A Cost Analysis of Switching Calcium Channel Blockers: A One-Year Post-formulary Decision Review

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**ABSTRACT** This study was a retrospective utilization and cost analysis based on the records of 314 patients using pharmacy services at Martin Army Community Hospital in Fort Benning, Georgia who had been prescribed amlodipine in the past and were switched to felodipine extended-release (ER) or nifedipine core coat (CC) beginning in January of 1999. The average cost per day for amlodipine therapy prior to the switch was $0.67. Post-conversion, the average per-day cost was $0.53 for felodipine ER and $0.48 for nifedipine CC. However, there was a substantial rise in the use of concomitant cardiovascular (CV) medications after the switch from amlodipine to either felodipine ER or nifedipine CC. Overall, 52.2% of patients were taking at least one additional CV drug prior to the switch. After the switch, this number increased to 84.5%. Calculation of the total monthly costs for the 314 patients whose records were reviewed indicated that the overall cost of calcium channel blockers decreased from $6,311 to $5,275 as a result of the switch, but that the cost for concomitant CV medications increased from $754 to $2,826, and the total cost for all CV drugs increased from $7,065 to $8,101. The average monthly per-patient cost for all CV drugs increased from $22.50 to $25.80 (14.7%). These findings support the conclusion that an evaluation of formulary changes must consider the overall cost of therapy and not just that of the agents being switched.

Effective management of patients with hypertension is a health care priority because of the increased risk for cardiovascular morbidity and mortality associated with this disease and the significant economic burden that results if it is left untreated. The American Heart Association (AHA) has estimated the annual total cost of cardiovascular disease and stroke to be $26.6 billion.

Many studies, including the sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of Hypertension (JNCVI), support the position that drugs from many different classes are suitable as initial therapy for patients with hypertension. The newer long-acting dihydropyridine (DHP) calcium channel blockers (CCBs) have been shown to be highly effective and well-tolerated in a wide range of patients with hypertension or angina. These drugs provide smooth 24-hour control over blood pressure with once-daily dosing and without excess activation of the sympathetic nervous system.

The cost of blood pressure-lowering medication for patients with hypertension is a significant component of the overall cost of treating hypertension and its associated risks. Results from a recent review indicated that the total cost of drugs used to treat hypertension in the U.S. in 1995 was $8.3 billion. The cost for CCBs alone was $2.86 billion. Drug acquisition costs are cited by managed care organizations as one of the major reasons for rate increases, and concern about the expense of antihypertensive drugs has prompted attempts to control their cost through formulary management. Some organizations switch patients from one CCB to another to reduce drug acquisition expenses. Although cost savings resulting from such a switch can be estimated from expected dosages and established drug prices, the true cost of treatment can also be strongly influenced by higher-than-anticipated drug doses, reduced or increased requirements for additional blood pressure-lowering medications, laboratory tests, and office visits for the management of adverse events.

For example, at Barksdale Air Force Base in Louisiana, a switch from amlodipine to felodipine extended-release (felodipine ER), motivated by a slight difference in drug acquisition cost, resulted in an increase in overall drug costs for control of blood pressure rather than the expected decrease, because of the need for higher-than-expected felodipine doses and additional antihypertensive medications. In another study, Zotto and associates evaluated the effects of converting patients from nifedipine gastrointestinal therapeutic system (GITS) to amlodipine at Patrick Air Force Base in Florida. Nifedipine GITS is another slow-release formulation of this CCB. Zotto et al.’s review included the records of 1,245 patients. At six months after the switch, 99% (1,233/1,245) of the switched patients remained on amlodipine and 80.5% were maintained at a dose of 5 mg/day or less. For the 1,233 patients who remained on amlodipine, the switch in therapy resulted in an annual savings of more than $106,000 in dihydropyridine acquisition costs alone. In addition, 213 patients who had required one or more concomitant antihypertensive drugs while receiving nifedipine GITS were managed with amlodipine monotherapy, further reducing the total cost of blood pressure-lowering therapy. Conversion to amlodipine provided good control of blood pressure and also increased patient satisfaction with therapy.
The present study was undertaken to evaluate changes in the cost of antihypertensive therapy associated with switching patients from amlodipine to either felodipine extended-release (ER) or nifedipine core coat (CC).

