The Pharmacist Activist

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Editorial

Concern for PATIENTS or PROTECTION of PROFITS?

Legislation Regarding Generic Antiepileptic Drugs is Not Needed!

For the last several decades, pharmacists in almost all states have had legislative authority to dispense the generic equivalent of a multisource medication when the brand-name product was prescribed, unless the prescriber specifically requested that the brand-name product be used. This system has worked very well with only isolated exceptions that have been reported in individual patients. However, there have been no or very few studies that have directly compared the clinical response and bioequivalence of brand-name and generic formulations of multisource drugs.

Legislative proposals have been developed recently in most states that would require pharmacists to inform physicians or obtain their approval before substituting a generic equivalent for an antiepileptic drug that is prescribed by brand name. The introduction of these legislative proposals comes at a time when patents for certain formulations of four of the most widely-prescribed antiepileptic drugs (divalproex [Depakote], lamotrigine [Lamictal], levetiracetam [Keppra], topiramate [Topamax]) will soon expire, and less expensive generic formulations will become available. Those introducing/supporting the legislative proposals primarily include the large pharmaceutical companies, most notably those who market antiepileptic drugs, and the Epilepsy Foundation, that receives substantial funding from large pharmaceutical companies.

Reasons and scare tactics

Several months ago I received a call from a manager with one of the pharmaceutical companies that markets an antiepileptic drug for which the patent will soon expire. He was hoping that I would support the legislative proposal that is currently being considered in Pennsylvania that would restrict the authority of pharmacists to dispense generic formulations of antiepileptic drugs. He identified his reasons for which he considered this legislation necessary including the difficulty in determining the best dosages of antiepileptic drugs (particularly when they are often used in combination), the challenge in maintaining a stable response to the antiepileptic regimens in individual patients, and the risk of serious, and even fatal, consequences if the effectiveness of an antiepileptic regimen is compromised. I responded that I agreed that these were important challenges in the treatment of patients with seizure disorders but that I did not consider legislative changes to be necessary in addressing them.

This is when the scare tactics regarding generic formulations began to emerge, including the observations that there were small permissible variations in the concentrations of the active ingredient in generic formulations, the inactive ingredients in generic formulations did not have to be the same as in the brand-name formulations, that meeting bioequivalence

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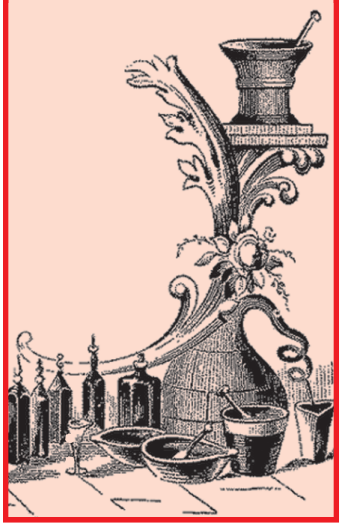


standards did not assure the same clinical response attained with the brand-name product, and that many patients with epilepsy would be at risk. I responded that I had confidence in the current system in which generic formulations are evaluated and approved, and that, even though patients with epilepsy may have some unique challenges, I did not consider legislative changes to be necessary. Furthermore, adopting legislation that pertains to one type of medical problem and the drugs developed to specifically treat it encourages similar initiatives for other classes of medications such as some have already proposed for immunosuppressants and antiarrhythmic agents.

I then indicated that I considered the pursuit of legislative changes to be a huge waste of money, as well as the time of many people. Such changes are particularly unacceptable when there is a course of action that is entirely within the control of the brand-name company that would permit essentially all of the patients currently being treated with its drug to continue receiving it once the generic formulations become available. He was interested—at least until I explained my recommendation.

