

Cost Savings in Migraine Associated With Less Chest Pain on New Triptan Therapy

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Abstract

Objectives: This article constructs an economic model to estimate cost of chest-pain-related care in migraine patients receiving almotriptan 12.5 mg compared with those receiving sumatriptan 50 mg.

Study Design: This population-based, retrospective cohort study used data from the MED-STAT Marketscan database (Ann Arbor, Michigan) to quantify incidence and costs of chest-pain-related diagnoses and procedures. After a 6-month exclusion period, the study used a pre-post design, with baseline and treatment periods defined, respectively, as 5 months before and after receiving sumatriptan therapy. An economic model was constructed to estimate annual cost savings per 1000 patients receiving almotriptan instead of sumatriptan as a function of differing rates of chest pain. Annual direct medical cost avoided was calculated for a hypothetical health plan covering 1 million lives.

Results: Among a cohort of 1390 patients, the incidence of chest-pain-related diagnoses increased significantly (43.6%) with sumatriptan, from 110 during the baseline period to 158 during the treatment period ($P = .003$). Aggregate costs for chest-pain-related diagnoses and procedures increased 33.1%, from \$22,713 to \$30,234. Payments for inpatient hospital services rose 10-fold; costs for primary care visits and outpatient hospital visits rose 53.1% and 14.4%, respectively. Payments for angiography increased from \$0 to \$462, and costs for chest radiographs and electrocardiograms increased 58.7% and 31.2%, respectively. Sumatriptan treatment was associated with a 3-fold increase in payments for services for painful respiration and other chest pain. The model predicted \$11,215 in direct medical cost savings annually per 1000 patients treated with almotriptan instead of sumatriptan. Annual direct medical costs avoided for the health plan totaled \$195,913.

Conclusion: Using almotriptan instead of sumatriptan will likely reduce the cost of chest-pain-related care for patients with migraine headaches.

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The introduction of the 5-HT_{1B/1D} receptor agonists (triptans) into clinical practice heralded a new era in migraine therapy.¹ Both in Europe and the United States, recent expert opinion recommends triptans as the drugs of choice for the treatment of acute migraine attacks.^{2,3} Although the tolerability profile of triptans is generally acceptable, adverse events associated with these agents are not uncommon and include central nervous system-related events and chest symptoms (eg, heaviness or pressure in the arms and chest, chest discomfort, palpitations, and chest pain), which many patients find disturbing.⁴⁻¹³ Most cases of triptan-associated chest pain are thought to be predominantly not of cardiac origin,⁴ but examples of electrocardiographic changes consistent with transient ischemic episodes have been reported with sumatriptan.¹⁴ Isolated instances of angina, arrhythmia, myocardial infarction, and death have also been temporally associated with sumatriptan administration.¹⁴

In a 2-year postmarketing survey, a striking 41% of migraine patients who received an oral dose of sumatriptan experienced chest symptoms, and 10% of patients discontinued treatment because of these symptoms.¹³ By contrast, long-term (1-year) studies of oral almotriptan 12.5 mg, a novel and selective triptan, have demonstrated placebo-like safety and tolerability, with an overall incidence of chest pain of less than 1%.¹⁵ A recent randomized, double-blind, parallel-group study comparing almotriptan 12.5 mg and sumatriptan 50 mg in 1173 acute migraine patients confirmed the superior

tolerability profile of almotriptan.¹⁶ In this study, equal proportions of patients in both groups achieved headache response at 2 hours, but drug-related adverse events were reported in significantly fewer patients receiving almotriptan 12.5 mg than sumatriptan 50 mg ($P = .001$). Notably, the rate of chest pain (discomfort, heaviness, pressure, tightness/pain, pressure in the upper chest, sensation of chest pressure, tightness in the chest, or tightness in the upper chest) among almotriptan-treated patients was only 0.3%, which is consistent with previous reports and significantly lower than that reported for patients taking sumatriptan (2.2%; $P = .004$).¹⁶

These data suggest that the incidence of chest pain (and overall drug-related adverse events) in migraine patients treated with almotriptan 12.5 mg is lower than with sumatriptan 50 mg, and thus the corresponding costs of care for chest pain associated with migraine therapy may be lower with almotriptan. A recent study reported a lower contractile effect of almotriptan versus sumatriptan on coronary arteries, which may contribute to lower chest pain with almotriptan.¹⁷ Accordingly, the main objective of the current study was to construct an economic model to estimate the cost of care for chest pain in migraine patients receiving treatment with almotriptan 12.5 mg instead of sumatriptan 50 mg.

