The Pharmacist Activist

Volume 1, No. 3 • March 2006

A Tribute and a Warning

A friend, a teacher, a mentor, a leader, a professional---Pharmacist Barbara Korberly was all of these and more. Most of her professional career was spent at the McNeil Consumer and Johnson & Johnson companies at which she held important positions. More than any other pharmacist, she was responsible for the comprehensive studies and regulatory changes that resulted in the switch of prescription medications to OTC status, including Nicotrol, Imodium, Nasalcrom, and Children's Motrin. My students and I enjoyed learning from her when she would speak in my Nonprescription Drug Therapy course about such changes that had already been made and OTC switches that she anticipated would occur in the future.

Barbara died on July 8, 2005 at the age of 55 following a courageous battle against colon cancer. With all her accomplishments, she recognized the opportunity to do even more. Her fine personal qualities are reflected, in part, by her concern as she was approaching the end of her own life, for the continued provision of care for her elderly mother. In the spring of 2005, her friends and colleagues paid tribute to her at an event at which McNeil Consumer and Johnson & Johnson announced the establishment of the Barbara H. Korberly Professorship in Women's Leadership and Health at the Philadelphia College of Pharmacy at University of the Sciences in Philadelphia. She was thrilled!

In a discussion with Barbara at an earlier stage of her illness, she indicated her determination to recover and her plan to be an advocate for colon cancer screening. The best way through which we can honor her is to convey her important message to our families, friends, patients, and colleagues.

Colorectal cancer is the second leading cause of cancer-related death in the United States. In 2002 more than 56,000 Americans died from this disease. Regular colorectal cancer screening (e.g., fecal occult blood test [FOBT], colonoscopy) is recommended for adults aged 50 and older. Individuals at higher risk (e.g., those with a personal or family history of colorectal polyps or colorectal cancer, those with inflammatory bowel disease) should begin screening at a younger age and may need to be tested more frequently. Comprehensive information and recommendations are available at www.cdc.gov/colorectalcancer.

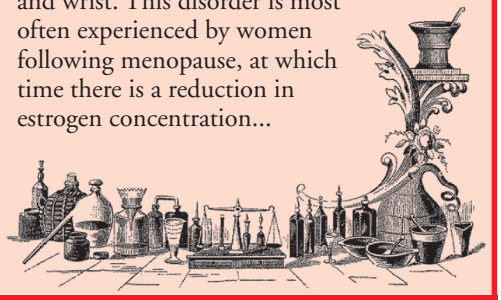
If you are older than 50, have you had a colonoscopy? If not, please arrange to do so, and convey this message to others.

- Daniel A. Hussar

Contents

Discussion

Osteoporosis is characterized by decreased bone mass and an increased risk of fracture, most often at the spine (vertebrae), hip, and wrist. This disorder is most often experienced by women following menopause, at which time there is a reduction in estrogen concentration...



Dear President Bush:

I wish to voice my strong objection to the comment you made about pharmacists in your discussion of the Medicaid program. Specifically, you noted, "People talked about how the decision to reform Medicaid was immoral. Well, it's not immoral to make sure that prescription drug pharmacists don't overcharge the system."

Your reference to "prescription drug pharmacists" is baffling as pharmacists are never described in this manner. However, of greatest concern, is your allegation that pharmacists overcharging the system is a reason to reform Medicaid. What is your basis for this statement that is so unfair and insulting to pharmacists?

You appear to be unaware of the severe financial restrictions under which pharmacists must practice. Pharmacists must purchase medications at prices that are established by the manufacturers/distributors of the drugs. In the Medicaid program, they must accept dispensing fees and product cost compensation that are determined/dictated by government agencies and/or managed care programs.

An unfortunate irony is that your comment was made so soon after Secretary Michael Leavitt praised pharmacists for their role in the implementation of the changes in the Medicare program. His specific observations were, "The efforts of pharmacists over the last month have been nothing short of heroic…They have been selfless, compassionate, and committed to service." This is the message that you also should have been communicating about pharmacists, instead of impugning them.

