracture efficacy was not demonstrated for hip and nonvertebral fractures.[113,114] The risk of invasive breast cancer was demonstrated to decrease by 72%.[117,118]

## Side effects, safety issues

In large placebo-controlled studies, raloxifene was associated with death from stroke and a 3-fold increase in occurrence of venous thromboembolic events (VTE).[119,120] FDA has a black box warning of increased risk of VTE and death from stroke. Raloxifene is contraindicated in women with an active or previous history of VTE or risk of VTE. A risk-benefit balance should be considered in women at risk for stroke.[111]

Common side effects associated with raloxifene include menopausal symptoms and leg cramps.[111] The risk-benefit profile of raloxifene (vertebral fracture benefit, breast cancer benefit, but no hip fracture benefit, and risk of thrombosis or risk of death from stroke) makes it better suited to the younger postmenopausal woman with osteoporosis who is at low risk of hip fracture and stroke.[121]

**Patient counseling.** Side effects with raloxifene can include blood clots, hot flushes, and leg cramps. Women who have had blood clots should not take this medicine. Raloxifene should be stopped at least 72 hours prior to and during prolonged immobilization such as postsurgical recovery because of the increased risk of blood clots. Patients should not take this drug if they have an increased risk for stroke, including women who have had a stroke, "mini-strokes," or transient ischemic attacks, AF, uncontrolled high blood pressure, and are smokers.

## Calcitonin

Calcitonin is a peptide produced by thyroid C cells that inhibits bone resorption by inhibiting osteoclast activity.[122] Salmon calcitonin (more potent antiresorptive than human calcitonin) is available in the United States as a nasal spray, subcutaneous injection, and in generic equivalents.[123] It is approved for postmenopausal osteoporosis treatment, but not prevention, in women at least 5 years beyond menopause. The main concern with calcitonin use has been its relatively modest fracture efficacy compared with other agents. The postmenopausal osteoporosis indication for calcitonin-salmon was based on data showing that the drug improved BMD.[123] One postmarketing RCT of intranasal spray calcitonin for 5 years reduced the risk of vertebral fractures by 33% compared to placebo. No effect was seen for nonvertebral or hip fractures.[124] After 5 years, calcitonin produced minimal increments to BMD of the spine alone.[124] In addition calcitonin has beneficial analgesic effects in women with acute painful compression fractures independent of its antiresorptive effects.[124,125]

Recent safety concerns of cancer risk with salmon calcitonin in osteoporosis led to its withdrawal in 2012 from the European market; only the injectable dosage form continues to be available for use in prevention of acute bone loss due to sudden immobilization, Paget's disease, or hypercalcemia.[126] In March 2013 FDA advisory committees reviewed safety data in trials of calcitonin (nasal and oral dosage forms) and concluded that even though the cancer signal is inconclusive, it is a consistent signal. Based on this finding and insufficient efficacy data to support its use in osteoporosis, the advisory committees voted to remove it from the United States market.[127] Effective October 1, 2013, calcitonin salmon nasal spray will be withdrawn from the Canadian market.[128] Pharmacists will need to know how to safely dispose of calcitonin nasal sprays.

## Estrogens

Hormone therapy is only approved in the United States for the prevention but not treatment of postmenopausal osteoporosis. Use of hormone therapy became controversial as a result of the Women's Health Initiative.[129] It should be noted, however, that in women younger than age 60 years hormone therapy provided an overall favorable effect on all-cause mortality.[130] A more extensive discussion on estrogen therapy is covered elsewhere.[18-20]

## Anabolic agents

Endogenous parathyroid hormone (PTH) is an 84 amino acid peptide secreted by the

Patients picking up denosumab from the pharmacy must be instructed on proper storage conditions for the single-use prefilled syringe prior to administration.

parathyroid gland and is critical to calcium homeostasis. PTH increases renal reabsorption of calcium and enhances intestinal calcium absorption via its effect on one hydroxylation of 25(OH)D3. Continuous secretion of PTH, such as in primary hyperparathyroidism, decreases bone mass, whereas intermittent secretion of exogenous PTH increases bone mass secondary to stimulation of osteoblastic bone formation and increased skeletal remodeling activity.[131-133]

Teriparatide, a recombinant fragment of human parathyroid hormone (PTH 1-34) is the sole anabolic agent approved in the United States for treating postmenopausal osteoporosis in women and in men at high risk for fracture.[134] It is available as a multidose prefilled pen for self-administration by subcutaneous injection once daily and treatment is restricted to 2 years over a lifetime because of bone cancer (osteosarcoma) found in rat studies.[135] Although this has not been observed in humans, FDA has a black box warning in the product labeling. It is contraindicated in patients at risk of osteosarcoma including children, those who have had radiation therapy, or who have Paget's disease.[134]

Fracture reduction was demonstrated in vertebral and nonvertebral categories (65% vs 53% vs placebo) in postmenopausal women. No improvement was seen in reduction of hip fractures.[136] Multiple studies demonstrate BMD increases at the lumbar spine, with more modest increases in the hip region.[136-139] On discontinuation of teriparatide therapy, substantial bone loss occurs and subsequent treatment with an antiresorptive medicine is recommended to preserve BMD.[140-142] The effect of pretreatment with bisphosphonates and the role of combination therapy are currently being evaluated.[143]

Common side effects include leg cramps, nausea, dizziness, and hypercalcemia.[134,136] Orthostatic hypotension may occur within 4 hours of administration and spontaneously resolves within minutes to a few hours. Patients should be counseled to immediately sit or lie down if symptoms occur.[134] PTH therapy is currently targeted in patients with severe osteoporosis who have had prior fractures while on other antiosteoporotic agents or have had intolerance to bisphosphonates.