METHODS

Study Design
This study was a retrospective utilization and cost analysis based on the records of patients using pharmacy services at Martin Army Community Hospital in Fort Benning, Georgia, who had been prescribed amlodipine in the past and were switched to either felodipine ER or nifedipine CC beginning in January of 1999.

All patients using the Martin Army Pharmacy who had been dispensed amlodipine were advised to have their physicians convert them to either felodipine ER or nifedipine CC beginning in January of 1999.

Physicians were also given the option of maintaining patients on amlodipine through a special purchase request program. Physicians within the hospital could request that their patients remain on amlodipine by presenting justification in writing to the P&T committee for review. The P&T committee had developed criteria to justify a patient remaining on amlodipine and authorized the hospital pharmacy to oversee the program. Thus, the pharmacy could authorize amlodipine if the patient met any of the following criteria: previous therapy failure caused by a lack of efficacy or documented adverse events to felodipine ER or nifedipine CC; concomitant angina or coronary heart disease; or blood pressure that was controlled with amlodipine after multiple failures with other medications. All other special requests were reviewed by a physician/pharmacist review board. The relatively stringent criteria for maintaining patients on amlodipine raises the possibility that they might have had more severe or complicated form of the disease than patients switched to felodipine ER or nifedipine CC. Nevertheless, the actual costs for treating these patients, rather than other historical data, were used for comparison with results from patients who changed their antihypertensive medications.

Selection of Records for Review
A computerized list was generated to determine all patients who had received a prescription for amlodipine in November or December of 1998. The list included 1,379 patients on amlodipine. Three hundred seventy-two patients were selected for evaluation using a table of random numbers. Eligible patient records, coded by specific patient identifier, were then retrospectively analyzed from the time of the conversion, beginning in January of 1999, through a one-year period ending in the early spring of 2000. Data were extracted and recorded using standardized forms developed for this study.

Data Collected
Data retrieved from each patient record included demographic characteristics, amlodipine dosage prior to conversion, and any use of concomitant cardiovascular (CV) medication pre-conversion, felodipine ER or nifedipine CC dose at conversion, changes in dosing or discontinuation of therapy within one year of post-conversion, and the number of concomitant CV medications used post-conversion. Concomitant medications were defined as prescription medications other than amlodipine, felodipine ER, or nifedipine CC prescribed for chronic CV-related illness. Concomitant CV medications were divided into eight classes: diuretics; β-blockers; angiotensin-converting enzyme (ACE)-inhibitors; CCBs other than amlodipine, felodipine ER, or nifedipine CC; α-blockers; angiotensin-receptor blockers; nitrates; and other antihypertensive agents.

It was assumed that patients whose records were reviewed were receiving all their CV medications from the pharmacy at

### Table 1 Patient Characteristics at the Time of Formulary Conversion

<table>
<thead>
<tr>
<th></th>
<th>All Patients</th>
<th>Control Group*</th>
<th>Conversion Group**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>314</td>
<td>62</td>
<td>252</td>
</tr>
<tr>
<td>Men</td>
<td>153 (48.7%)</td>
<td>28 (45.2%)</td>
<td>125 (49.6%)</td>
</tr>
<tr>
<td>Women</td>
<td>161 (51.3%)</td>
<td>34 (54.8%)</td>
<td>127 (50.4%)</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>66.6</td>
<td>66.8</td>
<td>66.5</td>
</tr>
<tr>
<td>Men: mean (range)</td>
<td>66.7 (40–90)</td>
<td>66.2 (46–84)</td>
<td>66.8 (40–90)</td>
</tr>
<tr>
<td>Women: mean (range)</td>
<td>66.5 (39–89)</td>
<td>67.4 (44–85)</td>
<td>66.2 (39–89)</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension only</td>
<td>245 (78%)</td>
<td>51 (82.3%)</td>
<td>194 (77%)</td>
</tr>
<tr>
<td>Hypertension + angina</td>
<td>69 (22%)</td>
<td>11 (17.7%)</td>
<td>58 (23%)</td>
</tr>
</tbody>
</table>

