

Impact of a Prior Authorization for Pregabalin on Health Plan Drug Expenditures

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Objective: The objective of this study is to examine the financial impact of a prior authorization (PA) intervention for pregabalin in a commercially insured US population via an economic model.

Methods: An Excel-based model was developed to simulate 2 hypothetical scenarios for health plans: one with a PA on pregabalin, and another without a PA. In the PA scenario, a variable percentage of pregabalin prescriptions were assumed to be approved and dispensed, the remainder being denied or a substitute product dispensed (branded or generic alternatives). In the “no PA” scenario, all pregabalin prescriptions were assumed to be filled. The market shares of these products, including pregabalin, were based on secondary prescription data. The model calculated the total drug acquisition cost and cost of PA administration in each scenario for a cohort of 1000 patients over a 1-year period. Patients switching to pregabalin following denial were accounted for in the model. Sensitivity analyses were carried out varying the PA approval rates and prescription share of pregabalin and limiting the range of substituted products.

Results: The pregabalin prescribing rate was set to 10.3% in both the PA and “no PA” scenarios, with a denial rate of 50% in the PA scenario, consistent with the IMS prescription volume. The calculated drug acquisition cost for the PA scenario was \$885,564 compared with \$888,822 for the “no PA” scenario, a difference of 0.4%, after factoring in the cost of PA administration. The calculated PA administration cost was \$4121. Eliminating the PA administration cost results in a cost for the PA scenario of \$881,443, 0.8% below the “no PA” scenario. Lowering the pregabalin PA approval rate from 50% to 10% decreased the costs of the PA scenario to \$879,660, 1.0% lower than the “no PA” scenario. Raising the pregabalin market share to 20% in the “no PA” scenario increased the costs of that scenario to \$902,714, 1.9% higher than the PA scenario. Limiting the substituted products for denied pregabalin prescriptions in the PA scenario to the 2 most common products, valproate sodium and gabapentin (both generics), lowered the cost of the PA scenario to \$875,412, 1.5% below the “no PA” scenario cost. With half of the denied pregabalin patients switching to pregabalin during the course of the year, the cost of the PA scenario increased to \$892,550, 0.4% higher than the “no PA” scenario.

Conclusion: Potential savings due to PA protocols on pregabalin are low, in the 1% to 2% range across a variety of scenarios, because of the relatively low pregabalin market share (about 10%) in typical health plans and the absence of a significant difference in cost for the most commonly substituted products. Patients who switch to pregabalin after an initial denial will further reduce savings to health plans.

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Health plans commonly establish prior authorization (PA) protocols primarily to reduce utilization of more expensive medications and thereby reduce drug expenditures, as well as to limit products to specific diagnoses and support appropriate use. Actual cost savings realized by a PA intervention depend largely on factors such as PA approval rates, costs of alternative medications, the cost of administering the PA, as well as the impact on overall patient outcomes.

A number of studies based on analyses of drug claims data assessing the impact of PA or step-edit protocols are reported in the literature. Yokoyama et al (2007) reported 13% lower antihypertensive drug costs in plans with a step-edit intervention for angiotensin receptor blocker (ARB) products that required prior use of an angiotensin-converting enzyme inhibitor or other antihypertensive products compared with plans with no such restriction.¹ Dunn et al (2006) found a 9% drug cost savings using a step-edit protocol for the antidepressant category, where a generic product, excluding tricyclies, was required prior to use of a brand product.² Stacy et al (2003) performed a cost-effectiveness analysis comparing the use of a PA protocol for cyclooxygenase (COX)-2 inhibitors with no intervention and found a total cost per success (no serious gastrointestinal event) of \$278 with the intervention versus \$422 with no intervention.³ Balkrishnan et al (2007) reported the results of an economic model using typical plan rejection rates for a PA intervention in state Medicaid plans in the sedative-hypnotic category that showed higher drug costs in the intervention scenario.⁴ In a 2001 review of the literature on PA programs, MacKinnon and Kumar concluded that PA programs appear to be effective at reducing drug-related costs, but they could not reach a definitive conclusion on the impact of these programs on overall patient outcomes.⁵