**Patient counseling.** Teriparatide multidose pen injection should be given once daily at the same time in the thigh or abdomen. The pen is stable for up to 28 days and must be discarded after this time. It should be stored under refrigeration (but not frozen) and should be used immediately on removal from the refrigerator. Patients should be instructed on the proper disposal of pens and needles and educated on signs and symptoms and management of low blood pressure and low blood calcium.[134]

Women with osteoporosis or at risk for osteoporosis should be counseled about self-care measures to reduce the risk of bone loss; bone loss accelerates significantly with the onset of menopause. Key recommendations that pharmacists should know are on vitamin D and calcium, physical activity, falls prevention, and lifestyle changes.

**Vitamin D and calcium.** Supplementation with calcium and vitamin D has long been a cornerstone of therapy in postmenopausal osteoporosis. Women should be advised of current calcium and vitamin D recommendations and the benefits of a good nutrition rich in calcium and vitamin D. Over-the-counter supplements should be recommended when dietary intake is inadequate. Pharmacists should monitor for potential drug interactions of calcium supplements with prescription drugs, such as levothyroxine, iron, proton pump inhibitors, and suggest possible strategies to manage these drug interactions.

**Physical activity.** Performing weight-bearing and muscle-strengthening exercises seems to stimulate osteoblastic activity to maintain bone mass and reduce the risk of falls. There is no evidence that physical exercise in osteoporosis reduces fracture incidence. Studies instead report an increase in BMD or a decrease in the propensity to fall. A Cochrane review showed that aerobics, weight-bearing, and resistance exercises are all effective in increasing the BMD of the spine in postmenopausal women, but walking was only effective at the hip.[144] Specific types and duration of effective exercise interventions are discussed in a recent review.[145,146] Nevertheless, exercise, even low impact walking, should be recommended because it improves mobility, muscle function, and balance and consequently reduces the risk of falling.

**Falls prevention.** All patients with osteoporosis or at risk of osteoporosis should be assessed for risk factors for falls. Pharmacists can assess older individuals living in the community for presence of risk factors such as a history of previous falls, muscle weakness, impaired balance, dizziness and orthostasis, visual impairment, presence of certain medications (sedatives, psychotropics, antihypertensives) and environmental risks (loose rugs, insufficient lighting). Pharmacists can educate patients on the effect of medications on falls, provide advice to prevent postural hypotension, review and reduce or switch medications if appropriate, assist the patient to adopt appropriate falls prevention strategies at home, and refer patient for further evaluation.

**Lifestyle.** Smoking, excessive alcohol (>3 drinks/day), and excessive caffeine (>4 cups/day) consumption are significant risk factors for fractures.[145,147] General lifestyle changes should incorporate assistance in smoking cessation and advice on reducing alcohol and daily caffeine intake.

## Conclusion

Community pharmacists are in an ideal position to provide patient-centered pharmaceutical care in osteoporosis management. Poor adherence to bisphosphonate therapy is common and associated with poor outcomes and increased treatment costs Pharmacists can improve osteoporosis care by screening and providing early detection of high-risk patients, educating patients on osteoporosis, the role of medications and adherence, performing medication reconciliation, educate on potential adverse effects, identify and prevent risk factors for falls, perform calcium intake assessment, and counsel patients on the importance of calcium and vitamin D and other lifestyle changes for good bone health. •

**References are available online.**

## TEST QUESTIONS

**1. Pharmacists can play an important role in reducing the gaps in osteoporosis management by identifying high risk individuals such as?**
- **a.** A patient with rheumatoid arthritis on chronic glucocorticoid therapy
- **b.** A patient taking over-the-counter calcium and vitamin D
- **c.** A patient on bisphosphonate therapy
- **d.** A patient with a BMD T-score of 1.6

**2. All of the following pharmacologic options for osteoporosis can be classified as antiresorptive agents except?**
- **a.** Denosumab
- **b.** Bisphosphonates
- **c.** Parathyroid hormone
- **d.** Calcitonin

**3. When comparing osteoporosis therapies, clinical treatment efficacy is best demonstrated by which of the following?**
- **a.** Increase in bone mineral density (BMD)
- **b.** Decrease in BMD
- **c.** Decrease in fracture risk
- **d.** A and C

**4. Which of the following is the correct dose for osteoporosis prevention in a post-menopausal woman?**
- **a.** Alendronate 35 mg by mouth once weekly
- **b.** Alendronate 70 mg by mouth once weekly
- **c.** Risedronate delayed-release 35 mg by mouth once a week
- **d.** Zoledronic acid 5 mg by intravenous infusion every year

**5. All of the following bisphosphonates are considered as first-line agents for use in postmenopausal osteoporosis except?**
- **a.** Zoledronic acid
- **b.** Ibandronate
- **c.** Alendronate
- **d.** Risedronate

**6. Which of the following is true with stopping bisphosphonate therapy for a "drug holiday"?**
- **a.** Patients with femoral neck BMD T-score > -2.0 and without a fracture history after 3 to 5 years
- **b.** Patients with femoral neck BMD T-score > -2.0 plus a fracture history after 3 to 5 years
- **c.** Patients with fracture history or BMD T-score < -2.5 after 5 years
- **d.** Patients with fracture history or BMD T-score < 3.0 after 5 years