*Patients remaining on amlodipine constituted the control group. **Patients converted to felodipine ER or nifedipine CC constituted the conversion group.

### Table 2 Comparison of Antihypertensive Therapy Before and After Conversion

<table>
<thead>
<tr>
<th>Initial Therapy</th>
<th>DHP No. of Patients</th>
<th>Avg. Therapy Dose (per day)</th>
<th>Therapy Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amlodipine</td>
<td>314</td>
<td>6.7 mg/day</td>
<td>$0.67</td>
</tr>
<tr>
<td>Felodipine ER</td>
<td>190</td>
<td>7.9 mg/day</td>
<td>$0.53</td>
</tr>
<tr>
<td>Nifedipine CC</td>
<td>53</td>
<td>55.5 mg/day</td>
<td>$0.48</td>
</tr>
<tr>
<td>No DHP therapy</td>
<td>9</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Converted patients</td>
<td>252</td>
<td>N/A</td>
<td>$0.52</td>
</tr>
<tr>
<td>Amlodipine</td>
<td>62</td>
<td>6.9 mg/day</td>
<td>$0.75</td>
</tr>
</tbody>
</table>

DHP = dihydropyridine
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Their records were also excluded. Thus, records from 314 patients form the basis for the results described in this section. The baseline demographic and clinical characteristics for these patients are summarized in Table 1. Despite the relatively restrictive criteria for maintaining patients on amlodipine, there were no substantive differences between the demographic and clinical characteristics of patients who did and did not switch antihypertensive therapy. Overall, 78% of the patients (n=245) had hypertension and 22% (n=69) had hypertension and angina. Prior to the switch, 65.9% of patients were being treated with amlodipine 5 mg once daily, and the remaining patients were taking 10 mg/day. The mean amlodipine daily dose prior to conversion was 6.7 mg.

**Current Therapy**
Current therapy for the patients whose records were reviewed is summarized in Table 2. The average felodipine ER dose post-conversion was 7.9 mg/day and the dose for nifedipine CC was 55.5 mg/day. The average post-conversion dose of the patients who remained on amlodipine was 6.9 mg/day.

The average cost per day for amlodipine therapy prior to the switch was $0.67. Post-conversion, the average per-day cost for felodipine ER was $0.35 and the cost for nifedipine CC was $0.32. The daily cost for patients who remained on amlodipine was $0.75.

**Concomitant CV Medications**
There was a substantial rise in the use of concomitant CV medications after the switch from amlodipine to either felodipine ER or nifedipine CC (Table 3). Overall, 52.2% of patients were taking at least one additional CV drug prior to the switch. After the switch, this value increased to 84.5%. In particular, there were increases in the use of ACE-inhibitors, α-blockers, angiotensin receptor blockers, β-blockers, diuretics, and nitrates. The use of additional CV medications fell to 43.5% in the patients maintained on amlodipine. The switch in therapy also resulted in an increase in doses for all CV medications, except for sublingual nitroglycerin and nitroglycerin patches (Table 4).

**Cost Analysis**
The costs for dihydropyridines (DHPs) and other CV drugs are summarized in Table 5. The results show that the switch had the intended effect of reducing acquisition costs for DHPs, but the unintended result of increasing the overall cost for CV medications. Switching significantly reduced the mean daily cost of DHPs from $0.67 to $0.56 (P<0.001). However, it significantly increased the mean daily cost for concomitant CV medications from $0.08 to $0.30 (P<0.001) and the mean total cost for all CV medications, including DHPs, from $0.75 to $0.86 per day (P<0.001).

