The Pharmacist Activist

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Editorial

Wal-Mart's Generics Scam

Ignores the Professional Role of Its Pharmacists

The announcement by Wal-Mart that it is initiating a program in which it will provide a 30-day supply of certain generic medications for $4 has generated extensive publicity. Target quickly responded by noting that it would match Wal-Mart's prices.

I view Wal-Mart's action as a deceptive publicity stunt designed to bring more people into their stores. It has already resulted in confusion and misinterpretation on the part of the media who are trying to describe the program and the patients who expect to benefit from it. Wal-Mart's program only covers a small fraction of the generic medications that are available (the lowest-priced ones) and it should have made that clear at the outset rather than trying to create the impression that the approximately 300 products they are including in the program (representing less than 150 different drugs) is a large number. This program will just add to the chaos of evaluating and comparing prescription prices and programs, particularly for the patients who are still baffled by the multiplicity of the Medicare prescription plans and formularies, "doughnut holes," etc. How will this new program interface with existing prescription benefit programs? As one example, for a patient who is participating in one of the Medicare plans, who is responsible for paying the $4?—the patient? the government? the PBM/insurance company administering the plan? all of the above? The battle lines are probably being drawn now as to how the responsibility for paying the $4 should be divided.

Reducing the cost of medications is a desirable goal. However, programs of this type create confusion and have the potential to fragment the provision of medications to patients (i.e., from multiple pharmacies) in a manner that will increase the risk of drug-related problems.

I sympathize with the pharmacists who are employed at Wal-Mart, Target, and the other companies that develop such a program. They will be inundated with questions, many of which they will not be able to answer to the patient's satisfaction (e.g., Why isn't my generic Zocor covered?). These pharmacists should insist on having additional staffing support if/when these programs are implemented.

Although the issues discussed above are highly problematic, I am most concerned by, and strongly object to, the manner in which these companies have ignored the value of the professional role and services of their pharmacists in the design of these programs. In various studies it has been determined that the cost of dispensing a prescription (e.g., salaries, overhead) in community pharmacies is far more than $4, and this does not include the cost of the medication. Notwithstanding the fact that the generic drugs included in the $4 program are the least expensive of all medications, $4 does not begin to cover the other costs associated with dispensing a prescription. What is the cost (exclusive of drug product cost) of dispensing a prescription at Wal-Mart and Target? Are their $4 generic prescriptions being dispensed below this cost?

Wal-Mart and Target should discontinue their misleading generic programs. If they do not, their pharmacists should strongly object to the way in which these programs ignore/devalue their professional role and services, and take appropriate action.

Daniel A. Hussar

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News, Information and Career Opportunities
NEWS - Line PUBLISHING

It is Almost Election Day!

Do You Know What Your Candidates Stand For?

I deplore the highly negative rhetoric that characterizes so many of the election campaigns. Character assassination is commonplace and both incumbents and challengers attack the record (or lack thereof) of their opponents. The criticism is so pervasive that it becomes very difficult to determine what a candidate stands for, and what her/his position is on important issues. Many incumbents actually prefer that we do not know or remember how they voted on certain issues, and many challengers are so intent on criticizing the incumbents that they try to escape taking any positions.

It is important that we be knowledgeable about multiple and varied issues, as well as the positions, voting records, and personal qualities of the candidates, in determining which individuals we will support. As pharmacists, however, we have a particular responsibility to determine the positions of the candidates on the issues that are extremely important to our profession's ability to serve our patients and communities.

In the state of Pennsylvania we have a hotly-contested senatorial election in which the incumbent Rick Santorum is being challenged by Bob Casey, Jr. Senator Santorum voted for the Medicare and Medicaid prescription programs legislation and budgets that have had such a devastating impact on many community pharmacists and patients.

I think that Bob Casey, Jr. understands the concerns of our profession in general and community pharmacists in particular. However, I am concerned that he has not confirmed this in any written communication or public statement. He is missing an opportunity to obtain strong and active support from pharmacists.

As Election Day approaches, the rhetoric and negativism escalates. I find the campaigns of both candidates to be disgusting. I do not want to be in a situation in which I vote for the candidate who "is the lesser of two evils" or who ran the least sleazy campaign. But I have been active and I will vote!

It is not too late for pharmacists to have a deciding influence in many of the 2006 elections. We are fortunate in that the issues that are very important for the profession of pharmacy are also important for our patients and communities. But we must communicate what we stand for! All of us should consider this to be a personal responsibility and, if our profession does not recognize this as a collective responsibility, we will experience the consequences. The observation, "If you stand for nothing, you will fall for anything," should be our warning. What do you stand for and what actions will you be taking?

Daniel A. Hussar

New Drug Review

Ranolazine (Ranexa)

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

Indications:

Treatment of chronic angina; should be reserved for patients who have not achieved an adequate response with other antianginal drugs; should be used in combination with amlodipine, a beta-blocker, or nitrate.

Comparative drugs:

Amlodipine (Norvasc), beta-blockers (e.g., atenolol [e.g., Tenormin]), long-acting nitrates (e.g., isosorbide mononitrate [e.g., Imdur]).

Advantages:

- Unique mechanism of action
- May increase the effectiveness of antianginal regimens in some patients in whom the previous regimens did not provide an adequate response

Disadvantages:

- May cause QT interval prolongation
- Interacts with more medications
- Contraindicated in patients with hepatic disease

Conclusions:

Ranolazine has a unique mechanism of action and may increase the effectiveness of regimens used for the treatment of chronic angina in some patients who have not responded adequately to previous therapy. It is not indicated for monotherapy and should be used in combination with amlodipine, a beta-blocker, and/or a long-acting nitrate. Because it may cause QT interval prolongation, it is not a first-line agent for the treatment of chronic angina, and its use should be reserved for patients who have not experienced an adequate response with other antianginal agents.