Materials and Methods

Study Design and Setting. This population-based, retrospective cohort study was designed to estimate the cost of care for chest pain-related care in almotriptan-versus sumatriptan-treated patients from a health plan perspective. The study used a pre-post design with baseline and treatment periods defined, respectively, as 5 months before and after receiving the first sumatriptan prescription minus 15 days (to account for drug samples given to patients). All patients were enrolled in self-insured health plans of Fortune 500 companies, which collectively covered approximately 3.5 million lives in 1996 through 1997 and nearly 4 million lives in

1997 through 1998. A total of 363,400 patients were continuously enrolled in 1996 through 1997 and 512,969 patients in 1997 through 1998.

Patient Selection. To be eligible for participation in the study, patients were required to be continuously enrolled for any 2 consecutive years between 1996 and 1998, and receive the first prescription for oral sumatriptan 25 or 50 mg between July 1, 1996, and June 30, 1998.

Exclusion criteria, applied in the 6 months before initiation of sumatriptan therapy, included any *International Classification of Diseases, Ninth Revision* (ICD-9) codes for contraindications to triptans, including history of ischemic cardiac, cerebrovascular, or peripheral vascular disease; uncontrolled hypertension; or severe renal impairment. Patients were also excluded from participation if they had risk factors for coronary artery disease, such as a history of essential hypertension or hypertension with heart disease, hypercholesterolemia, diabetes, smoking, or obesity. Patients with cardiovascular disease, cardiomyopathy, conduction disorders, dysrhythmias, heart failure, acute myocarditis, or occlusion or stenosis of precerebral arteries were excluded. In addition, male patients aged > 40 years, and female patients with menopausal or postmenopausal disorders, surgical menopause, or excision of the ovary were not eligible to participate in the study. Other exclusion criteria included a diagnosis of nonspecific chest pain before and after receiving the first sumatriptan prescription, possibly suggesting a preexisting, chronic condition. Patients were also excluded if they used any antimigraine drug other than sumatriptan during the study.

Data Collection and Outcomes Assessment. Data used in the study were extracted from the MEDSTAT MarketScan database (Ann Arbor, Michigan), an employer-based fee-for-service medical and pharmacy claims database obtained from third-party administrators of self-insured Fortune 500 companies through-

Figure. Economic Model of the Estimated Annual Cost Savings per 1000 Patients Receiving Almotriptan Instead of Sumatriptan

$$\frac{(\text{Base Cost} - \text{Treat Cost}) \cdot [1 - (\text{Almo Rate}/\text{Suma Rate})] \cdot 12 \text{ months} \cdot 1000 \text{ Pts}}{(\text{Study Period} \cdot \# \text{ Study Pts})}$$

Substituting

$$\frac{(\$22,713 - \$30,234) \cdot [1 - 0.3/2.2] \cdot 12 \cdot 1000}{(5 \cdot 1390)} = (\$11,215)$$

Base Cost = Total claims cost of chest-pain-related care in baseline period (ie, \$22,713)
 Treat Cost = Total claims cost of chest-pain-related care in treatment period (ie, \$30,234)
 Almo Rate = Chest pain rate for almotriptan patients (ie, 0.3)
 Suma Rate = Chest pain rate for sumatriptan patients (ie, 2.2)
 Pts = Almotriptan patients
 Study Period = Number of months of baseline or treatment period (ie, 5 months)
 # Study Pts = Total number of sumatriptan patients in the study cohort (ie, 1390 patients)

out the United States (with major representation from the Midwest, parts of New England, and the West Coast). The occurrence of chest-pain-related care was quantified based on relevant ICD-9 codes identifying chest-pain-related diagnoses or procedures, such as acute myocardial infarction, anginal syndromes, and “other chest pain.”