Additional analyses indicated the same outcome as above when the results for patients maintained on amlodipine were compared with those from patients switched to either felodipine ER or
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Table 5 Mean Daily Per-Patient Costs for Cardiovascular (CV) Drugs (All Patients) *

<table>
<thead>
<tr>
<th>Drug Therapy</th>
<th>Initial Therapy (Amlodipine)</th>
<th>Current Therapy</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>DHPs</td>
<td>$0.67 ± 0.13</td>
<td>$0.56 ± 0.31</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>Concomitant CV medications</td>
<td>$0.08 ± 0.15</td>
<td>$0.30 ± 0.37</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>All CV medications</td>
<td>$0.75 ± 0.20</td>
<td>$0.86 ± 0.49</td>
<td>P&lt;0.001</td>
</tr>
</tbody>
</table>

*Mean ± standard deviation. DHP = dihydropyridine

The mean daily DHP costs, the costs for concomitant CV drugs, and the total CV drug costs for patients maintained on amlodipine were $0.75 ± 0.56, $0.07 ± 0.18, and $0.82 ± 0.58, respectively; the corresponding values for the patients switched from amlodipine were $0.52 ± 0.17, $0.36 ± 0.38, and $0.88 ± 0.42. The between-group differences in DHP and concomitant CV medication costs were both statistically significant (P=0.0007 and P<0.001, respectively).

A calculation of the total monthly costs for the 314 patients whose records were included in the analysis indicated that the overall cost of DHPs decreased from $6,311 to $5,275 as a result of the switch. The cost for concomitant CV medications increased from $7,065 to $8,101 (Figure 1). The average monthly per-patient cost for all CV drugs increased from $22.50 to $25.80 (14.7%). Importantly, this analysis includes patients maintained on amlodipine in the post-switch averages. The average monthly per-patient cost for all CV medications in the amlodipine group was $24.59, whereas the cost for the patients who changed antihypertensive therapies was $26.40.

**Results for Patients with Hypertension Alone Versus Those for Patients with Hypertension Plus Angina**

A review of the results in Table 4 suggests that a substantial portion of the increased use of concomitant CV medications after the switch from amlodipine was for additional drugs (e.g., isosorbide mononitrate, nitroglycerin or possibly atenolol, metoprolol) that were required for the control of angina symptoms. Therefore, it was important to assess the effects of the switch on patients with hypertension alone versus those with hypertension and angina. The results of this analysis are presented in Table 6. They show that the costs of concomitant CV drugs for patients switched to felodipine ER or nifedipine CC were higher than those prior to the switch. They also demonstrate that the cost of concomitant CV drugs for patients switched to felodipine ER or nifedipine CC were higher than those for patients maintained on amlodipine. This applied to individuals with hypertension alone and to those with hypertension plus angina. For patients with hypertension, the average daily costs for concomitant CV drugs for individuals receiving amlodipine before and after the switch were $0.05 and $0.03, respectively. The respective values for hypertensive patients switched to felodipine ER and nifedipine CC were $0.21 and $0.28. For patients with hypertension plus angina, the average daily costs for concomitant CV drugs for individuals receiving amlodipine before and after the switch were $0.18 and $0.23, respectively. The corresponding values for the patients switched to felodipine ER and nifedipine CC were $0.78 and $0.52, respectively.