**7. All of the following patient counseling facts are accurate with the new delayed-release, 35-mg, once weekly formulation of risedronate except?**
- **a.** Should be taken with at least 4 ounces of plain water 30 minutes before breakfast and remain in an upright position
- **b.** Should be taken with at least 4 ounces of plain water immediately after breakfast and remain in an upright position
- **c.** It is approved only for treatment of postmenopausal osteoporosis
- **d.** It has improved bioavailability

**8. Orally or intravenously administered bisphosphonates should be contraindicated in which of the following patients?**
- **a.** Patients with a creatinine clearance <35 mL/min
- **b.** Patients with a creatinine clearance <50 mL/min
- **c.** Patients with hypercalcemia
- **d.** Patients with atrial fibrillation

**9. Your patient has heard on the news about atypical fractures and osteonecrosis of the jaw (ONJ) associated with bisphosphonate use and she is very concerned. Which of the following statements is best to include in your patient education?**
- **a.** Atypical fractures and ONJ are definitely caused by prolonged use of bisphosphonates.
- **b.** Atypical fractures and ONJ are considered to be unusual adverse effects, and the benefit of bisphosphonates in reducing fracture risk far outweighs the potential risk of these adverse effects.
- **c.** You should stop using bisphosphonates and follow up with your provider.
- **d.** You should continue to use bisphosphonates.

**10. A 72-year-old woman is filling a new prescription for denosumab. You proceed to provide this patient with advice on this medication. All of the following are accurate statements except?**
- **a.** Report symptoms of muscle cramps or spasms and numbness or tingling in your fingers, toes, or around the mouth.
- **b.** Store the injection in the refrigerator (do not freeze) until it is time for the injection to be administered.
- **c.** You should receive this medication once every 6 months.
- **d.** Its major advantage is that it can be used in patients with poor kidney function without any problems.

**11. Denosumab inhibits bone resorption by?**
- **a.** Decreasing BMD
- **b.** Blocking endogenous receptor activator of nuclear factor kappa B ligand
- **c.** Increasing premature osteoclast cell death
- **d.** Stimulating endogenous parathyroid hormone

**12. Raloxifene has been shown to?**
- **a.** Decrease the risk of invasive breast cancer
- **b.** Increase BMD
- **c.** Have no effect on hip and nonvertebral fractures
- **d.** All of the above

**13. Contraindications to raloxifene include:**
- **a.** Patients at risk or with previous history of venous thromboembolic events (VTE)
- **b.** Patients with endometrial cancer
- **c.** Patients with history of stroke
- **d.** A and C

**14. Teriparatide therapy is not recommended to exceed 24 months due to:**
- **a.** Significant increases in VTE
- **b.** Possible increased risk of osteosarcoma
- **c.** It stops working after 24 months.
- **d.** The body starts to reject the drug.

**15. Common counseling points of teriparatide include all of the following except?**
- **a.** The approved dosage is 20 µg once daily injected subcutaneously in thigh or abdomen.
- **b.** The disposable multidose pen syringe must be discarded after 28 days.
- **c.** Orthostatic hypotension may occur within 4 hours of injection.
- **d.** It is a first-line therapy to prevent osteoporosis in postmenopausal patients

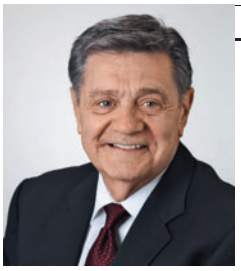
**16. Which of the following statements regarding salmon calcitonin in the U.S. is false?**
- **a.** It is approved for osteoporosis treatment in women at least 5 years beyond menopause.
- **b.** It is approved for prevention of osteoporosis in women at least 5 years beyond menopause.
- **c.** It has beneficial analgesic effects in women with acute painful compression fractures.
- **d.** It has modest fracture efficacy compared to other agents.

**17. Which safety concern with salmon calcitonin in osteoporosis led FDA advisory committees to recommend its removal from the U.S. market?**
- **a.** Ventricular arrhythmias
- **b.** ONJ
- **c.** Cancer risk
- **d.** Fatal stroke

**18. Which of the following lifestyle modifications is associated with promoting bone health?**
- **a.** Smoking cessation
- **b.** Alcohol use in moderation
- **c.** Daily coffee consumption in moderation
- **d.** All of the above

**19. Which of the following has not been shown to be a benefit of physical activity in osteoporosis?**
- **a.** Stimulates osteoblastic activity to maintain bone mass
- **b.** Reduces fracture incidence
- **c.** Decreases propensity to fall
- **d.** Improves balance and mobility

**20. Teriparatide therapy is currently targeted for use in patients with?**
- **a.** Prior fractures while on a bisphosphonate agent
- **b.** Intolerance to a bisphosphonate agent
- **c.** BMD T-score of -1.8
- **d.** A or B



**ETHICAL DECISION-MAKING IN PHARMACY** Kenneth R. Baker, BS Pharm, JD

# Making ethics work: Manage your counseling time

Every year I ask my students, "How many of you came to pharmacy school to be the least pharmacist you could possibly be?" Not a single hand has ever gone up. The point is to explain the difference between pharmacists' legal duty and their ethical duty.[1]

The legal standard is usually said to be what the "reasonably prudent" pharmacist would do under the same circumstances. It is the minimum every pharmacist is legally required to do. There is a higher standard — a professional, ethical standard. Every pharmacist aspires to this higher standard. We all want to be, not the least, but the best pharmacist.

