Assessing Step-Therapy Programs:
A Step in the Right Direction

Managed care organizations (MCOs) and pharmacy benefits managers (PBMs) use utilization management programs such as prior authorization (PA) and step therapy to improve the cost-effectiveness of therapeutic selection. Utilization management pharmacy benefit programs were first introduced in the 1980s and grew in popularity with the implementation of multiple-copayment (tiered) open formularies. Step therapy is appealing because it is generally applied to a select drug class with the goal of encouraging generic use and decreasing costs without compromising the quality of care. Step therapy requires a member to try the first-line medication(s) within the drug class, usually a branded product. Currently, most PBMs implement step therapy using “smart edit” logic, and grandfathering those members who had received the target (second-line) drug previously. At the point of service, the “smart edit,” electronically and in real time, reviews the member’s claims history for evidence of use of first-line agent(s). If a claim is found, the system covers the second-line agent automatically. Otherwise, the claim is rejected. After claim rejection, members have the opportunity to have their prescriber change the prescription to another medication, preferably the first-line medication, or in most step-therapy programs, permit the prescriber to submit a request for coverage through a PA. The pharmacist is typically involved in step-therapy programs in the capacity of directing the member to the prescriber for the change or PA or performing this service for the member directly with the prescriber.

An opportunity exists for a step-therapy intervention for the renin-angiotensin-system (RAS)-blocking drug class consisting of first-line therapy with angiotensin-converting enzyme inhibitors (ACEIs) and second-line therapy with angiotensin II receptor blockers (ARBs). In this issue of JMCP, Yokoyama et al. report the first evidence in the literature of the outcomes in drug cost and therapeutic selection of step-therapy intervention for the RAS drugs. Using the standard pharmacy benefit smart-edit technology, with grandfathering, the authors found an adjusted $0.03 per member per month (PMPM) savings and an estimated unadjusted savings of $0.05. However, about 7% of members whose claim was rejected at the point of service did not have any antihypertensive medication claims during 12 months of follow-up. The results by Yokoyama et al. have been replicated using a comparable step-therapy program implemented in 2006, which led to an unadjusted PMPM savings of $0.11. In this study, 9% of members whose claims were rejected at the point of service received no antihypertensive medication during a minimum of 4-month follow-up. The higher pharmacy savings and percentage of members without any antihypertensive medication claims during the analysis period are likely due to the shorter duration of follow-up. Step-therapy PMPM savings have been shown to be greatest in the months following implementation, and it is intuitive that the longer members are followed, the greater the likelihood they will initiate therapy. Based on the data from the RAS-blocker step-therapy studies, it is possible that some of the pharmacy savings from this managed care intervention may come at the cost of some members going without antihypertensive medication.

An important limitation for both of these studies is the absence of the medical costs and clinical outcomes assessment. Further research is needed to better understand the potential clinical outcomes and medical costs associated with step-therapy programs, especially those programs impacting use of medication for which clinical trials have documented lower rates of endpoint events such as hospitalization or death. Of special concern are high-risk members (such as those who are postmyocardial infarction or have congestive heart failure or renal insufficiency) who may go without a RAS-blocking agent, for which studies have documented a clinical outcomes benefit. Unfortunately, the current step-therapy studies lack medical claims assessment. Thus the proportion of high-risk members going without antihypertensive therapy after their step-therapy claim rejection is unknown, as are the total health care costs.

The RAS-blocking drug class step-therapy program is one of many step-therapy programs in use today (see table). Only 3 other programs have been assessed to an extent similar to the evaluation of the RAS-blocking drug class. These programs include the nonsteroidal anti-inflammatory drugs (NSAIDs) including cyclooxygenase-2 (COX-2) inhibitors, proton pump inhibitors (PPIs), and selective serotonin reuptake inhibitors (SSRIs). The reported savings ranged from zero to $0.36 PMPM with SSRIs to $0.48 with PPIs. The lack of SSRI savings in one study and the substantial savings in another may be the result, in part, of the sole availability of fluoxetine as a generic drug in the first analysis and the subsequent availability of 3 generic SSRIs at the time of the more recent study.

The prevalence of members without a medication claim in the drug class after their point-of-service claim rejection ranged from 7% with RAS-blockers to 22% with PPIs. The pharmacy benefit savings in direct drug cost occurred as anticipated due to greater use of generics and a portion of members receiving no medication. The higher rate of members with no medication claims following the step-therapy claim rejection for the PPI and NSAID drug classes is likely due to the availability of over-the-counter alternatives. For the SSRIs and RAS-blocker drug classes, the rate of no medication claims following the step-therapy claim rejection was similar, at approximately 1 in 10 members or less. It has become clear that one outcome of step-therapy programs
is that a portion of members with a claim rejection at the point of service go on to have no claims in that class of medications. The PBM industry has already begun to address this potential concern. Two methods are currently in use by some PBMs to decrease rates of the no-medication outcome. One method is to perform rapid retrospective drug utilization review (RetroDUR). The second method involves a medical and pharmacy claims integrated smart edit.

