

GABAPENTIN AND PREGABALIN USE IN MISSISSIPPI MEDICAID

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BACKGROUND

The prescribing of gabapentin and pregabalin, collectively referred to as gabapentinoids, has risen sharply in recent years. In 2016, gabapentin was the 10th most commonly prescribed medication in the United States with 64 million prescriptions dispensed, up from 39 million in 2012. Additionally, pregabalin (Lyrica) sales in dollars more than doubled from 2012 to 2016 to \$4.4 billion nationally.¹ These medications consistently rank in the top 10 drug categories by dollars paid monthly by Mississippi's Division of Medicaid (DOM).

Gabapentin is FDA approved for the treatment of partial onset seizures, with and without secondary generalization, in adults and pediatric patients ≥ 3 years of age and in the management of postherpetic neuralgia in adults.² Pregabalin is FDA approved for the management of neuropathic pain associated with diabetic peripheral neuropathy or spinal cord injury, postherpetic neuralgia, partial onset seizures in adults, and fibromyalgia.³ Both medications are increasingly being prescribed for non-FDA approved indications, particularly for the management of various pain syndromes.

Increased prescribing of gabapentin and pregabalin may be due in part to clinicians seeking alternatives to opioids in the treatment of pain. Prescription drug misuse or abuse is a growing problem in the United States. According to the National Institute on Drug Abuse, results from a 2014 survey report estimate that 52 million Americans (approximately 20% of the U.S. population age ≥ 12 years) have used a prescription medication for nonmedical purposes.⁴ Opioid abuse is largely implicated in this trend. With recent attention focused on the opioid crisis, many clinicians are looking to gabapentinoids as additional options to treat pain. These medications can be used to decrease or eliminate opioid use in certain patients. However, there is evidence of increasing abuse of gabapentin and pregabalin. Literature reviews referencing gabapentinoid abuse cite a 1.6% prevalence of gabapentinoid abuse in the general population. Within populations of people who abuse opioids, the prevalence of gabapentinoid abuse increased to 15-22%.^{5,6}

¹ Goodman, C and Brett, Allan. "Gabapentin and pregabalin for pain – Is increased prescribing a cause for concern?" *N Engl J Med* 2017; 377:411-414.

² Neurontin[®] [package insert]. New York: Pfizer, Inc. 2015.

³ Lyrica[®] [package insert]. New York: Pfizer, Inc. 2016.

⁴ Volkow ND. National Institute of Health National Institute on Drug Abuse. <https://www.drugabuse.gov/publications/research-reports/prescription-drugs/director>. (last updated Aug 2016)

⁵ Evoy, Kirk E., Megan D. Morrison, and Stephen R. Saklad. "Abuse and misuse of pregabalin and gabapentin." *Drugs* (2017): 1-24.

⁶ Smith, Rachel V., Jennifer R. Havens, and Sharon L. Walsh. "Gabapentin misuse, abuse and diversion: a systematic review." *Addiction* 111.7 (2016): 1160-1174.

The mechanism of action of gabapentinoids and the association with abuse is not fully understood. Gabapentin and pregabalin are both analogues of gamma-aminobutyric acid (GABA), a neurotransmitter that slows down the activity of nerve cells in the brain. While these medications do not directly bind to GABA receptors, they are thought to exert GABA-mimetic properties. They share many similarities with other medications associated with abuse potential in that they produce withdrawal syndrome and certain psychoactive effects.⁷

Due to the potential for abuse, MS-DUR examined use of gabapentinoids in DOM beneficiaries. The analysis included reviewing the daily dosage ranges prescribed, diagnoses and concomitant opioid use.

METHODS

A retrospective analysis was conducted for the period of January 1, 2017 through June 30, 2017 using DOM prescription claims data from the Fee For Service (FFS) and the two coordinated care organizations, United Healthcare (UHC) and Magnolia (MAG). Claims were identified using national drug codes (NDC) for gabapentin and pregabalin. For beneficiaries with claims for these gabapentinoids during the study period, any concurrent claims for opioids were also identified. For gabapentinoid claims that had a concomitant opioid claim, days of overlap were calculated. Each beneficiary's gabapentinoid claim was assessed to determine if it can be classified as an early refill, based on the previous prescription fill date and the days of medication supplied for that previous claim. For each gabapentinoid claim, the daily dosage level was calculated based on the strength of the medication filled, quantity supplied, and days of supply. Daily dosage levels were also categorized.