Nothing in pharmacy practice today illustrates that point better than pharmacist counseling, particularly at the community, retail level. Every state requires the pharmacist at least to make an offer to counsel. In these states, the pharmacist who asks, "Do you have a questions for me?" has met the legal duty.

Several states today require actual counseling for all patients who receive drugs that they have not previously taken. In these states, the pharmacist is to tell the patient what the medication is, what it is normally used to treat, how it is to be taken, and other information the pharmacist believes is important, including common severe side effects and what to do if a dose is missed.[2]

## The time crunch

Over the years, pharmacists' attitudes toward counseling have changed. Today one is more likely to hear pharmacists complain that they do not have the time they need to give counseling to patients who need it. In one study, 29% of pharmacists said they thought "not enough time to counsel patients" was a cause of prescription errors.[3] In other studies, 84% of pharmacists blame high prescription volume for medication errors.[2,4]

While most studies have not found a direct correlation between prescription volume and errors[2,3], one fact does seem clear. Pharmacist counseling can improve compliance and increase the effectiveness of drugs, particularly drugs used to treat chronic illness.[2,3] The problem in a busy pharmacy is how to find the time to do the counseling pharmacists would like to do.

Like my students, most pharmacists aspire to be the best pharmacists they can be and to make a difference in patient's lives.[3,5] The problem is not that pharmacists do not want to live up to their ethical duties, but how they can organize their time to do so.

## Try an algorithm

One answer may be to find a way to select those patients who most need the pharmacist's advice and counsel. Consider creating an algorithm to identify these most needy patients. An algorithm is defined as "a set of rules for solving a problem."[6] In a pharmacist's counseling algorithm, the pharmacist makes a form noting the disease states, patient characteristics, and drugs that could signify a patient who would particularly benefit from counseling. An example might be a fictional Sam Jones:

**Sam Jones**

- ☑ Patient over 65
- ☑ On Coumadin
- ☑ On more than 5 meds
- ☑ Heart condition
- ☑ High blood pressure

All patients' needs are not equal. The trick lies in finding the ones who need your services the most. DT

### References


1. Mr. Baker teaches Ethical Decision Making at Midwestern University College of Pharmacy, Glendale, Ariz.
2. See for example *Arizona Board of Pharmacy Rules R4-23-402 (E) through (J).*
3. Gianutsos, G, *Identifying Factors That Cause Pharmacy Errors, U.S. Pharmacist*, December 1, 2008, citing Massachusetts Board of Registration in Pharmacy Medication Error Study. Massachusetts Office of Health and Human Services. *www.mass.gov*. Accessed October 1, 2008.
4. Phillips DP, Jarvinen JR, Phillips RR. A spike in fatal medication errors at the beginning of each month. *Pharmacotherapy*. 2005;25:1-9.
5. See Phillips, DP, op. cit. "The results of several studies suggest that up to 10% of hospital admissions and 23% of nursing-home admissions are related to noncompliance" (McKenney and Harrison,1976; Strandberg, 1984). A review of published studies of drug-related hospital admissions reported that 22.7% of adverse drug reaction hospitalizations were induced by noncompliance (McKenney et al., 1973)."
6. See Merriam Webster Dictionary, *http://www.merriam-webster.com/dictionary/algorithm* (accessed 8/21/2013).


*These articles are not intended as legal advice and should not be used as such. When a legal question arises, the pharmacist should consult with an attorney familiar with pharmacy law in his or her state.*

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**LEGAL COMPLIANCE** Ned Milenkovich, PharmD, JD

# Refill reminder programs in jeopardy

## HHS Office for Civil Rights squelches reimbursements

Federal healthcare privacy regulators and the nation's pharmacies, as well as drug manufacturers, are at odds over part of the Health Insurance Portability and Accountability Act (HIPAA): the Omnibus Rule (Rule) released by the Department of Health and Human Services (HHS) in January 2013. The section in contention deals with restrictions imposed on reimbursements for refill reminders sent to patients.

In general, with respect to its marketing provisions, the Rule strengthened HIPAA's existing privacy rule. Specifically, patients must authorize use of their protected health information (PHI) in any communication that is paid for by a drug manufacturer, if the patient information relates to the product promoted in the communication. The Rule sets forth the more stringent privacy provisions pursuant to the statute better known as the American Recovery and Reinvestment Act of 2009 (ARRA).

### The problem

Notwithstanding the patient authorization restriction, ARRA carved out a specific exemption for the use of PHI without patient authorization for third-party-funded marketing of prescription-reminder refills.

ARRA permits payments from drug manufacturers to pharmacies for reminder-refill mailings, but only if the payments are found to be "reasonable in amount."

However, rather than define this term itself, Congress tasked HHS to define what the term "reasonable" means in this context. HHS, in turn, concluded that the term "reasonable in amount" should mean that pharmacies should not be able to profit from refill reminders.

Historically, payments made by drug manufacturers to pharmacies vary, but are typically in the range of $1.50 for each refill reminder. With its interpretation, HHS effectively eliminated such a reimbursement.

### The critics' viewpoint

Critics complain that HHS' Office of Civil Rights narrowly interpreted the exception to the authorization requirement for paid refill reminders. These same critics want "reasonable" compensation defined much more broadly, to account for specific costs when profitability is calculated.

At least one major retail pharmacy chain has decided to end its refill-reminder program as a result of HHS' interpretation of the ARRA provisions, to the possible detriment of patient medication adherence and compliance programs.

