The Pharmacist Activist

Volume 1, No. 11 • November 2006

Editorial

NO MORE EXCUSES!

Let's Get Cigarettes Out Of Pharmacies!

Since 1977, the Great American Smokeout has been observed on the third Thursday in November. On at least this one day out of the year, many think about, and some take action regarding, the devastating smoking-related illnesses and suffering that result in the deaths of more than 440,000 Americans each year. Why does our society that, in many respects, seems preoccupied with the problems of healthcare, its cost, and insurance coverage, tolerate this situation?

Some years ago I was a participant in a program on the consequences of smoking in which a physician panel member made the following statement that was so bold that I still recall it verbatim: "The tobacco industry should be treated as a criminal enterprise that thrives on addiction and murder." The latest outrage perpetrated by this industry is the recent discovery that some companies have been quietly increasing the nicotine content of cigarettes, thereby increasing the likelihood of addiction and the difficulty of quitting.

As pharmacists, we value and take pride in our role as health professionals. This role is not limited to our important responsibility in assuring the effective and safe use of medications, but also includes other steps that we are in a position to take to protect and improve public health. We should have no association with an industry that for many years denied that its products were addictive and carcinogenic, and which, most recently, has deceptively increased the nicotine content of cigarettes. We must not sell cigarettes in pharmacies when we want pharmacies to be considered as sources of healthcare.

Most independent pharmacies do not sell cigarettes, and I am particularly pleased to commend John Lorenzo and Anthony Zweier of Mackey's Pharmacy in my community of Newtown Square, PA on their decision earlier this year to stop selling cigarettes. Most chain pharmacies (with Target and FamilyMed being commendable exceptions) continue to sell cigarettes. In 2000, and again in 2003, I wrote letters to the CEOs of 25 of the largest chain pharmacy organizations in the country encouraging them to assume a leadership position in chain pharmacy by discontinuing the sale of tobacco products. I did not receive one response. However, their silence sends a clear and unfortunate message—they just don't care about the health of the people who buy cigarettes in their stores. In fact, some, when challenged by evidence of sales of cigarettes to minors, would rather spend substantial amounts of money to reprogram cash registers and to implement other systems than discontinue the sale of these products.

I have heard all the reasons that some have used in an attempt to defend the continued sale of cigarettes in their pharmacies. All these reasons can be reduced to one word—MONEY. However, no pharmacy has ever gone out of business, or from profitable to unprofitable, as a result of a decision to stop selling cigarettes. Therefore, the question becomes whether the owner/executives of a pharmacy are willing to accept the possibility of a pharmacy being slightly less profitable. Actually, I am confident that a reduction in profit does not have to be experienced as the space and resources currently allocated to tobacco products can be devoted to products and services that can provide a similar or better financial return.

Daniel A. Hussar

As individual pharmacists, and as a profession, we should take the necessary actions to get tobacco products out of pharmacies. The following are among the steps that we can take:

— Pharmacists and pharmacy students who are employed in pharmacies that sell tobacco products should urge the owner/manager/executive to discontinue their sale. If there is a hesitation to do that, please provide them with a copy of this commentary.

— Colleges of pharmacy should not use pharmacies that sell tobacco products as experience sites to send students.

— Colleges of pharmacy and pharmacy organizations should encourage pharmacy students and pharmacists who are seeking employment in a community pharmacy to first consider pharmacies that do not sell tobacco products.

Contents

Paying $155 Million Means Never Having to Say You are Sorry (or Admit to any Wrongdoing)
Page 2

New Drug Review
Sitagliptin phosphate (Januvia)
Page 3

Discussion
Incretins are naturally occurring hormones that increase insulin secretion in the presence of elevated glucose concentrations (e.g., following meals). In 2005, exenatide (Byetta) was marketed as the first agent for the treatment of diabetes mellitus that acts by increasing the action of incretins.
Page 4

Free Subscription

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

The Pharmacist Activist will be provided FREE via e-mail 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: _____

E-mail: _____

Home Address: _____

City/State/Zip: _____

Work Address: _____

City/State/Zip: _____

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

Publishers
Christopher J. Polli • G. Patrick Polli II

Assistant Editor
John Buck

Publications Director
Jeff Zajac

Graphic Artist/Designer
Joe Monte

The opinions and recommendations are those of the author and do not necessarily represent those of his full-time employer or the publisher.