Pregabalin was first marketed in the United States in 2005. Pregabalin is indicated for adjunctive therapy for adult patients with partial-onset seizures, neuropathic pain associated with diabetic peripheral neuropathy (pDPN), postherpetic neuralgia (PHN), and fibromyalgia. Painful DPN, which impacts 10% to 20% of all patients with diabetes, significantly impacts health-related quality of life and is associated with a tremendous burden in terms of its direct and indirect costs.⁶ Currently, only pregabalin and duloxetine, a serotonin and norepinephrine reuptake in-

hibitor (SNRI), are indicated for the treatment of pDPN. However, the most common treatment for pDPN based on a large insurance database for the year 2000 is short-acting opioids, followed by nonsteroidal anti-inflammatory drugs (NSAIDs), including COX-2 inhibitors, benzodiazepines, and selective serotonin reuptake inhibitors (SSRIs).⁷ First-tier treatment recommendations for pDPN issued by the Mayo Clinic include pregabalin, duloxetine, oxycodone CR, and tricyclic antidepressants (TCAs), followed by a second tier including the anticonvulsants carbamazepine, gabapentin, and lamotrigine, the SNRI venlafaxine ER, and the narcotic analgesic tramadol.⁸

Fibromyalgia afflicts 2% to 4% of the US population.⁹ Its predominant symptom is chronic widespread musculoskeletal pain. As with pDPN, few drug treatments are currently approved for fibromyalgia and include pregabalin, duloxetine, and milnacipran. The most commonly used drug therapies based on an analysis of insurance claims from 2002 to 2005, however, are TCAs such as amitriptyline, SSRI antidepressants, and opioid analgesics. Anticonvulsants, NSAIDs (including COX-2s), and benzodiazepines are also commonly used.⁹

The incidence of PHN is between 9% and 14% 1 month after the herpes zoster eruption. As many as 40% of patients with PHN will continue to have long-term problems because of incomplete or no pain relief from therapy.¹⁰ TCAs (amitriptyline, nortriptyline, desipramine, and maprotiline), gabapentin, pregabalin, opioids, and topical lidocaine patches are supported in the American Academy of Neurology guidelines as having strong evidence for efficacy in the treatment of PHN.¹¹ The prevalence of active epilepsy is approximately 3 million individuals in the United States.¹² A wide variety of generic and brand products are used in the treatment of epilepsy.

Thus, both generic and/or brand product alternatives are available to treat each of these indications for which pregabalin is approved. Some health plans have placed a PA on pregabalin, although many of the substituted products are not approved by the US Food and Drug Administration for the same indications.

The objective of this study is to examine the financial impact of a PA intervention for pregabalin in a commercially insured US population via an economic model that incorporates actual market shares of pregabalin and alternative products derived from secondary data sources.

METHODOLOGY

An Excel-based model was developed from the health plan perspective to simulate 2 hypothetical scenarios:

(1) a health plan in which a PA intervention is placed on pregabalin (PA scenario), and (2) a health plan in which there is no intervention (“no PA” scenario). In the PA scenario, a variable percentage of pregabalin prescriptions were assumed to be approved and dispensed. The remainder was assumed denied, and a substitute product was dispensed. In the “no PA” scenario, 100% of pregabalin prescriptions were assumed to be filled. In both scenarios, a mix of brand and generic products was assumed dispensed to patients who did not receive a pregabalin prescription or who were denied pregabalin in the PA process. The prescription shares of these products, including pregabalin, were based on IMS (Plymouth Meeting, PA) data for all approved pregabalin indications across the United States. The **Figure** shows a patient flow diagram of the PA and “no PA” scenarios.

The model calculated the total drug acquisition cost and cost of a PA administration in each scenario for a cohort of 1000 patients over a 1-year period, with one quarter of the patient cohort entering treatment at the start of each calendar quarter. All patients were assumed to be fully compliant with the dispensed medication and remain on the medication for the balance of the 1-year period. This algorithm resulted in a mean of 7.5 monthly prescriptions per patient in the 1-year period. Product unit costs were based on 2009 wholesale acquisition cost (WAC) for single-source products and 2009 federal upper limit (FUL) prices, where available, for multiple-source products. Daily product cost was based on the unit cost and the mean daily dosage stated in the product package insert. Monthly prescription cost was calculated as the daily product cost times 30 minus the member copayment. A \$10 copayment was assumed for all generic products and a \$25 copayment for all brand products, consistent with national copay trends.¹³ No manufacturer rebates were included in the analysis. The cost of a single PA adjudication was assumed to be \$40.⁴

Analyses were also performed in which a percentage of patients denied a pregabalin prescription in the PA scenario were assumed to switch to pregabalin during the course of the year. Upon switching to pregabalin after a denial, the health plan was assumed to incur an additional PA administration cost plus the cost of a single incremental specialist physician office visit at a cost of \$125. The incremental office visit would likely be required to obtain the new prescription and discuss the treatment failure of the product originally dispensed.