A statement from the Center for Democracy and Technology has indicated that "clarifications would make the regulatory language regarding the refill reminder exception more consistent with other public health exceptions to the patient authorization requirement, such as the sale of PHI for research purposes. They also would bring HHS in line with Congress' original intent in drafting the refill-reminder exception in the HITECH Act, which is to promote and encourage these important medication adherence and patient education programs."

The same interest group specifically asked HHS' Office for Civil Rights "to clarify that: (1) entering into a business associate agreement with a third party in order to carry out a refill reminder program — a common practice among pharmacies — does not automatically trigger a patient authorization requirement; and (2) 'reasonable in amount' payment for refill reminder programs includes all reasonable direct and indirect costs related to them."

### The workaround

Even though HHS has determined that a pharmacy is entitled only to an amount that is not profitable, one possible workaround for the interested parties would be to obtain patient permission or an official "authorization" to receive the refill reminders. In that case, a pharmacy would be able to market to the patient until the patient withdraws the authorization.

If such a workaround could be realized operationally, then the "reasonable in amount" requirement would not apply, and pharmacies could continue to profit from the refill reminders.

Notably, on September 5, 2013, Massachusetts' Adheris Inc. filed suit in a District of Columbia federal district court against HHS and its Secretary Kathleen Sebelius, arguing the constitutionality of the Rule's restrictions on reminder payments. Adheris also filed a preliminary injunction motion to enjoin Sebelius' enforcement of these restrictions, which were otherwise set to begin on September 23, 2013. DT

*This article is not intended as legal advice and should not be used as such. When legal questions arise, pharmacists should consult with attorneys familiar with the relevant drug and pharmacy laws.*

**Ned Milenkovich** *is a partner and chair of the drug and pharmacy legal practice at Roetzel and Andress LPA. He is also vice-chairman of the Illinois State Board of Pharmacy. Contact Ned at 312-582-1676 or at nmilenkovich@ralaw.com.*


The DivaCup, available in two sizes, can be cleaned easily with DivaWash.


Dulcolax Laxative Suppositories with New DulcoGlide Applicators are a mess-free option for suppository use.

OTC

# Unmentionables worth mentioning

JULIA TALSMA, CONTENT CHANNEL DIRECTOR

Some young women, perhaps even some in their 30s, may not want to ask for certain feminine products that they consider embarrassing, such as products for the monthly menstrual cycle, constipation, overactive bladder, feminine odor, or lubrication, but they'll be looking for them. A number of new products in these categories are worthy of mention, for stocking on your shelves.

## The menstrual cycle

Women who want 12 hours of leak-free protection during their menstrual cycles may want to consider the **DivaCup** by Diva International Inc. The reusable bell-shaped silicone cup is placed in the vaginal canal for the collection of the menstrual flow. Free of latex, plastic, PVC, acrylic, and colors and dyes, the DivaCup is intended to provide comfort and durability. The product also features extra grip ridges for easy removal. It can be cleaned with **DivaWash,** made of plant-based ingredients. **(sales@divacup.com / 866-444-3482)**.

The **Lunette menstrual cup,** developed in Finland by Lune Group Oy Ltd and available in the United States, comes in sizes 1 and 2. The smaller one, Lunette size 1, is recommended for younger women who have not given birth, have a short vagina, and are active in sports. The larger one, Lunette size 2, is recommended for younger women who have given birth, adult women who have or have not given birth, and for individuals with heavy menstrual flow. The Lunette menstrual cup is made of medical-grade silicone and is latex-free. The cup should be emptied two to four times daily and can be used at night. Individuals can monitor the menstrual flow with the measuring lines on the inside of the cup. **(www.lunette.com)**

For women who prefer to use tampons, Proctor & Gamble offers the **Tampax Radiant** tampon product line, which includes Tampax Radiant Regular for regular menstrual flow, Tampax Radiant Super for heavy-flow, Tampax Radiant Super Plus for heavier flow, and Tampax Radiant Duopack for regular and heavy flow. These products offer leak protection and a resealable wrapper for disposal. **(http://m.tampax.com/en-US/products)**

Playtex Products LLC also has developed tampons for leak protection, including its **Playtex Gentle Glide 360° Protection line,** which includes Playtex Gentle Glide Regular Absorbency, Playtex Gentle Glide Super Absorbency, Playtex Gentle Glide Super Plus Absorbency, and Playtex Gentle Glide Ultra Absorbency tampons. This product line offers three layers of production, with a unique design made to custom fit the product to a woman's body. The applicator has a contoured tip and there is a small tube plunger for fast and easy

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PHOTOS COURTESY OF DIVA INTERNATIONAL INC. / BOEHRINGER INGELHEM PHARMACEUTICALS

# Unmentionables worth mentioning

Continued from pg. 47

insertion. **(www.playtexplayon.com/gentle-glide)**.

### Constipation relief

For fast, reliable constipation relief, Boehringer Ingelheim Pharmaceuticals has developed **Dulcolax Laxative Suppositories with New Dulco-Glide Applicators**. Recommended for the temporary relief of occasional constipation, these bisacodyl suppositories provide relief within 15 minutes to one hour. According to the company, the applicators offer a mess-free option for suppository placement. Each suppository comes individually wrapped for easy disposal of the applicator. This product can be used once daily for one week, if needed, by adults and children 12 years of age and older. **(www.dulcolaxusa.com/dulcoglide-applicators.html)**

Adding fiber to one's diet can help prevent constipation. It is now made easy, according to Procter & Gamble, with **Metamucil Fiber MultiGrain Wafers**, which come in two flavors — apple crisp and cinnamon spice. Just two wafers provide 5 g of dietary fiber, or 20% of the daily fiber needed, and only 4.5 g of fat per serving — 7% of the daily total fat content in a 2,000-calorie diet, according to the manufacturer. Adults and children 12 years of age and older can consume up to three servings daily. **(www.metamucil.com/metamucil-fiber-wafers.php)**