**DISCUSSION**

The results of this study indicate that switching patients from amlodipine to either felodipine ER or nifedipine CC resulted in the expected reduction in acquisition costs for DHPs, but a significant increase in the overall cost of therapy for patients with hypertension or hypertension and angina. This rise in the overall cost of therapy resulted from increases in both the number and doses of additional CV medications required by patients who were switched from amlodipine. The use of concomitant CV medications increased from 52.2% of patients to 76.4% after the change in antihypertensive therapy. When patients who remained on amlodipine were removed from the analysis, the change was even more striking: 83.1% of the patients who were switched to felodipine ER and 86.8% of those treated with nifedipine CC required one or more concomitant CV medications. The percentages of patients in these two groups taking concomitant CV medications prior to the switch were 54.3% and 56.6%, respectively. Importantly, the increased requirement for concurrent CV drugs after the switch was noted for patients with hypertension alone as well as for those with hypertension and angina. Prior to the switch, 42.4% of hypertensive patients receiving amlodipine required at least one additional CV drug at an average daily cost of $0.05. After the switch, the respective values for the hypertensive patients who received felodipine ER were 77.6% and $0.23, and the values for the hypertensive patients treated with nifedipine CC were 84.1% and $0.28. An interesting point to consider is that drug costs were calculated using FSS pricing; however, most institutions do not qualify for FSS pricing. Thus, a higher drug acquisition cost would potentially create an even greater difference in overall costs.

The reason for the increased need for additional CV drugs in the patients switched to either felodipine ER or nifedipine CC could not
be determined by our analysis. It might be caused by disease progression, but this seems unlikely, given the fact that similar percentages of patients who were switched and who remained on amlodipine had hypertension and angina at baseline.

The increased need for additional CV drugs observed in patients with hypertension and angina who were switched from amlodipine might follow directly from the indications for felodipine ER and nifedipine CC. Amlodipine is indicated for the treatment of patients with hypertension, as well as those with either chronic stable or vasospastic angina, whereas felodipine ER and nifedipine CC are both indicated only for the treatment of hypertension. Most importantly in the present context, amlodipine might follow directly from the indications for felodipine ER.

In addition to increasing costs, the need for additional CV medications in patients switched to felodipine ER or nifedipine CC might also reduce the probability of good therapeutic outcomes. McCombs and associates reported that 86% of hypertensive patients interrupt or discontinue their therapy during the first year of treatment, and noncompliance is now considered to be a major reason for the failure of antihypertensive therapy, as well as for significant increases in the overall cost of treatment. The complexity of treatment has a negative effect on compliance. Although they did not assess the role of treatment complexity, Detry et al. and Mouzin-Vehier et al. reported that compliance with amlodipine therapy was significantly better than that for a slow-release formulation of nifedipine in patients with either hypertension or angina.

The strengths of observational studies such as this include the use of population-based case-control subjects, comparable confounding factors, and the use of pharmacy records to assess drug use in a comparable and unbiased fashion. An important limitation of the present study is that the database observed did not document blood pressure readings. Another limitation is that patients were randomly selected from the overall amlodipine population, but not randomly assigned within each therapy cohort. Physicians decided whether the patient was to be switched or remain on amlodipine, and this might have introduced bias. Residual confounding because of incomplete clinical variables or unmeasured confounders, such as risk stratiﬁcation, cannot be excluded.

Randomized controlled trials (RCTs) are the preferred design method to compare antihypertensive therapies. However, when clinical trial results are lacking or conflicting, well-designed observational studies can complement them. Furthermore, the highly selective nature of participants of RCTs and the strict, protocol-driven conditions under which they are conducted might preclude extrapolating findings from RCTs to clinical practice. The common use of a large number of antihypertensive drugs makes evaluation of these therapies in an observational setting feasible.

Another limitation of the present study is that the only costs considered were those for DHPs and other CV drugs. The switch in treatment might also have affected a variety of other expenses, including those for physician and emergency department visits and hospitalization.

In summary, the results of this drug-therapy evaluation showed that switching patients with hypertension or hypertension plus angina from amlodipine to either felodipine ER or nifedipine CC resulted in a small decrease in acquisition costs for DHPs, but a significant rise in the overall cost of therapy resulting from marked increases in both the numbers...
and doses of additional CV medications required by these patients. These findings support the conclusion that the evaluation of formulary changes must consider the effects of those changes on the overall cost of therapy and not just the cost of the agents being switched.

REFERENCES