RESULTS

Table 1 provides an overview of claims for gabapentin and pregabalin as well as concomitant opioid use. During the 6 month observation period, 177 claims were processed for a daily dosage > 3600mg, the maximum FDA approved daily dose. For pregabalin, the maximum FDA approved daily dose is 600mg. A total of 65 pregabalin claims were processed for a daily dosage >600mg during the 6 month observation period. More than 50% of gabapentinoid claims in this timeframe are associated with concomitant opioid use.

⁷ Schifano F. Misuse and abuse of pregabalin and gabapentin: cause for concern? *CNS Drugs*. 2014;28:491–6.

Table 1: Prescription Claims for Gabapentinoids and Concomitant Opioid Use (January 1, 2017 thru June 30, 2017 - FFS and CCOs)						
Drug	Daily Dosage levels	Total # Claims	Claims With Concomitant Opioid Use	% of Claims With Concomitant Opioid Use	Mean Days of Overlap	# Claims with Early Refills (%)
Gabapentin	< 1200 mg	21,809	11,427	52%	24.6	11,445 (26.3)
	1200 mg - 2400 mg	19,380	11,606	60%	24.8	
	2400 mg - 3600 mg	2,185	1,327	61%	23.6	
	> 3600 mg	177	126	71%	27.3	
Pregabalin	0 - 600 mg	8,420	5,696	68%	24.8	2,360 (27.8)
	601 mg - 1200 mg	63	34	54%	21.9	
	1200 mg - 2400 mg	2	2	100%	4.0	

Table 2 illustrates the daily dosing for total gabapentinoid prescriptions by DOM's three pharmacy programs. There was a noticeable difference in the number of claims for daily dosage > 3600mg of gabapentin in FFS as compared to UHC and MAG. In regards to pregabalin, both UHC and MAG had substantially more claims for a daily dosage > 600mg compared to FFS.

Table 2: Number of Prescriptions By Dose Level and Pharmacy Program (January 1, 2017 thru June 30, 2017)				
Drug	Daily Dosage Level	Pharmacy Program		
		FFS	UHC	MAG
Gabapentin	< 1200 mg	4,495	7,400	9,914
	1200 mg - 2400 mg	3,354	6,840	9,186
	2401 mg - 3600 mg	73	1,014	1,098
	> 3600 mg	114	45	18
Pregabalin	0 - 600 mg	1,670	3,110	3,648
	601 mg - 1200 mg	4	21	38
	1201 mg - 2400 mg	0	1	1

Table 3 displays the prevalence of appropriate diagnoses present in medical claims. Appropriate diagnoses were determined by both FDA-approved diagnoses for each agent or an acceptable diagnoses supported by CMS approved pharmacy compendia. Approximately two-thirds of gabapentinoid prescriptions did not have an appropriate diagnosis found in the medical claims. Through MS-DUR's literature review, follow-up discussions with providers support that gabapentinoids are often used in various pain syndromes to reduce or eliminate the use of opioids.

Table 3: Prevalence of Appropriate Diagnoses for Gabapentinoid Claims by Pharmacy Program (January 1, 2017 thru June 30, 2017)		
Plan	Number of gabapentinoid claims	Percent of claims associated with appropriate diagnoses*
FFS	9,758	31.3%
UHC	18,454	33.2%
MAG	23,911	33.4%

* Appropriate diagnosis found in medical claims.

CONCLUSIONS AND RECOMMENDATIONS:

There is substantial evidence supporting the increased utilization of the gabapentinoid class of medications in recent years. Although providers may use these medications to limit opioid prescribing, these agents are not void of potential side effects. Data shows that although there is not significant use of these products above FDA recommended dosing for DOM beneficiaries, it does occur on a limited basis. Based on current utilization patterns for these products, MS-DUR proposes the following recommendations to the DUR Board for consideration.

Recommendations:

1. DOM should set a maximum daily dosage of 3600mg for gabapentin products.
2. DOM should set a maximum daily dosage of 600mg for pregabalin products.
3. DOM should conduct a one-time educational mailing outlining the proposed changes to include all prescribers writing gabapentin and pregabalin prescriptions during the last six months that exceeded the recommended maximum daily dosage limits.
4. DOM should monitor concomitant opioid use with pregabalin /gabapentin claims to determine impact of pregabalin/gabapentin on reducing or eliminating opioids.