The new Medicare prescription program is widely perceived as having been developed by and for lobbyists and their clients, and being poorly planned and implemented. I recognize that you disagree with that assessment, but the serious problems in implementing the new program can not be denied. The situation would have been much worse were it not for the dedicated efforts of pharmacists who put the interests of their patients before their own interests. Unfortunately, many of these pharmacists are now experiencing cash-flow crises and severe financial hardships as a consequence, without any promise of relief from those who have the authority to provide it.

I am enclosing a copy of my letter to my Senator, Rick Santorum, in which I go into greater detail regarding problems associated with the Medicare program. For the reasons noted in that letter, I have urged him to initiate the administrative and/or legislative actions necessary to provide pharmacies with an administrative fee of $25 for every patient in the Medicare program who obtains prescriptions in that pharmacy. Although this amount does not begin to cover the costs incurred by pharmacists with respect to the implementation of the changes in the Medicare program, it represents a positive step in recognizing the value of the services provided by pharmacists. I urge you to support the provision of this administrative fee, and to arrange for the involvement of practicing pharmacists in efforts to make changes in the Medicare and Medicaid prescription programs that will facilitate the provision of needed medications to patients.

Another irony exists. Polls of pharmacists indicate that a large majority voted for you in both of your Presidential elections. While you have been President, I do not recall hearing you make any comments at all about pharmacists prior to your allegation about them overcharging the system. Why should these pharmacists continue to support you or the Republican candidate who will want to succeed you when you have publicly vilified them?

I urge you to retract your statement and to apologize to the nation's pharmacists.

Sincerely,

Daniel A. Hussar

New Drug Review

Ibandronate sodium (Boniva)

New Drug Comparison Rating (NDCR) = 4
(Significant Advantage[s])
in a scale of 1 to 5, with 5 being the highest rating

Indications (for oral use):

Treatment and prevention of osteoporosis in postmenopausal women.

Comparative drugs:

Alendronate (Fosamax), risedronate (Actonel)

Advantages:

- May be administered in a once-a-month dosage regimen that is more convenient for some patients
- Less frequent (once-a-month) administration reduces the number of times at which a patient is at risk of upper gastrointestinal (esophageal) adverse events associated with administration of the drug
- Is available in a formulation that is administered intravenously once every three months and provides an additional treatment option that may be preferred for certain patients

Disadvantages:

- Has fewer labeled indications
- Has not been demonstrated to reduce the incidence of nonvertebral fractures
- A longer time period (60 minutes compared with 30 minutes for the other agents) should elapse between the administration of the drug and consuming food or beverages, or lying down
- Some patients may find it difficult to remember to take the drug at monthly intervals

Conclusions:

The properties of ibandronate are generally similar to those of alendronate and risedronate. The new drug was not directly compared with the other agents in clinical studies prior to its approval, and there are no data that indicate that it is more effective or better tolerated than alendronate and risedronate. The feature that most distinguishes ibandronate from its predecessors is its formulation that may be administered just once a month, compared to the once-a-week regimens in which alendronate and risedronate are usually administered. The once-a-month regimen may be more convenient for some patients (and caregivers), particularly those in long-term care facilities. In addition, administering just one dose a month significantly reduces the number of occasions in which patients must observe sometimes inconvenient restrictions associated with taking the medication (i.e., must be standing up or sitting in an upright position, must wait to consume food, beverages, and some medications) and be at risk for the occurrence of esophageal adverse events.

The advantages for some patients of less frequent administration of ibandronate are at least partially offset by the lack of documentation that it reduces the incidence of nonvertebral fractures, the longer interval that should elapse between administration of the drug and consuming food or beverages (or lying down), and the possibility that some patients may find it difficult to comply with a regimen in which the medication is administered as infrequently as once a month.

The once-a-week regimens for alendronate and risedronate have been effective, well tolerated by most patients, and generally convenient, notwithstanding the restrictions associated with the administration of the medications. Alendronate is the agent with which there has been the most extensive experience and, for most patients, it should be the first choice among these three drugs unless there are circumstances that make the less frequent administration of ibandronate a compelling advantage.