Sensitivity analyses were conducted to determine the impact of the PA adjudication cost, PA approval rates,

Table 1. Products and Prescription Share of Products Used to Treat Pregabalin Indications (Diabetic Peripheral Neuropathy, Fibromyalgia, Postherpetic Neuropathy, Partial-Onset Seizures)

Product	Share, %	Average WAC or FUL per Unit, \$	Units per Day	Copayment, \$	Net Monthly Medication Cost After Copayment, \$ ^a
Valproate sodium (generic)	27.81	0.59 ^b	6.0	10	96.36
Gabapentin (generic)	22.17	1.00 ^c	3.0	10	79.86
Lyrica (pregabalin)	10.30	2.14	2.5	25	135.64
Lamotrigine (generic)	7.48	4.34	2.0	10	250.46
Topiramate (generic)	6.75	5.07	2.0	10	293.92
Phenytoin (generic)	5.02	0.28 ^b	3.0	10	15.43
Keppra (levetiracetam)	3.84	4.04	3.0	25	338.99
Carbamazepine (generic)	3.81	0.17 ^b	3.0	10	5.60
Oxcarbazepine (generic)	3.42	2.01 ^b	2.0	10	110.60
Opioid analgesics	2.15	0.47 ^d	4.0	25	31.40
Cyclobenzaprine (generic)	1.93	0.25 ^b	3.0	10	12.28
Cymbalta (duloxetine)	1.58	3.61	1.0	25	83.27
Amitriptyline (generic)	1.38	0.12 ^b	2.5	10	0.00
Ultram (tramadol HCl)	0.73	0.31 ^b	4.0	25	11.82
Lidoderm (lidocaine) patch	0.70	6.13	1.0	25	158.79
Naproxen (generic)	0.53	0.16 ^b	2.0	10	0.00
Celebrex (celecoxib)	0.26	2.94	1.0	25	63.25
Effexor XR (venlafaxine)	0.05	3.68	1.0	25	85.55
Lexapro (escitalopram)	0.05	2.70	1.0	25	55.96
Citalopram (generic)	0.05	0.31 ^b	1.0	10	0.00

FUL indicates federal upper limit; WAC, wholesale acquisition cost.

^aA net cost of zero results when the member copayment is greater than the acquisition cost.

^bFUL price.

^cFUL for 100- to 400-mg dosages; WAC for 600- and 800-mg dosage.

^dFUL for Vicodin 5/500 mg.

Sources: Share: IMS; WAC price: *Redbook* June 2009 average wholesale price divided by 1.25; FUL price: Centers for Medicare & Medicaid Services Web site; Units per day: product package insert; Net monthly medication cost after copayment: calculated as unit price x units per day x 30 minus copayment.

market share of pregabalin, switch rates to pregabalin, and limitations on alternative drug treatments.

RESULTS

Table 1 shows the IMS-derived market basket of products, including pregabalin, used to treat the 4 approved indications for pregabalin. The Table shows the product name, US market share (Source: IMS), unit cost (WAC or FUL), daily dosage (product package insert), member copayment

(\$10 generic, \$25 brand), and net monthly prescription cost to the health plan.

Baseline Analysis

The baseline analysis uses the market share and cost data in Table 1. Of the 103 prescriptions (1000 × 10.3%) written for pregabalin in the 1-year analysis, half are approved and filled with pregabalin and the other half are filled with an alternative product in proportion to the market shares of the other products in the market basket. It is assumed

that all patients remain on the product initially dispensed for the full 1-year period (no switching). The calculated drug acquisition cost for the PA scenario was \$885,564 compared with \$888,822 for the “no PA” scenario, a difference of 0.4%, after factoring in the cost of PA administration. The calculated PA administration cost was \$4121. Eliminating the PA administration cost results in a cost for the PA scenario of \$881,443, 0.8% below the “no PA” scenario.