Through the rapid RetroDUR program, providers are notified of their patients who have a step-therapy claim rejection and have not yet obtained their medication. The rapid RetroDUR program works through a process of frequently querying the pharmacy claims data to identify members with a step-therapy claim rejection and no medication claim following the claim rejection. Prescribing providers are sent a letter or telephone call informing them that their patient had experienced a step-therapy edit and that the PBM had not processed any comparable medications for the patient within a set period of days. The letter outlines the process for the member to seek second-line medication coverage.8

The smart-edit method to manage absence of medication in a class associated with a step-therapy intervention includes real-time integration of a member’s medical diagnosis into the point-of-service transaction. According to David Lassen, PharmD (senior director of Care Management, Prime Therapeutics LLC; February 26, 2007), this method allows members with a high-risk diagnosis to bypass the edit. Integration of the medical diagnosis can be accomplished through the review of historical medical claims International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes by the PBM or by the pharmacist electronically entering ICD-9-CM code(s) at the point of service. It can also be accomplished by the prescriber entering the ICD-9-CM diagnosis code(s) during the e-prescribing event. All of these processes require medical diagnosis information to be integrated in some fashion with the pharmacy electronic claims processing system.

Currently, PBMs who receive medical data are capable of performing an integrated medical and pharmacy smart edit. For example, the edit for RAS-blockers might allow members who have a medical claim for a myocardial infarction, congestive heart failure, or renal insufficiency to electronically obtain approval for second-line coverage of the ARB. Similarly, the edit for PPIs might provide approval for second-line coverage to members with Barrett’s disease or Zollinger-Ellison syndrome. The edit for statins might allow members at high cardiovascular risk to obtain the second-line therapy; and the edit for COX-2 inhibitors might allow members with a diagnosis of prior upper gastrointestinal tract bleed or familial adenomatous polyposis to receive second-line coverage. Ideally, a combination of the rapid RetroDUR and an integrated medical and pharmacy smart edit would be applied to step-therapy programs in order to reduce the rate of members going without medication.

Understanding the impact pharmacy step-therapy programs have on therapeutic selection is the first step in an ongoing assessment of the programs. It is only through assessments of PBM utilization management programs, as reported by Yokoyama et al., that the next steps can be taken to fully understand the risks and benefits. The direct pharmacy financial outcomes appear clear. Less clear are the risks. The current pharmacy-only smart-edit step-therapy program appears to result in as many as 1 in 10 members who experience claim rejection for SSRIs or RAS-blocking medication going on to have no pharmacy claims for drugs in that class. PBMs and MCOs might do better in step-therapy program development by adding medical diagnosis

<table>
<thead>
<tr>
<th>Core Area</th>
<th>First Line</th>
<th>Second Line</th>
<th>PMPM Savings</th>
<th>No Medication After Step-Therapy Claim Rejection</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADHD</td>
<td>Generic stimulants</td>
<td>Strattera or brand stimulants</td>
<td>No published data</td>
<td>No published data</td>
</tr>
<tr>
<td>Allergy</td>
<td>Nasal steroids</td>
<td>Leukotriene modifiers</td>
<td>No published data</td>
<td>No published data</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>Generic statins</td>
<td>Brand statins</td>
<td>No published data</td>
<td>No published data</td>
</tr>
<tr>
<td>Depression</td>
<td>Generic SSRIs</td>
<td>Brand SSRIs, brand SNRIs</td>
<td>$0.00-$0.36</td>
<td>11%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Generic ACEIs</td>
<td>Brand ACEIs, brand ARBs</td>
<td>$0.03-$0.11</td>
<td>7%-9%</td>
</tr>
<tr>
<td>Pain</td>
<td>Generic NSAIDs</td>
<td>Brand NSAIDs, COX-2s</td>
<td>$0.29</td>
<td>15%</td>
</tr>
<tr>
<td>Pain</td>
<td>Generic gabapentin or tricyclic antidepressants</td>
<td>Lyrica or Topamax</td>
<td>No published data</td>
<td>No published data</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>Methotrexate</td>
<td>TNF-blockers</td>
<td>No published data</td>
<td>No published data</td>
</tr>
</tbody>
</table>

ACEIs = angiotensin-converting enzyme inhibitors; ARBs = angiotensin II receptor blockers; COX-2s = cyclooxygenase-2 inhibitors; NSAIDs = nonsteroidal anti-inflammatory drugs; PMPM = per member per month; PPIs = proton pump inhibitors; SNRIs = serotonin norepinephrine reuptake inhibitors; SSRIs = selective serotonin reuptake inhibitors; TNF = tumor necrosis factor.
information to the smart-edit program and following up with the rapid RetroDUR prescriber notification. The next analytic step should be assessments of the impact of step-therapy programs on clinical outcomes and total medical costs, including pharmacy provider and administrative costs.

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DISCLOSURES
The author discloses that he is employed by Prime Therapeutics, LLC, a pharmacy benefits management company.

REFERENCES