### Overactive bladder

An OTC treatment is now available for women dealing with symptoms of overactive bladder. At the beginning of the year, FDA approved **Oxytrol for Women,** the first OTC product for overactive bladder in women 18 years of age and older. The OTC Oxytrol product is not available for men with the condition. Appropriate users of this product include women who have had two or more symptoms of urinary frequency, urinary urgency, and urge incontinence for three months. Oxytrol for Women is a patch that contains oxybutynin to help relax the bladder muscle. Applied to the skin, the patch delivers 3.9 mg of oxybutynin per day. The patch should be removed and a new patch applied every four days. Oxytrol for Women is available in 16- and 32-day supplies. **(www.oxytrolforwomen.com)**

### Odor elimination

The Poise offerings from Kimberly-Clark Worldwide Inc. have received the stamp of approval from consumers, winning in the feminine wellness category of Product of the Year, according to an annual consumer survey compiled by TNS, a custom research agency that is part of Kantar, which queried more than 50,000 individuals. The **Poise FreshCare Femme Wash** helps eliminate vaginal odor with its pH-balanced formula. For women who need a gentle wash, **Poise GentleCare Femme Wash** was developed without glycerin, parabens, or dyes. For women on the go, **Poise Intimate Cleansing Cloths** provide a "shower-fresh feeling." These hypoallergenic cloths contain no alcohol, glycerin, parabens, or dyes, and according to the manufacturer are safe for daily use. **(http://www.poise.com/products)**


**Oxytrol for Women** is available nationwide for overactive bladder treatment.

Another convenient feminine product is **Poise Panty Fresheners**, individual-use fresheners that can be attached to the outside of an undergarment. They provide up to four hours of a clean, fresh scent. **(www.poise.com)**

Formulated to freshen the vaginal area and eliminate odor-causing bacteria, **Summer's Eve Cleansing Wash** products from Fleet Laboratories include Simply Sensitive, Delicate Blossom, Morning Paradise, Island Splash, and Naturally Normal. The company also offers the convenient **Summer's Eve Cleansing Cloths**, which can be carried in a purse or gym bag for occasions when women don't have time to take a shower. **(http://www.summerseve.com)**

### Hot flashes

For women who experience hot flashes, **Poise Upper Body Cooling Towelettes** were developed to quickly and conveniently ameliorate the discomfort. The towelettes offer the comfort of a cold washcloth in a resealable package of 20. Women can apply them to their faces, necks, or chests for an instantly cooling sensation. **(www.poise.com)**

It's 2 Cool, LTD, offers **Cool Off**, natural herbal towelettes for fast heat relief. Applied to the neck or inner arms, or behind the knees, the towelettes can bring relief to hot flashes or after exercise. **(www.allstarhealth.com)** DT

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## Advertiser Index



*Indicates a demographic advertisement.

RX & OTC

# New products

JULIANNE STEIN, CONTENT CHANNEL MANAGER



PHOTOS COURTESY OF JANSSEN PHARMACEUTICALS / PERRIGO CO.

## RX CARE

### New Rx

Astellas Pharma U.S has announced that **Astagraf XL** (tacrolimus extended-release capsules), approved in July, is now available in U.S. pharmacies. The first once-daily oral tacrolimus formulation available in the United States for the prophylaxis of organ rejection in patients receiving a kidney transplant, it is used with mycophenolate mofetil (MMF) and corticosteroids, with or without basiliximab induction. **(www.Astellas.us)**

### New indication

In September, FDA approved Janssen's **Stelara** (ustekinumab) **[1]**, alone or combined with methotrexate, to treat active psoriatic arthritis, a chronic autoimmune disease characterized by joint inflammation and psoriasis skin lesions, in patients 18 years of age or older. Stelara is the first treatment approved for psoriatic arthritis since the introduction of anti-TNF biologics more than a decade ago. It is currently the only therapy available that targets the cytokines interleukin-12/13, two proteins that may play a role in the development of psoriatic arthritis. **(http://www.stelarainfo.com)**

FDA has approved **Abraxane for Injectable Suspension** (paclitaxel protein-bound particles for injectable suspension) (albumin-bound) for the first-line treatment of patients with metastatic adenocarcinoma of the pancreas, in combination with gemcitabine. Adenocarcinoma, a subtype of exocrine tumors, accounts for about 95% of cancers of the pancreas. Abraxane is the first new treatment approved for metastatic pancreatic cancer in nearly eight years. **(www.abraxane.com)**

Allergan has received approval from FDA to market **Botox Cosmetic** (onabotulinumtoxinA), for an additional indication for temporarily reducing the appearance of moderate to severe lateral canthal lines, commonly known as "crow's feet." It is the first and only product of its kind approved for this indication. Botox Cosmetic received FDA approval in 2002 for the temporary improvement of moderate to severe glabellar lines (frown lines between the brows) for patients aged 18 to 65 years. According to the manufacturer, it remains the foremost minimally invasive aesthetic medical treatment globally. **(www.botoxcosmetic.com)**