■ **Table 2. Summary of Results**

Analysis	PA Scenario Cost, \$	“No PA” Scenario Cost, \$	% Cost Difference (“No PA” – PA)
Baseline analysis	885,564	888,822	0.4
No PA administration cost	881,443	888,822	0.8
Reduce pregabalin PA approval rate to 10%	879,660	888,822	1.0
Increase pregabalin share in “no PA” scenario to 20%	885,564	902,714	1.9
Limit substituted products to valproate sodium and gabapentin	875,412	888,822	1.5
All sensitivities above combined	857,266	902,714	5.0
50% of denied patients switch to pregabalin in PA scenario	892,550	888,822	–0.4
All sensitivities combined	874,093	902,714	3.2
PA indicates prior authorization.			

Sensitivity Analyses

Sensitivity analyses were carried out based on adjustments in the pregabalin approval rate, market share, the range of substituted products and switches from substituted products to pregabalin. Lowering the pregabalin PA approval rate from 50% to 10% decreased the costs of the PA scenario to \$879,660, 1.0% lower than the “no PA” scenario. Raising the pregabalin market share to 20% in the “no PA” scenario increased the costs of that scenario to \$902,714, 1.9% higher than the PA scenario. Limiting the substituted products for denied pregabalin prescriptions in the PA scenario to the 2 most common products, valproate sodium and gabapentin (both generics), lowered the cost of the PA scenario to \$875,412, 1.5% below the “no PA” scenario cost. Combining the above 3 variations to the baseline scenario and setting the PA administration cost to zero results in savings of 5% in the PA scenario (\$857,266 vs \$902,714).

We tested for switches from the substituted product to pregabalin as follows. Starting with the baseline scenario, we assumed half of the denied pregabalin patients switched to pregabalin during the course of the year. We further assumed each of these patients has an incremental PA cost and physician office visit at a cost to the health plan of \$125. These assumptions increased the cost of the PA scenario to \$892,550, 0.4% higher than the “no PA” scenario. Combining all of the above variations to the baseline scenario (approval rate, market share, substituted products, and switching) resulted in savings of 3.2% in the PA scenario (\$874,093 vs \$902,714).

Table 2 summarizes the results of the baseline and sensitivity analyses.

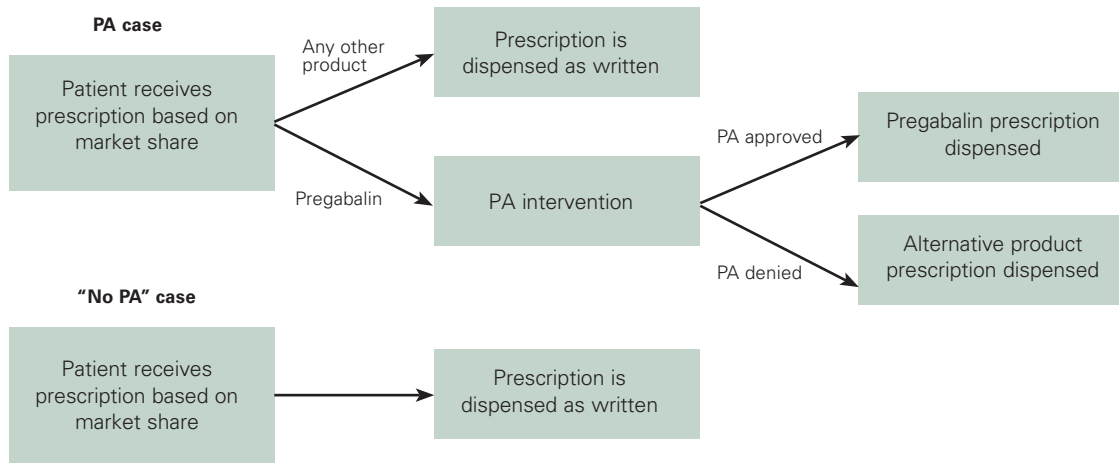
DISCUSSION

All of the baseline and individual sensitivity analyses described result in relatively small savings from the PA intervention, under 2%. The key drivers of savings will be (1) the comparative cost of alternative products, (2) the PA approval rate, (3) the prescribing rates of the restricted product in the PA and “no PA” scenarios, and (4) the likelihood of switching back to the denied product. We discuss each of these factors.

