The Pharmacist Activist

Volume 11, No. 8 • August 2016

Editorial

The PBM Formulary FOLLIES

Express Scripts and CVS Health have recently announced the list of prescription products that will be excluded from their pharmacy benefit manager (PBM) formularies in 2017. There is no pretense that the products identified as alternatives are more effective or safer than those that are being excluded from the formularies. Rather, the sole criterion that results in the exclusion of a product from these formularies is that it costs more than the alternative products and that cost savings will result. This situation prompts the following question:

By excluding products from PBM.formularies, who experiences the greatest cost savings?

a. Patients
b. PBM clients
c. Pharmacists
d. PBMs

Answer "c" can be quickly excluded because, aside from their own mail-order pharmacies and other pharmacies that their companies own, pharmacies are viewed as no more than a needed distribution network. Although the PBMs would like it to be believed that it is patients and PBM clients who will benefit from the cost savings, I contend that it is the PBMs themselves (answer "d") that experience the greatest cost savings from exclusions from the formularies.

In announcing its 2017 National Preferred Formulary, Express Scripts makes the following comments:

"Express Scripts' National Preferred Formulary (NPF) is the most widely used drug list in the United States, providing prescription drug coverage guidelines for 25 million Americans. In 2017, our members and plan sponsors will see small changes in their coverage, which will allow a large increase

in value. Approximately 0.12% of our NPF members will be asked to use a different medication that achieves the same health outcome than one they are currently using. If any of these patients have rare clinical needs that require a medication that's not on the formulary, we have provided a pathway to have that drug covered.

Out of more than 3,900 drugs on the market, the 2017 NPF excludes 85. We exclude medications only when clinically equivalent alternatives are already covered on our formulary, and only when those exclusions will result in significant cost savings for our clients and patients. Participating plan sponsors will save approximately $1.8 billion throughout the year, the biggest annual savings since the NPF was introduced in 2014."

These statements invite the following observations:

1. It is clear that the cost of a product is the only factor that will result in its exclusion from the Formulary.

2. The inclusion on the Formulary of "clinically equivalent alternatives" to the excluded products is debatable in certain situations (examples to follow).

3. Reference is made to savings for plan sponsors of approximately $1.8 billion which is intended to sound impressive. However, neither the total cost for plan sponsors nor the cost savings for Express Scripts is identified.

4. Express Scripts' Formulary is identified as providing coverage guidelines for 25 million Americans – a very large number. However, the number of members who will be asked to use a different medication is identified as 0.12% - a statistic intended to suggest a very small number. But 0.12% of 25 million is 30,000 patients – a not so small number of individuals who are likely to be disadvantaged and/or inconvenienced by having to use a different medication so that Express Scripts and its plan sponsors will benefit financially.

5. A "pathway" will be provided for patients with "rare" clinical needs to be considered for coverage of a medication that is not on the formulary. Does anyone anticipate that such coverage will be provided often, and on a timely basis?

Formularies have important value

I am a strong advocate for the use of formularies in a manner in which patients will not experience a reduction in the effectiveness and safety of their treatment, or other important disadvantages, and in which cost savings and other efficiencies can be achieved. Indeed, I can fully support many of the decisions that Express Scripts has made in excluding certain medications from its preferred formulary. However, I disagree with certain of the decisions that, in my opinion, place patients at greater risk and/or significant disadvantage, and the following are examples.

For patients with chronic hepatitis C virus (HCV) genotype 1 infection, Viekira Pak (ombitasvir, paritaprevir, and ritonavir, copackaged with dasabuvir) is the only preferred alternative on the formulary, although Express Scripts includes a notation that this category is being reviewed based on recent product launches. However, Express Scripts has not provided coverage for Harvoni (sofosbuvir and ledipasvir) or the newer product Epclusa (sofosbuvir and velpatasvir), and includes Zepatier (elbasvir and grazoprevir) on the list of excluded medications. I agree that Viekira Pak is similarly effective to Harvoni, Epclusa, and Zepatier for the treatment of chronic HCV genotype 1 infection but, in my opinion, Viekira Pak presents greater risk for patients. The primary reasons for this greater risk are that Viekira Pak contains four active ingredients, compared with two for the other options, and Viekira Pak includes ritonavir that interacts with dozens of other medications (please see my editorial, "Express Scripts Made the Wrong Formulary Decision that is a Disservice to its Customers," in the January 2015 issue at www.pharmacistactivist.com).