The use of ranolazine is contraindicated in patients with pre-existing QT prolongation and in patients taking other QT-prolonging drugs (e.g., many of the antiarrhythmic agents). It is extensively metabolized via the CYP3A pathway and its use is contraindicated in patients being treated with a potent or moderately potent CYP3A inhibitor, including diltiazem (e.g., Cardizem) and verapamil (e.g., Covera-HS) that have an indication for the treatment of angina. It may also interact with other medications via other mechanisms.

Discussion

Ranolazine (Ranexa-CV Therapeutics) is the first drug to be approved for the treatment of chronic angina in more than a decade, and its structural and pharmacologic characteristics differ from those of the long-acting nitrates (e.g., isosorbide mononitrate [e.g., Imdur]), beta-blockers (e.g., atenolol [e.g., Tenormin]) and calcium channel blocking agents (e.g., amlodipine [Norvasc]). It has been described as a late sodium current inhibitor, but the specific mechanisms through which it provides its antianginal and anti-ischemic effects have not been identified. The clinical benefit attributed to its use does not depend on reductions in heart rate or blood pressure.

Ranolazine is indicated for the treatment of chronic angina, and should be used in combination with amlodipine, a beta-blocker, or a long-acting nitrate. Amlodipine is designated as the calcium channel blocking agent that is appropriate for concurrent use because the concurrent use of ranolazine and other dihydropyridine calcium channel blockers has not been evaluated, and the use of ranolazine with diltiazem (e.g., Cardizem) or verapamil (e.g., Covera-HS) is contraindicated because of the risk of serious interactions. Because it is known to prolong the QT interval of the electrocardiogram, ranolazine is not a first-line agent for the treatment of chronic angina and should be reserved for use in patients who have not achieved an adequate response with other antianginal drugs.

In several clinical studies of ranolazine, patients who were already being treated with other antianginal drugs received either the new drug or placebo. The patients treated with ranolazine experienced, in general, one less angina episode a week (e.g., three episodes instead of four), and the need for sublingual nitroglycerin for the treatment of acute episodes was reduced. The effect of ranolazine on angina rate or exercise tolerance was observed to be smaller in women than in men.

Ranolazine prolongs the QT interval in a dose-related manner. Although problems associated with this effect were

not identified in the clinical studies, other drugs causing this response have been associated with the occurrence of torsades de pointes-type arrhythmias and sudden death. Because of the risk of additive effects on the QT interval, ranolazine is contraindicated in patients with pre-existing QT prolongation (e.g., congenital long QT syndrome, uncorrected hypokalemia) and in patients taking other QT-prolonging drugs (e.g., Class Ia antiarrhythmic agents [e.g., quinidine], Class III antiarrhythmic agents [e.g., dofetilide (Tikosyn), sotalol (e.g., Betapace)], thioridazine [e.g., Mellaril], ziprasidone [Geodon]).

Ranolazine is extensively metabolized, primarily via the CYP3A pathway, and the concurrent use of another medication that inhibits this pathway will increase the concentration of the new drug, as well as the risk associated with QT prolongation. Accordingly, ranolazine is contraindicated in patients treated with a potent or moderately potent CYP3A inhibitor (e.g., azole antifungal agents [e.g., ketoconazole (e.g., Nizoral), itraconazole (e.g., Sporanox)], diltiazem, verapamil, clarithromycin [e.g., Biaxin], erythromycin, HIV protease inhibitors, grapefruit-containing products).

The QT prolonging effect of ranolazine is increased approximately three-fold in patients with hepatic dysfunction, and ranolazine is contraindicated in patients with mild, moderate, or severe hepatic disease.

The adverse events experienced most frequently in the clinical studies with ranolazine include dizziness (6%), headache (6%), constipation (5%), and nausea (4%). Syncope was reported in less than 1% of patients but, because of the possibility of dizziness and syncope, patients should be advised to determine how they respond to the medication before they drive or engage in other activities that require alertness and coordination. Approximately 6% of the patients treated with ranolazine discontinued treatment because of an adverse event, compared with 3% of those receiving placebo.

Small, reversible elevations in serum creatinine and BUN concentrations have been observed in some patients treated with ranolazine, although there was not evidence of renal toxicity. Patients with severe renal impairment have experienced increases in blood pressure of about 15mm Hg while being treated with ranolazine, and the use of the new drug should generally be avoided in these patients.

In addition to being a substrate for CYP3A, ranolazine is a substrate for P-glycoprotein (P-gp) and caution should be exercised when it is used concurrently with P-gp inhibitors such as cyclosporine (e.g., Neoral). The results of in vitro studies suggest that ranolazine may inhibit the CYP3A, CYP2D6, and P-gp metabolic pathways. Digoxin is a substrate for P-gp and concurrent use with ranolazine has resulted in a 1.5-fold increase in digoxin concentrations. Ranolazine has also has been reported to cause an approximately two-fold increase in the concentration of simvastatin (e.g., Zocor), a CYP3A substrate. The new drug should also be used with caution in patients who are also being treated with medications that are CYP2D6 substrates (e.g., tricyclic antidepressants).

Approximately 75% of a dose of ranolazine is excreted in the urine as metabolites and approximately 25% is eliminated in the feces. Because it is extensively metabolized, less than 5% of a dose is excreted in unchanged form.

The recommended initial dosage of ranolazine is 500 mg twice a day. The dosage should be increased as needed to 1000 mg twice a day, but this dosage should not be exceeded. Baseline and follow-up electrocardiograms should be obtained to evaluate effects on the QT interval.

Ranolazine extended-release tablets are supplied in a 500 mg-potency. Patients should be advised that the tablets should not be crushed, chewed, or broken.

Daniel A. Hussar