Costs of chest-pain-related care by setting (eg, primary care, hospital visits), costs for specific diagnostic tests and services, and aggregate costs during the baseline and treatment periods were analyzed based on the incidence of chest-pain-related diagnoses and procedures during the 2 study periods. The incidence of chest-pain-related diagnoses and procedures during baseline and treatment periods were compared using the McNemar test.

Model Specification for Cost Avoidance. An economic model was con-

structed to estimate the annual cost savings per 1000 patients receiving almotriptan instead of sumatriptan as a function of total claims for cost of chest-pain-related care during the 2 study periods and differing rates of chest pain between the 2 drugs (**Figure**). From this model, the cost avoided per patient-year when using almotriptan instead of sumatriptan was estimated. The predicted annual direct medical cost savings from the perspective of a health plan with 1 million covered lives was also calculated as a product of the estimated cost avoided per patient-year, migraine prevalence (12.6%), proportion of patients treated with prescription drugs (41.0%), and oral sumatriptan market share (33.8%).¹⁸

Several key assumptions were made in constructing the model. It was assumed that the amount of utilization of health-care resources for chest pain management varied proportionally with the incidences of chest pain. Further, it was assumed that the incidences of chest pain for oral almotriptan and sumatriptan were 0.3% and 2.2%, respectively, based on results derived from a head-to-head clinical trial.¹⁶ The model was limited to quantifying the relative costs of managing complaints of chest pain; it was not influenced by nor did it account for differences in the cost of the drugs.

Results

Patient Demographics. A total of 1759 patients meeting the inclusion criteria were identified. Of these, 369 were excluded, leaving a final cohort size of 1390 patients entered into the study. Patients with nonspecific chest pain in both periods were excluded (n = 40); thus, no patients with an ICD-9 code for a chest-pain-related diagnosis in the baseline period were represented in the treatment period. Such patients were excluded from the analysis to reduce variation between the treatment groups. Female patients comprised 89% of the study population, and approximately 85% of the patients were aged 15 to 54 years.

Incidence and Costs Analysis. The data showed that the incidence of

patients with chest-pain-related diagnosis increased significantly by 43.6% with sumatriptan treatment, from 110 during the baseline period to 158 during the treatment period ($P = .003$). Furthermore, the aggregate costs associated with chest-pain-related diagnoses and procedures increased 33.1%, from \$22,713 during the baseline period to \$30,234 during treatment with sumatriptan (Tables 1 and 2). Payments for primary care physician visits and inpatient and outpatient hospital visits all increased during the treatment period. Specifically, payments for inpatient hospital services increased 10-fold, rising from \$726 at baseline to \$7314 during treatment with oral sumatriptan. In addition, costs for visits to primary care physicians rose from \$6650 during the baseline period to \$10,179 during the treatment period, a 53.1% increase. Payments for outpatient hospital services increased by 14.4%, from \$8208 to \$9386.

Examination of costs for specific diagnostic tests revealed increases from baseline for angiography, chest radiographs, electrocardiograms (ECGs), and echocardiograms. Payments made for angiographic tests increased from \$0 at baseline to \$462 during sumatriptan treatment, and costs for chest radiographs increased 58.7%, rising from \$2251 at baseline to \$3572 during treatment. Payments for ECGs rose from \$2077 to \$2725, a 31.2% increase. Payments for echocardiograms rose from \$3141 to \$3411, an 8.5% increase.

The costs of medical care services for painful respiration and other chest pain also increased in the treatment period compared with the baseline period. With regard to chest-pain-related services, greater than 3-fold increases in payments for services for both painful respiration (from \$485 to \$1530) and other chest pain (from \$2440 to \$7348) were observed from the baseline period to the treatment period in those receiving sumatriptan.