The solution

The solution I propose for this and similar situations is that, when the patent for a brand-name drug expires, the company should reduce its price so that it is competitive with the prices of the generic formulations that become available. If the price is competitive, it removes the reason for which insurance companies, government agencies, or others might expect the patient to be switched from the brand-name formulation to a generic formulation. The brand-name company for a product going off patent can lower its price substantially and still make a profit. If a generic company can make a profit on the product at the price it charges, certainly the company that has the greatest expertise and experience with that product can also make a profit at that price.

With respect to the antiepileptic drugs for which the patents will soon expire, each of them has already brought billions of dollars of revenue into its respective company. Will the brand-name company be willing to accept a level of profit for this product that is much lower (but a profit, nevertheless) than the one to which it has become accustomed (but will lose when generic formulations become available)?

The ultimate question

The reasons that the brand-name companies identify in promoting legislative changes with respect to antiepileptic drugs focus on what they contend is an increased risk to patients of potentially serious consequences if their treatment is changed to generic formulations of the same medications. However, are the companies willing to accept a reduction in their profits if they could greatly reduce or even eliminate the risks they contend are so important? The ultimate question is whether the companies give the highest priority to their stated concerns about the safety and welfare of the patients using their medications, or to protecting their profits? If it is the latter, it represents blatant hypocrisy!

Legislative changes with respect to antiepileptic drugs are not needed, and efforts of pharmaceutical companies and the Epilepsy Foundation to pursue such should be abandoned. When the patents for antiepileptic drugs expire, the companies should reduce their prices to be competitive with the generic formulations.

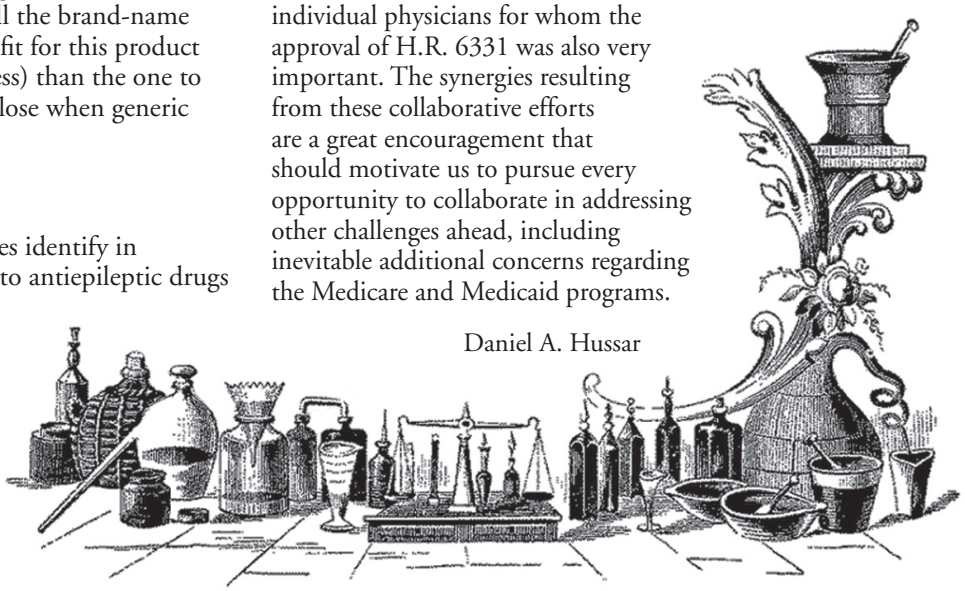
Daniel A. Hussar

Synergies from Working Together

The development and approval of H.R. 6331, and then the override of the President's veto, represent extremely important accomplishments for the profession of pharmacy. First, this legislation delays implementation of provisions of the Medicare and Medicaid prescription programs that would have had a devastating financial impact on many community pharmacies, as well as very negative implications for the patients and communities served by these pharmacies. Thanks to the legislators who supported pharmacy's concerns, and congratulations to the pharmacists who provided the leadership in this effort and our professional organizations (e.g., NCPA, APhA, NACDS, state pharmacy associations) that were responsible for the attainment of such important results.