### New formulation

Orexo U.S. has announced that once-daily **Zubsolv** (buprenorphine and naloxone sublingual tablets [CIII]) is now commercially available in pharmacies across the United States. Approved by FDA in early July, Zubsolv is a maintenance treatment for people suffering from opioid dependence. The product's higher bioavailability means less drug is available for inappropriate use. Each Zubsolv tablet is wrapped in an individual blister pack, reducing chances of tampering by children. Zubsolv should be used as part of a complete treatment plan that includes counseling and psychosocial support. Orexo is also launching RISE, an around-the-clock support program designed with input from patients in recovery. **(www.zubsolv.com / http://www.rise-us.com)**

### New generics

In late September, FDA approved Perrigo's **nitroglycerin lingual spray [2]** (generic for Arbor Pharmaceuticals'

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# New Products

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PHOTO COURTESY OF ABBOTT LABORATORIES

Nitrolingual Pumpspray) in the 400-µg-per-spray strength. The drug is used to relieve or prevent attacks of angina pectoris resulting from coronary artery disease. Perrigo was awarded 180 days of generic drug exclusivity, as it was the first company to submit an ANDA containing a paragraph IV certification. The product is shipping now. **(http://www.perrigo.com)**

In mid-September, Dr. Reddy's announced FDA approval of its **azacitidine for injection** (100 mg/vial), a bioequivalent generic version of Celgene's Vidaza. The product, which treats patients with myelodysplastic syndromes, is available in single-use vials. The company expects to launch the product soon. **(http://www.drreddys.com)**

At the end of August, FDA approved the emetic **ondansetron injection USP**, 4 mg/2 mL (2 mg/mL), the third prefilled generic injectable in the BD Simplist line from BD Rx Inc. Used to prevent postoperative nausea and vomiting, the product is currently on the FDA drug shortage list. BD Rx also manufactures metoclopramide injection, USP, and diphenhydramine hydrochloride injection, USP, and plans to launch between 20 and 30 generic drugs, concentrating on injectables commonly used in hospitals and surgical centers. **(http://bit.ly/ondansetron)**

In September 2012, following reports of differences in efficacy between GlaxoSmithKline's Wellbutrin XL, indicated for the treatment of major depressive disorder (MDD), and some generic versions, FDA asked companies making generic bupropion hydrochloride (HCl) extended-release tablets to conduct studies to demonstrate that their versions were as effective as the branded version.

Mylan has announced FDA approval of its supplemental Abbreviated New Drug Application, which provided bioequivalence study results for its generic **bupropion HCl extended-release (ER) tablets USP (XL)**, 300 mg. Mylan had launched 150-mg and 300-mg formulations of its bupropion HCl ER tablets USP (XL) in the U.S. market in September 2010. **(http://www.mylan.com)**

FDA has also approved Par Pharmaceutical's **bupropion HCl ER tablets** in the 300-mg strength. Par already markets generic bupropion in the 150-mg strength. Par had also conducted a study demonstrating that its version was equivalent to GSK's. **(http://www.parpharm.com)**

Continued on pg. 55

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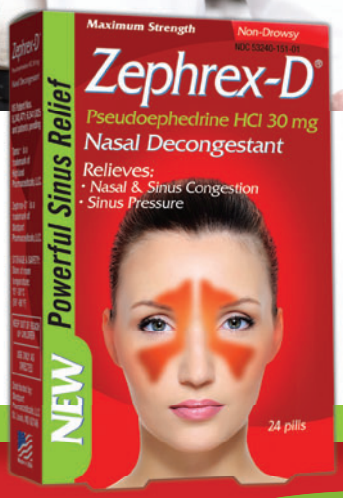


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# Products & Services



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## Financing



## Education

# New Products

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PHOTOS COURTESY OF MISSION PHARMACAL / PERFECTA PRODUCTS / PHARMAVITE

## NEW OTC

In September, Abbott introduced **Glucerna Advance [3]**, a new shake offering people with diabetes targeted nutrition formulated to minimize blood sugar spikes while supporting heart health and the immune system. Ingredients include slowly digested carbohydrates, plant-based phytosterols and omega-3s for heart health, antioxidants for the immune system (vitamins C and E, and selenium), and chromium from chromium picolinate for carbohydrate metabolism. The product comes in chocolate and vanilla flavors. **(http://glucerna.com/diabetes-shakes-advance)**

Perrigo has received final FDA approval for bubble-gum flavored **cetirizine hydrochloride oral solution USP** (1 mg/mL), the store-brand equivalent to Children's Zyrtec Allergy Syrup from McNeil. Perrigo expects to begin shipments of the product during the upcoming cough/cold/flu season. The product is indicated for indoor and outdoor allergies in children 2 years of age and older. **(http://www.perrigo.com)**

Westport Pharmaceuticals has announced the national availability of **Zephrex-D**, a pseudoephedrine-based decongestant formulated to resist breakdown by meth-makers. The product's meth-resistant properties are provided by an innovative locking technology that provides 100% pseudoephedrine relief while deterring misuse of the medication. In eight months of test-marketing at more than 300 stores in Missouri, the nation's top meth-lab seizure state, Zephrex-D was not connected with a single seizure, according to the Missouri Narcotics Officers Association. **(www.zephrex-d.com)**

Seen at the NACDS Total Store Expo in Las Vegas:

• **Dr. Smith's Diaper Rash Ointment [4]** from Mission Pharmacal, now available at Walgreens and Kroger's, as well as in many Walmart stores and regional retailers. Online purchase can be made through *walgreens.com*, *amazon.com*, and *drugstore.com*. **(http://doctorsmiths.com/)**