Many patients with diabetes are being treated with at least two antidiabetic medications, and considerable time has been devoted to identifying the most appropriate medications and determining their dosages. A common challenge in striving for optimal treatment is that many patients are noncompliant in using their medications. Express Scripts has excluded Victoza (liraglutide), the most widely-prescribed glucagon-like peptide-1 (GLP-1) agonist from its preferred formulary. Although the preferred alternatives identified (Bydureon, Byetta, Trulicity) would be expected to be similarly effective and could be easily justified for initiating treatment with a GLP-1 agonist, many patients currently being treated effectively with Victoza will experience inconvenience, dosage adjustments, and associated risk in having to switch to an

(Continued on Page 4)

New Drug Review

Pimavanserin tartrate (Nuplazid – Acadia)

Antipsychotic Agent

New Drug Comparison Rating (NDCR) = 5
(important advance)
in a scale of 1 to 5 with 5 being the highest rating

Indication:
Treatment of hallucinations and delusions associated with Parkinson's disease psychosis.

Comparable drugs:
Atypical antipsychotic drugs (e.g., risperidone).

Advantages:
- Is the first drug to be demonstrated to be effective in the treatment of hallucinations and delusions associated with Parkinson's disease psychosis;
- Has a unique mechanism of action (a combination of inverse agonist and antagonist activity at serotonin 5-HT2A receptors);
- Does not act at dopamine receptors and is not likely to cause extrapyramidal effects;
- May be less likely to cause serious adverse events (e.g., tardive dyskinesia, neuroleptic malignant syndrome).

Disadvantages:
- Is more likely to cause QT interval prolongation and increase the risk of arrhythmias (the atypical antipsychotic drug ziprasidone is also associated with this risk).

Most important risks/adverse events:
Increased risk of death in elderly patients with dementia-related psychosis (boxed warning; is not approved for the treatment of patients with dementia-related psychosis unrelated to the hallucinations and delusions associated with Parkinson's disease psychosis); prolongs the QT interval (use should be avoided in patients with QT prolongation, congenital prolongation of the QT interval, a history of cardiac arrhythmias, symptomatic bradycardia, hypokalemia, and/or hypomagnesemia, or in combination with other drugs known to prolong the QT interval including Class 1A antiarrhythmics [e.g., quinidine, procainamide, disopyramide], Class 3 antiarrhythmics [e.g., amiodarone, sotalol], certain antipsychotic medications [e.g., ziprasidone, chlorpromazine, thioridazine], and certain antibacterial agents [e.g., moxifloxacin]); is a substrate of the CYP3A4 metabolic pathway and action may be increased by the concurrent use of a strong CYP3A4 inhibitor (e.g., clarithromycin, itraconazole: dosage should be reduced); action may be reduced by the concurrent use of a strong CYP3A4 inducer (e.g., carbamazepine, rifampin, St. John's wort), and it may be necessary to increase the dosage; use is not recommended in patients with hepatic impairment or in patients with severe renal impairment.

Most common adverse events:
Nausea (7%), peripheral edema (7%), confusional state (6%).

Usual dosage:
34 mg (two 17 mg tablets) once a day; in patients treated concurrently with a strong CYP3A4 inhibitor, the recommended dosage is 17 mg once a day.

Products:
Tablets – 17 mg (pimavanserin base provided by 20 mg pimavanserin tartrate).

Comments:
An estimated 40% of patients with Parkinson's disease experience psychosis characterized by hallucinations and delusions. Serotonin 5-HT2A receptors are thought to play an important role in Parkinson's disease psychosis. Pimavanserin has a unique mechanism of action that preferentially targets 5-HT2A receptors and is mediated through a combination of inverse agonist and antagonist activity at these receptors. Unlike other antipsychotic drugs, it does not act at dopamine receptors. Therefore, it does not interfere with patients' dopaminergic therapy (e.g., levodopa) and does not impair motor function. The FDA granted pimavanserin a breakthrough therapy designation that is designed to expedite the development and review of drugs that are intended to treat a serious condition and where preliminary evidence indicates that the drug may demonstrate substantial improvement over available therapy.