Based on the WAC and FUL pricing used in our model, the alternative products have a weighted mean monthly cost of \$116.54 compared with \$135.64 for pregabalin, a ratio of 86%. When we limited the substituted products to the most commonly used generics (top 2), this lowered the weighted mean price of the alternative products to \$89.04, a ratio of 66%. Although these are substantial differences, about 5% of patients are affected (10.3% pregabalin prescribing share × 50% denial rate). Increasing the PA denial rate to 90% raises the affected population to only 9% of patients.

The small savings due to the PA largely result from the relatively low market share of pregabalin compared with available alternatives. Health plans may be concerned that removing restrictions on products will result in increased prescribing. We tested a doubling of the pregabalin market share to 20% in the “no PA” scenario, which resulted in

■ **Figure. Model Algorithm**



PA indicates prior authorization.

savings of almost 2%. Given current prescribing patterns and the wide availability of generics in all approved indications for pregabalin, it is unlikely that the pregabalin prescribing share would rise above this level in a health plan, even with no restrictions. Patients who switch back to the denied product due to treatment failures diminish the drug cost savings from a PA protocol. In our analysis, a 50% switch rate to pregabalin resulted in higher costs for the PA scenario compared with the “no PA” scenario.

In evaluating the potential cost savings of placing a PA on a product, Yokoyama et al¹ found that step-therapy protocols on ARBs resulted in a 13% savings in daily drug costs per patient. We can compare the above factors in the Yokoyama study with the current study. Yokoyama et al found a mean daily cost of \$1.39 for patients taking an ARB product compared with \$0.76 for patients taking alternative products, a ratio of 54% compared with 86% in this study. The approval rate for the ARB PA was 44%, close to our assumption of 50%. The ARB prescribing rates in the study by Yokoyama et al were 19.2% in the PA plans and 25.8% in the “no PA” plans, considerably higher than the current pregabalin market share of 10.3%. Switch rates to ARBs for patients initially denied an ARB reached 51% within 1 year in the PA plans. The difference in the cost ratios and target product prescribing shares accounts for the difference in savings between the Yokoyama study and the current study.

The “sentinel effect” takes place when physicians reduce their prescribing of products they know may be denied by the health plan through a step-edit or PA intervention. This is difficult to measure, since the patient population in a plan

with a PA intervention may differ in disease prevalence and severity from the patients in a plan with no intervention.

If the denial rate for a PA intervention is low, the health plan can easily spend more on administration costs than it saves in lowered drug acquisition costs. Based on a \$40 PA administration cost and the full market basket of products in our model, the health plan would have to deny 28% of pregabalin prescriptions to break even. A lower denial rate would result in higher costs compared with no intervention.

Limitations

This study uses a market basket of products most commonly prescribed for the approved indications of pregabalin. Market shares for these products were based on IMS retail prescribing data in the United States. Individual health plans may provide access to different products and have varying utilization patterns. Product prices were based on WAC or FUL prices where available. Health plans may be able to obtain lower prices due to either manufacturer rebates or state maximum allowable cost prices for generics. Net prescription prices used in this study were based on member copayments of \$10 for generics and \$25 for brand products. Copayments may differ for individual health plans.

This study made no attempt to assess patient outcomes or evaluate nondrug medical costs associated with utilization of specific products. Additionally, treatment persistency in this study is assumed to be 100% for all products, except for patients switching to pregabalin who were initially denied therapy. A potential consequence of PA interventions is

that the patient will not seek an alternative product if the PA request is not approved. These “walk-away” patients may go without treatment for their condition. In the ARB study by Yokoyama et al,¹ 6.6% of patients who were denied the ARB in the step-edit process received no drug treatment. Patients who are not treated with products specifically indicated for their condition may use higher doses of substituted medications. Margolis et al have shown higher concomitant analgesic medication use and overall costs in Medicaid programs with a pregabalin PA compared with those without such a restriction.¹⁴

CONCLUSION

Potential savings due to PA protocols on pregabalin are low, in the 1% to 2% range across a variety of scenarios. This is due to the relatively low pregabalin market share (about 10%) in typical health plans and the absence of a significant difference in cost for the most commonly substituted products. Patients who switch to pregabalin after an initial denial will further reduce savings to health plans.

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