• Perfecta Products' new Zim's Advanced and Zim's Arnica Max product lines. **Zim's Advanced with Hydrocortisone [5]** is a topical treatment for rashes, insect bites, eczema, and psoriasis. **Zim's Advanced Gel with Acemannan** is formulated to treat cuts, scrapes, abrasions, and burns. The arnica and aloe in **Zim's Arnica Max** help bring temporary relief to the joint and muscle pain of simple backache, arthritis, strains, bruises, and sprains. **(http://www.zimsusa.com)**

• Pharmavite's three new adult gummy vitamins, **Nature Made Adult Gummies Multi + Omega-3**, **Nature Made Adult Gummies Energy B12 [6]**, and **Nature Made Adult Gummies Immune Complex with Zinc**, as well as **Nature Made VitaMelts Multi** and **Nature Made VitaMelts Hair, Skin & Nails**. **(www.naturemade.com)**

• Naturally based products from TCCD International, including **Detox Complex**, **Naturally Fresh Crystal Deodorant Foot Spray**, **GEODEO Natural Deodorant**, and **BuckPower Deer Velvet** spray. **(http://www.tccd.com)**

## New devices

FDA has approved Novo Nordisk's **Novopen Echo**, which, according to the company, is the first insulin injection device for diabetes patients to combine half-unit dosing with a memory function that records the dose and time passed since the last injection. The pen will be available to patients for use with NovoLog (insulin aspart [rDNA origin] injection) PenFill cartridges. The manufacturer suggests that this product may be especially helpful to children with diabetes and their caregivers, since half-unit dose increments allow for finer adjustments that can be particularly important for children. Different removable skins will be available for a "kid-friendly customized look." The pen will be available in the United States early in 2014. **(http://www.nonvolog.com)** DT

**JP AT LARGE** Jim Plagakis, RPh

# You might as well ask the dog

We saw Rosalie, the only female member of the grounds crew where I live, at the end of our walk. My dog is still a puppy, so I stood there as Rosalie did what most women do with a puppy. She squealed, "Oh, you widdle baby boy, Buddy." She rubbed Buddy's head until he rolled onto his back. She scratched his belly. "You are a precious puppy-wuppy." Then she rotated her right arm and held it with her left hand, and grimaced.

"Pain?" I asked. Rosalie is thirty-something and fit. She does what some people think is a man's job, and she does it well. I knew she could take care of herself. However, I had heard Katja, a member of the building maintenance crew, tell Rosalie that a certain pain medicine *goes right to the pain and stays away from the rest of your body.*

The drug is naproxen. According to Katja, *it has no side effects.* I reminded Rosalie that I am a pharmacist. After dispelling Katja's counseling fantasy, I advised Rosalie to talk to a pharmacist about drugs. I added that she should always disregard anything she hears about drugs from Katja.

## Out of the frying pan

Americans get themselves into big trouble with drugs — legal drugs. Years ago, OTC analgesic ear drugs were removed from the market. They were too good. Without pain, an ear infection became mastoiditis, and that led to surgery.

Everywhere you looked, there was the message: Drugs were good for you, they could solve any problem, they were safe. This has been a moneymaking proposition for close to 50 years. *Plop, plop, fizz, fizz. Oh, what a relief it is.*

Americans do not respect the fact that drugs have dangerous properties. Why should we? They tell us how good the drug is, but the dangers are recited so quickly that we never really hear the four words *sudden death is possible*.

## For example

Axiron is a deodorant-style, testosterone-based muscle-builder for "Low T." Of course, every parent knows that a Title IX girly-girl volleyball ace better not use it. Or do they? What's not to like about increased muscle mass for a daughter heading for a major college scholarship? You can get anything on the black market, and Americans just do not respect drugs.

Serena Williams recently appeared in a *Saturday Night Live* spoof called "Excedrin for Racial Tension Headaches." There are people out there who think that a syndrome called Racial Tension Headache really exists. *Of course it's real. I saw it on TV.*

Whose job is it to educate our culture in the idea that every single drug is a poison? Death is a function of dosage and frequency. You should see the look on their faces when I say, *You take enough often enough, and you are dead*. Priceless.

## 50 years and waiting

In 1964 *Drug Topics* reported that APhA Executive Director Willam S. Apple was all in for a fourth drug class: Rx drugs that could be refilled at the discretion of the pharmacist. Some years later, Apple went to the wall for a third class of OTC drugs: BTC, Behind the Counter.

Instead of BTC, what did we get? Greed, with no concern for the health and welfare of the consumer. Some OTC products are hazardous, but a lot more money is made when anyone can buy them. BTC would make a dent in profits.

Apple championed pharmacists and pharmacy. What has happened at APhA? Who will take up the mantle now?

## Don't ask Alice

The poster children for this proposition are Auntie Alice's favorites: the drugs for yeast infection. Auntie Alice has diagnosed more incidents of vaginal candidiasis than any doctor or pharmacist you can name.

"It's yeast, dear." Auntie Alice always knows. "They have drugs now."

The problem, Alice, is that bacterial vaginosis is much more prevalent than yeast. A pharmacist will ask the right questions. *Is there a foul odor? What does the discharge look like?* No odor and cottage-cheesy discharge, and Auntie Alice is good. A fishy odor and a grayish-white or yellow discharge, and you have bacteria.

If she listens to you, Alice, your favorite niece may end up with pelvic inflammatory disease. She may end up infertile. You want grandnieces and nephews, Alice? Refer Brenda to her pharmacist.

William S. Apple was out front on this, but he was left twisting in the wind.

BTC = Superior patient care.

OTC = More profits.

The difference? Greed. *Greed.* GREED. DT

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