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

News, Information and Career Opportunities
NEWS - Line PUBLISHING

Paying $155 Million Means Never Having to Say You are Sorry (or Admit to any Wrongdoing)

In late October it was announced that Medco Health Solutions would pay $155 million to settle charges brought against it by the Department of Justice. The charges brought by the government were based, in part, on information provided by several whistle-blowing pharmacists who used to work for Medco and included allegations that Medco submitted false claims to the government, solicited and accepted kickbacks from pharmaceutical companies to favor their drugs, paid kickbacks to health plans to obtain business, destroyed valid prescriptions it could not dispense on a timely basis to avoid paying penalties under its contracts, underfilled prescriptions, used drugs other than those prescribed to earn rebates from pharmaceutical companies, and more.

As is often the case with settlements, the agreement does not require Medco to admit any wrongdoing. This is the point that is emphasized in Medco's statement regarding the settlement; "After nearly seven years of inquiry, these issues end as they began - with no finding of wrongdoing by Medco or any of its people… Even though we did nothing wrong, for our company and our clients it is the right decision to put these aged matters in the past."

These statements invite several questions. Did the Department of Justice, the whistle-blowing pharmacists, and others make up these allegations? If there was no wrongdoing, would not an individual or company want to do everything possible to demonstrate innocence? If there was no wrongdoing, would a company be willing to pay as much as $155 million to avoid further investigation and a trial? Does the statement, "…these issues end as they began…," somehow ignore that most would consider payment of $155 million to be a major difference between the end and the beginning?

One thing is very clear. *Admitting* to no wrongdoing is not the same thing as *committing* no wrongdoing. Indeed, statements made by Medco earlier in the investigation indicated that concerns of the government were based on the actions of some "rogue" employees who broke Medco's rules and were subsequently fired. Most would interpret such actions to be wrongdoing on the part of individuals who were employed by Medco.

The Medco statement at the time of the settlement also noted, "Our business practices today are widely regarded as setting the standard for our industry." This comment invites the question – If what has happened at Medco is "setting the standard," what must things be like in the rest of this industry?

There have been numerous charges brought against Medco and other large pharmacy benefit managers (PBMs) in recent years by government agencies/officials. However, as in this case, settlements have been reached that usually involve payment of millions of dollars. The settlements do not resolve the questions and suspicions that continue to exist. Government agencies should accept the responsibility to pursue a definitive determination of whether alleged actions are wrongdoing or not wrongdoing. The events that are alleged are sufficiently serious that PBMs should be prevented from buying the opportunity to claim that they were not involved in wrongdoing.

Daniel A. Hussar

New Drug Review

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

Sitagliptin phosphate (Januvia)

Indications:

As an adjunct to diet and exercise to improve glycemic control in patients with Type 2 diabetes mellitus; used as monotherapy or in combination with metformin or a thiazolidinedione (pioglitazone, rosiglitazone) when the single agent alone, with diet and exercise, does not provide adequate glycemic control.

Comparative drugs:

Exenatide (Byetta), metformin (e.g., Glucophage), pioglitazone (Actos), rosiglitazone (Avandia)

Advantages:

- Has a unique mechanism of action;
- Less likely to cause adverse events (e.g., less likely than exenatide and metformin to cause gastrointestinal effects; less likely than pioglitazone and rosiglitazone to cause edema and weight gain);
- Less likely to interact with other drugs;
- May be used in patients with renal impairment (with adjustment of dosage; compared with metformin that is contraindicated);
- May be used in patients with congestive heart failure (compared with metformin that is contraindicated in patients requiring treatment for congestive heart failure);
- Is administered orally (compared with exenatide that is administered subcutaneously);
- Is in Pregnancy Category B (compared with exenatide, pioglitazone, and rosiglitazone that are in Category C [metformin is in category B]).

Disadvantages:

- May reduce hemoglobin A1C to a lesser extent than the other agents;
- Indications are more limited (e.g., compared with metformin, pioglitazone, and rosiglitazone that are also indicated for use in combination with sulfonylureas and insulin);
- Not available in combination formulations with other antidiabetic agents (compared with metformin, pioglitazone, and rosiglitazone).

Conclusions:

Sitagliptin has a mechanism of action that is unique among the antidiabetic agents. It inhibits dipeptidyl peptidase-4 (DPP-4), an enzyme that inactivates incretins (hormones that increase insulin secretion). Inhibition of DPP-4 slows the inactivation of incretins, thereby increasing and prolonging their action. Sitagliptin is effective in improving glycemic control when used as monotherapy or in combination with metformin, pioglitazone, or rosiglitazone. However, the reduction of hemoglobin A1C reported with its use (0.6%-0.8%) is not as pronounced as with other agents (e.g., metformin).