Cost Avoidance With Almotriptan. Based on results from the economic model, the estimated annual direct med-

Table 1. Healthcare Utilization Associated With Care for Chest Pain in Migraine Patients

Services	Baseline Period (n = 110)		Treatment Period (n = 158)	
	Number of Claims*	Payment (\$)	Number of Claims*	Payment (\$)
PCP visit	94	6650	172	10,179
Specialist visit	21	2193	20	1787
ED visit	16	2294	2	833
Inpatient hospital	17	726	33	7314
Outpatient hospital	94	8208	165	9386
Other	33	2642	13	735
Total		22,713		30,234

*Some patients had claims for > 1 type of service related to chest-pain-related diagnosis.
ED = emergency department; PCP = primary care physician.

Table 2. Summary of Costs for Diagnostic Tests and Services for Chest Pain in Patients With Migraine

	Payment (\$)	
	Baseline Period (n = 110)	Treatment Period (n = 158)
Diagnostic Tests		
Cardiac enzymes	223	20
Stress test	388	167
Angiography	0	462
Chest radiograph	2251	3572
Electrocardiogram	2077	2725
Echocardiogram	3141	3411
Services		
Unspecified chest pain	11,588	9510
Precordial pain	120	76
Angina	NA*	1413
Painful respiration	485	1530
Other chest pain (discomfort, pressure, tightness)	2440	7348
Total	22,713	30,234

*NA = not applicable (exclusion criteria).

Table 3. Costs Avoided for Migraine Treated With Almotriptan Instead of Sumatriptan for a Health Plan With 1 Million Covered Lives

■ Health plan members	1,000,000
■ Migraine prevalence	12.6% ¹⁸
■ Proportion of migraine patients treated with prescription drugs	41.0% ¹⁸
■ Oral sumatriptan market share of antimigraine bundle	33.8% ¹⁹
■ Estimated cost avoided per patient-year when using almotriptan instead of sumatriptan	\$11.22
$1,000,000 \cdot 0.126 \cdot 0.41 \cdot 0.338 \cdot 11.22 = 195,913$	
■ Predicted health plan annual direct medical cost avoided from migraine patients using almotriptan instead of sumatriptan	\$195,913

ical cost savings per 1000 patients treated with almotriptan instead of sumatriptan was \$11,215 (Figure). This amount translated into an estimated cost avoidance of \$11.22 per patient-year when using almotriptan instead of sumatriptan. Therefore, the annual direct medical costs avoided from patients using almotriptan instead of sumatriptan was estimated to be \$195,913 for a health plan with 1 million covered lives (Table 3).

Discussion

Although triptans are the drugs of choice for acute migraine treatment,^{2,3} chest symptoms associated with their use can potentially lead to increased medical costs.^{6,7,9-14} Results from the present analysis confirmed that the incidence and costs for chest-pain-related diagnoses and procedures rise markedly after use of oral sumatriptan, with costs increasing by about one third over baseline. Almotriptan, in contrast, exhibits an extremely low incidence of chest pain,¹⁶ which will likely translate into substantial cost savings. Based on the lower rate of chest pain, the economic model presented here predicted annual direct medical cost savings in excess of \$11,200 per 1000 patients for health plans that use almotriptan in place of sumatrip-

tan. Further analysis indicated that a health plan with 1 million members could avoid nearly \$200,000 per year in direct medical costs by treating migraine patients with almotriptan instead of sumatriptan, based on the lower rate of chest pain and reduction in associated care.

With regard to specific healthcare settings, increased chest-pain-related costs associated with sumatriptan were primarily the result of payments for primary care visits plus inpatient and outpatient hospital visits. Therefore, much of the savings realized by using almotriptan instead of sumatriptan would be derived from a reduction in these visits for chest-pain-related episodes. The same is probably true with regard to specific diagnostic tests and services. From the retrospective data, it is impossible to determine the level of patient or physician expectation of chest symptoms in the sumatriptan versus almotriptan groups. Given its lower incidence of chest pain, use of almotriptan could reduce or eliminate the increase in payments for angiograms, chest radiographs, and ECGs observed during treatment with sumatriptan.

Although these results are encouraging, it should be noted that the economic model presented in this study was limited to quantifying the relative costs of managing complaints of chest pain. The model was not influenced by nor did it account for differences in acquisition costs of the drugs. Nevertheless, the present data underscore that substantial savings can be realized by using almotriptan in place of sumatriptan because of reducing the costs of care for chest pain in patients receiving treatment for migraine.

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