The new formulation of ibandronate that is administered intravenously just once every three months offers an option that is not associated with the risk of esophageal adverse events or the restrictions in administering doses of the orally-administered formulations. However, renal function (serum creatinine) should be determined prior to the administration of each dose of the drug, and the cost of intravenous treatment is considerably higher than the oral use of any of the three agents. Accordingly, the use of the intravenous formulation should be reserved for patients who are not suitable candidates for oral therapy.

Cost to the pharmacist for a 3-month supply:

(adapted from Medi-Span Price Alert, March 15, 2006)

Actonel 35 mg tablets---$273.91
Boniva 150 mg tablets---$263.83
Fosamax 70 mg tablets--$273.91

Discussion

Osteoporosis is characterized by decreased bone mass and an increased risk of fracture, most often at the spine (vertebrae), hip, and wrist. This disorder is most often experienced by women following menopause, at which time there is a reduction in estrogen concentration and bone resorption exceeds bone formation.

Ibandronate sodium (Boniva-GlaxoSmithKline; Roche) is the third bisphosphonate derivative to be approved in the United States for the treatment and prevention of osteoporosis in postmenopausal women, joining alendronate (Fosamax) and risedronate (Actonel). The bisphosphonates inhibit osteoclast activity, reduce bone resorption and turnover, increase bone mineral density, and reduce the incidence of fractures.

A formulation of ibandronate that is administered once a day was initially approved in 2003, but the marketing of the product was delayed because of the recognition that it would not successfully compete with once-weekly formulations of alendronate and risedronate. In 2005, the FDA approved a formulation of ibandronate that is administered once a month and, in early 2006, approved a formulation that is administered intravenously every three months.

The effectiveness and safety of the daily administration of ibandronate were demonstrated in placebo-controlled studies. Monthly administration was evaluated in a noninferiority trial comparing it with daily use, and the effectiveness and safety of the two regimens were generally similar. Ibandronate is effective in reducing the incidence of vertebral fractures; however, the incidence of nonvertebral (e.g., wrist, forearm, hip) osteoporotic fractures was similar to that experienced by those in the placebo group. In contrast, alendronate and risedronate have been reported to reduce the incidence of both vertebral and nonvertebral fractures. Ibandronate was not directly compared with alendronate or risedronate in clinical studies prior to its approval.

In addition to the treatment and prevention of osteoporosis in postmenopausal women, alendronate and risedronate are also indicated for glucocorticoid-induced osteoporosis and Paget disease of bone. Alendronate is also indicated for increasing bone mass in men with osteoporosis. However, these are not labeled indications for ibandronate at the present time.

The presence of uncorrected hypocalcemia is a contraindication to the use of ibandronate and the other bisphosphonates. This condition should be corrected before initiating treatment, and patients should receive supplemental calcium and vitamin D if dietary intake is not adequate.

The primary concern with the oral use of bisphosphonates is the risk of upper gastrointestinal (GI) adverse events such as dysphagia, esophagitis, and esophageal or gastric ulcer. To reduce the risk of esophageal irritation/ulceration, the transit of ibandronate through the esophagus to the stomach should be facilitated

Free Subscription

Go to www.pharmacistactivist.com to sign-up for a FREE subscription.

The Pharmacist Activist will be provided FREE to interested pharmacists and pharmacy students who request a complimentary subscription by providing the information below. The opportunity to provide this newsletter without charge is made possible by the generous support of individuals who are committed to the provision of objective and unbiased information regarding new drugs, as well as editorial opinion about important issues facing the profession.

It is important that the development and distribution of *The Pharmacist Activist* be as cost efficient as possible. Therefore, we prefer to send the monthly issues to you via e-mail.

Sign-up online at:
www.pharmacistactivist.com

To assure that you will receive *The Pharmacist Activist*, sign-up online or complete this form and mail to address noted below.