Sitagliptin is well tolerated and is less likely than the other antidiabetic agents to cause adverse events and to interact with other medications. It is much less likely than exenatide and metformin to cause gastrointestinal adverse events, and much less likely than pioglitazone and rosiglitazone to cause edema and weight gain. Although its clearance is reduced in patients with impaired renal function, it can be used (in a reduced dosage) even in patients with severe renal impairment. In contrast, the use of metformin is contraindicated in patients with impaired renal function because of the increased risk of lactic acidosis.

The effectiveness of sitagliptin following oral administration is an advantage over exenatide that is administered subcutaneously. It is administered once a day without regard to food.

Sitagliptin is a very useful addition to the group of antidiabetic agents. Its unique mechanism of action and excellent safety profile may extend the effectiveness of combination regimens that are administered orally and avoid the need to initiate the use of insulin. The greatest value of sitagliptin is in patients with diabetes who also have other complications (e.g., impaired renal function, congestive heart failure) that contraindicate or otherwise limit the use of metformin, pioglitazone, or rosiglitazone.

Discussion

Incretins are naturally occurring hormones that increase insulin secretion in the presence of elevated glucose concentrations (e.g., following meals). In 2005, exenatide (Byetta) was marketed as the first agent for the treatment of diabetes mellitus that acts by increasing the action of incretins. Exenatide is administered subcutaneously as adjunctive therapy in patients with type 2 diabetes who have not achieved adequate glycemic control with the use of metformin (e.g., Glucophage) and/or a sulfonylurea (e.g., glyburide).

In late 2006, sitagliptin phosphate (Januvia-Merck) was marketed as the first of a new class of antidiabetic agents that can be administered orally to increase the action of incretins. The incretins are rapidly inactivated by the enzyme dipeptidyl peptidase-4 (DPP-4). Sitagliptin is a DPP-4 inhibitor that slows the inactivation of incretins, thereby increasing and prolonging their action. The new drug is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus, either as monotherapy or in combination with metformin or a thiazolidinedione (pioglitazone [Actos], rosiglitazone [Avandia]) when the single agent alone does not provide adequate glycemic control. It is not effective in the treatment of type 1 diabetes mellitus or in the treatment of diabetic ketoacidosis.

In the clinical studies, treatment with sitagliptin provided clinically significant improvements in hemoglobin A1C, fasting plasma glucose, and 2-hour postprandial glucose compared to placebo. When used as monotherapy, sitagliptin reduced A1C by 0.6% - 0.8% compared with placebo and, when used with metformin or pioglitazone, reduced A1C by approximately this same percentage compared to the placebo plus metformin or pioglitazone regimens.

Sitagliptin is well tolerated and the overall incidence of adverse events reported in the clinical studies was similar to that reported with placebo. The adverse events reported most often include upper respiratory tract infection (6%), nasopharyngitis (5%), and headache (5%). The new agent does not cause hypoglycemia and is not likely to cause hypoglycemia when used in combination with metformin or a thiazolidinedione. However, its concurrent use with an agent that is known to cause hypoglycemia (e.g., sulfonylureas, insulin) should be closely monitored.

The use of some antidiabetic agents (e.g., sulfonylureas, thiazolidinediones) has been associated with weight gain, whereas the use of exenatide has been associated with weight loss. In the studies of sitagliptin, there was no or little change in body weight compared with baseline.

Like metformin, sitagliptin is classified in Pregnancy Category B, whereas exenatide, pioglitazone, and rosiglitazone are classified in Category C. The effectiveness and safety of sitagliptin in pediatric patients have not been established.

Following oral administration, sitagliptin is rapidly absorbed and it may be administered without regard to food. It is metabolized to only a limited extent and approximately 80% of a dose is excreted unchanged in the urine. The concurrent use of sitagliptin and digoxin has been reported to cause a slight increase in the AUC (11%) and peak concentration (18%) of the latter agent. An adjustment in dosage is not considered necessary but concurrent use should be closely monitored. Sitagliptin is less likely than most other antidiabetic agents to interact with other medications.

The recommended dosage of sitagliptin is 100 mg once a day. The clearance of the drug is reduced in patients with renal insufficiency and the dosage should be reduced to 50 mg once a day in patients with moderate renal insufficiency and to 25 mg once a day in patients with severe renal insufficiency.

Sitagliptin phosphate is supplied in tablets in quantities equivalent to 25 mg, 50 mg, and 100 mg of sitagliptin base. A formulation containing a combination of sitagliptin and metformin is under development. Several other DPP-4 inhibitors are being evaluated in clinical trials.

Daniel A. Hussar