Pimavanserin is metabolized primarily via the CYP3A4 pathway to a major active metabolite. Its effectiveness was evaluated in a 6-week placebo-controlled study that included 199 patients. A Parkinson's disease (PD)-adapted Scale for the Assessment of Positive Symptoms (SAPS-PD) was used to evaluate efficacy. This is a 9-item scale adapted for PD from the Hallucinations and Delusions domains of the SAPS. The new drug was demonstrated to be superior to placebo in decreasing the frequency and/or severity of both hallucinations and delusions, without worsening the primary motor symptoms of Parkinson's disease.

Daniel A. Hussar

alternative covered by their prescription plan.

The formulary exclusions recently announced by CVS Health also include a widely-used antidiabetic agent. Lantus (insulin glargine) will no longer be covered because the biosimilar product Basaglar has become available and is identified as the preferred alternative. For the first time, CVS will also be excluding coverage of certain drugs for the treatment of cancers. Xtandi (enzalutamide) for the treatment of prostate cancer is being excluded from the formulary and Zytiga (abiraterone) is the recommended alternative although there are some significant differences in the properties and use of the two agents. However, the oncology coverage exclusions will only apply to new patients, and patients who are already being treated with a drug that is to be excluded from the formulary will be permitted to continue using it.

Who makes the decisions?

The August 14th edition of the *St. Louis Post-Dispatch* includes an article (Samantha Liss) titled, "A secretive board controls access to prescription drugs for millions of Americans." The article describes the situation at Express Scripts in determining the products to be excluded from its formulary. A 16-member committee, described by Express Scripts as independent and objective, makes the recommendations of products to be excluded from the formulary. The committee is comprised almost entirely of physicians, and a pharmacist. It is noteworthy that this huge company with revenues that are dependent on the dispensing of medications only includes one pharmacist in such an important role. This is a very telling indictment of the lack of respect that Express Scripts has for pharmacists and the profession of pharmacy.

The identity of the 16 members of the committee is not disclosed. The explanation for this secrecy is that the company is shielding the committee members from the "tremendous" influences of pharmaceutical companies, lobbyists, patient advocacy groups, and others. Committee members are required to disclose their financial relationships with drug and device makers but the chief medical officer of Express Scripts acknowledges the impossibility of finding experts who haven't received money from the industry.

The secrecy regarding the membership of the formulary committee can't be justified. Their recommendations have important implications for tens of thousands of patients. If their recommendations can be challenged with valid questions, and if they don't have the courage of their convictions to justify their recommendations, the formulary process has no credibility. The identity of the committee members and their specific pertinent financial disclosures should be revealed, as is expected from individuals in most other healthcare organizations and activities.

Recommendations

For many, the secrecy surrounding the committee membership and formulary decisions of Express Scripts is not a surprise because there has been a lack of transparency and resultant concerns with respect to so many of the company's activities, financial operations, and working relationships with pharmaceutical companies and pharmacies. Notwithstanding its lack of credibility for many, Express Scripts has such size and influence that many conclude that it can't be effectively challenged. A coalition of patient/consumer, pharmacy, and medical organizations must challenge the policies and decisions that compromise the provision of optimal drug therapy for patients. Just as Express Scripts insists that its committee members need to function independently and objectively, we must insist that patients have the right to obtain their medication in the pharmacy they choose, physicians have the right to determine the most appropriate medications for their patients, and pharmacists have the right to continue to serve their patients in prescription programs that encourage counseling and treatment management that will result in optimum therapy, and are equitable.

Daniel A. Hussar

Author/Editor - Daniel A. Hussar, Ph.D.
Philadelphia College of Pharmacy, University of the Sciences in Philadelphia
Publisher - G. Patrick Polli III
Publications Director - Jeff Zajac
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, 15 Shoemaker Rd., King of Prussia, PA 19406
610-337-1050 • Fax: 610-337-1049
E-mail: pharmacistactivist@news-line.com
NEWS-Line PUBLISHING