☐ YES, I would like to receive a FREE subscription to
The Pharmacist Activist

Name: _____

Home Address: _____

City/State/Zip: _____

Work Address: _____

City/State/Zip: _____

E-mail: _____

Job Title/Student: _____

Employer: _____

Educational Facility/School: _____

Signature (required): _____ Date: _____

Mail this subscription form to:
The Pharmacist Activist
215 W. Church Rd., Suite 102, King of Prussia, PA 19406

Author/Editor
Daniel A. Hussar, Ph.D.
Philadelphia College of Pharmacy
University of the Sciences in Philadelphia

News, Information and Career Opportunities
NEWS - Line PUBLISHING

Publishers
Christopher J. Polli
G. Patrick Polli II

Assistant Editor
John Buck

Publications Director
Jeff Zajac

Graphic Artist/Designer
Joe Monte

The Pharmacist Activist
215 W. Church Rd., Suite 102
King of Prussia, PA 19406
610-337-1050 • Fax: 610-337-1049
E-mail: pharmacistactivist@news-line.com

by having patients swallow the tablet whole with a full glass of water while standing or sitting in an upright position. They should not lie down for 60 minutes after administering the drug, and should not chew or suck the tablet because of a potential for oropharyngeal ulceration.

The adverse events reported most often with the daily administration of ibandronate and at a higher incidence than with placebo include back pain (14%), pain in extremity (8%), dyspepsia (12%), diarrhea (7%), bronchitis (10%), headache (7%), and myalgia (6%). In the study in which the 150 mg once a month and the 2.5 mg once a day regimens of ibandronate were compared, the adverse events that occurred more frequently with the monthly regimen included abdominal pain (8%) and arthralgia (6%). In the postmarketing experience with the bisphosphonates there have been infrequent reports of severe bone, joint, and/or muscle pain. There have been rare reports of osteonecrosis (primarily in the jaw in patients undergoing dental procedures) associated with the use of the bisphosphonates, and the labeling for these agents has been revised to include a precaution regarding this possibility. Most of the reported cases have involved intravenous administration of the bisphosphonate in patients with cancer.

Following oral administration only a small fraction of a dose of ibandronate is absorbed and the oral bioavailability is approximately 0.6%. Both the bioavailability and the effect of the drug on bone mineral density are reduced if food or beverages are taken less than 60 minutes following administration of the drug. Accordingly, ibandronate should be administered with plain water (not mineral water) at least 60 minutes before the first food or drink of the day and before taking any oral medications or other products containing multivalent cations (e.g., antacids, supplements [e.g., calcium], milk). The oral bioavailability of alendronate and risedronate is similar to that of ibandronate, and it is recommended that these agents be administered at least 30 minutes before the first food or drink of the day or the use of potentially interacting medications.

The fraction of the dose of ibandronate that is absorbed either rapidly binds to bone (an estimated 40% to 50% of the circulating dose) or is excreted in the urine. The drug is not metabolized and is eliminated via the kidneys in unchanged form. Its use is not recommended in patients with severe renal impairment (creatinine clearance less than 30 mL/minute). Most of a dose of ibandronate is not absorbed and is excreted unchanged in the feces.

Ibandronate is supplied in tablets in 2.5 mg and 150 mg potencies. The 2.5 mg once-a-day regimen is rarely used because the once-a-month regimen is much more convenient. The recommended dosage is 150 mg once a month on the same date each month, administered at least 60 minutes before food, beverages (except plain water), or interacting medications. The once-a-month regimen is the feature that most distinguishes ibandronate from its predecessors. This regimen may be more convenient for some patients (and caregivers), particularly those in long-term care facilities, although there is also a possibility that some patients may find it difficult to comply with a regimen in which the medication is administered as infrequently as once a month. Once-a-month administration also reduces the number of occasions in which patients must observe sometimes inconvenient restrictions associated with taking the medication and be at risk for the occurrence of esophageal adverse events.

If the monthly dose of ibandronate is missed and the next scheduled dose is more than seven days away, the patient should take a 150 mg tablet in the morning following the day it is remembered. If the next scheduled dose is seven or fewer days away, the missed dose should not be replaced and the next dose should be taken according to the original schedule.

The recent marketing of a formulation of ibandronate that is administered intravenously just every three months offers an option that is not associated with the risk of esophageal adverse events or the restrictions in administering doses of the orally-administered formulations. However, renal function (serum creatinine) should be determined prior to the administration of each intravenous dose of the drug, and the cost of intravenous therapy is considerably higher. Therefore, the use of the intravenous formulation should be reserved for patients who are not suitable candidates for oral therapy.

- Daniel A. Hussar