An added benefit of this experience was to observe the synergies that can be attained when so many of our associations and individual members work together on behalf of our profession toward a common goal. We also had the added benefit of working in concert with the American Medical Association and many individual physicians for whom the approval of H.R. 6331 was also very important. The synergies resulting from these collaborative efforts are a great encouragement that should motivate us to pursue every opportunity to collaborate in addressing other challenges ahead, including inevitable additional concerns regarding the Medicare and Medicaid programs.

Daniel A. Hussar



New Drug Review

Methylnaltrexone bromide (Relistor – Progenics; Wyeth)

Agent for Opioid-Induced Constipation

New Drug Comparison Rating (NDCR) = 4

(significant advantages) in a scale of 1 to 5, with 5 being the highest rating

Indication:

Administered subcutaneously for the treatment of opioid-induced constipation in patients with advanced illness who are receiving palliative care, when the response to laxative therapy has not been sufficient.

Comparable drugs:

Laxatives (e.g., senna [e.g., Senokot]), stool softeners (e.g., docusate [e.g., Colace]).

Advantages:

- Is often effective in relieving opioid-induced constipation in patients whose response to laxatives has not been sufficient;
- Has a unique mechanism of action for the treatment of opioid-induced constipation.

Disadvantages:

- Must be administered by injection (subcutaneously);
- May be more likely to cause gastrointestinal adverse events.

Most important risks/adverse events:

Contraindicated in patients with known or suspected mechanical gastrointestinal obstruction; if severe or persistent diarrhea occurs during treatment, the drug should be discontinued; dosage should be reduced in patients with severe renal impairment; if the opioid analgesic is discontinued, the use of methylnaltrexone should also be discontinued.

Most common adverse events:

Abdominal pain (29%), flatulence (13%), nausea (12%), dizziness (7%), diarrhea (6%).

Usual dosage:

Administered subcutaneously and the usual frequency of administration is one dose every other day as needed; no more than one dose should be administered in a 24-hour period; recommended dose is 8 mg for patients weighing 38-61 kg (84-135 pounds), and 12 mg for patients weighing 62-114 kg (136-251 pounds); for patients weighing less than 38 kg or more than 114 kg, a dosage of 0.15 mg/kg should be used; in patients with severe renal impairment (creatinine clearance less than 30 mL/minute), the dosage should be reduced by one-half.

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NEWS - Line PUBLISHING

New Drug Review (cont.)

Product:

Vials – 12 mg (in 0.6 mL of solution); should be kept away from light.

Comments:

Opioid analgesics such as morphine are often used on a continuous basis to relieve pain associated with incurable cancers and other advanced illnesses. In addition to acting at opioid receptors in the central nervous system to provide their analgesic action, the opioid analgesics also act at opioid receptors in peripheral tissues such as the gastrointestinal tract, one of the consequences of which is that almost all patients who are treated with these analgesics on a continuous basis will experience constipation. To reduce the likelihood of constipation, the use of a bowel regimen (e.g., laxatives, stool softeners) is usually recommended for patients who are to be treated with an opioid analgesic on a regular basis. For many patients, however, even the use of a bowel regimen is insufficient to prevent opioid-induced constipation.

Methylnaltrexone is an opioid antagonist that is related to naltrexone (e.g., ReVia, Vivitrol) that has been used for the treatment of alcohol and opioid dependence. However, methylnaltrexone does not cross the blood-brain barrier and it functions as a selective peripherally-acting mu-opioid receptor antagonist in tissues such as the gastrointestinal tract. Therefore, it decreases the constipating action of opioid analgesics without reducing the centrally-mediated analgesic effects. The effectiveness of methylnaltrexone was demonstrated in placebo-controlled studies. In a single-dose study, approximately 60% of the patients experienced a laxative action within 4 hours following administration, compared with 14% of those receiving placebo. When administered every other day, those receiving the drug had a higher rate of laxation within 4 hours of the first dose (48%) than placebo-treated patients (16%).

Daniel A. Hussar