

## A Study into Trends on the Application of Gabapentinoid Medicine in Srinagarind Hospital

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**Background and objectives:** Gabapentinoids are considered as a class of new antiepileptic drugs (AEDs) used in combination with standard AEDs to treat partial seizures. Gabapentinoids are also indicated for the treatment of other conditions, such as neuropathic pain, chronic muscle pain with fibromyalgia, and anxiety disorders. Drugs affiliated with the gabapentinoid class are considered clinically important because of their efficiency to treat multiple diseases. Srinagarind Hospital has adopted the Drug Utilization Evaluation (DUE) form to monitor and direct the application of this class of medicine, and the action conforms to the restriction of the Cabinet Resolution issued on February 3, 1998. The objective of this study was to examine the application trends of both the original and the generic types of the gabapentinoid class medicines. The costs, yielded from the usage of this medication, were also investigated. The data, which was obtained from this research, should be exploited as a guideline for the medication planning and the prescribing system.

**Materials and Methods:** This descriptive research study was conducted with a group of patients from Srinagarind Hospital, whose records showed the use of gabapentinoid medications from the 1 January 2015 to 31 December 2020. The active ingredients, found in both the original and the generic types of gabapentinoid drug under this investigation, were Pregabalin and Gabapentin.

**Results:** There were 31,379 gabapentinoid-treated patients; 12,018 were men (38.30%) and 19,361 were women (61.70%), with a mean age of 57.68 years. Most of the patients (19,659 or 62.65%) had used the civil service for their medical payments. The Department with the highest number of gabapentinoid prescriptions had been the Orthopedic Department (70.86%). It was also observed that the application of the gabapentinoid medicines had increased annually. The drugs in the gabapentinoid class with the first three-highest rate of consumption as sorted by name and medical strength were as follows: 1) Gabapentin 300 mg, 2) Lyrica® 75mg, and 3) Gabapentin 100 mg. Based on this research study's timeframe, the total cost of the gabapentinoid drug prescription was found to be 79,061,537.73 Baht. The first three medicines with the highest prescription cost were: 1) Lyrica® 75 mg, 2) Lyrica® 150 mg, and 3) Gabapentin 300 mg. Based on the type of medical service payment, the highest description value was on the civil servant benefits (89.61%), followed by the self-paid value of 5.13 percent.

**Conclusion:** The usage and the description values of the drugs in the gabapentinoid class in Srinagarind Hospital were found to be increasing every year. Therefore, the importance of both the drug supply assessment and restrictions on the use of drugs in the hospital should be taken into account in order to direct reasonable drug usage, as well as to be able to reduce hospital expenses.

**Keywords:** Gabapentinoid; Trends; Usage

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Drugs in the gabapentinoid class of compounds are gabapentin and pregabalin, which can be active when bound with  $\alpha 2\delta$ -1 protein that is a component of the sub-unit of voltage-gated calcium channels<sup>(1,2)</sup>. This type of drug,

which is known for not assimilating with protein in the blood, can be absorbed well into the brain. Moreover, the drug is characterized by not being metabolized by the liver and not binding with CYP 450 enzyme, which helps to prevent the substances in the gabapentinoid class of drugs from reacting with chemicals from other medicines. The substances from this group of drugs can be excreted in form of urine without being processed by the kidneys<sup>(3)</sup>. Despite their similarities of their activation mechanism, Pregabalin is found to have a higher pharmacokinetic efficiency—faster absorption and steadier activeness—than its counterpart substance, gabapentin. It has been observed that the absolute bioavailability of gabapentin in the blood was reduced from 60% to 33% after the dose had been increased from 900 mg. to 3,600 mg. To the contrary, the observed value of pregabalin had been detected at a steady level of 90% or above regardless of the prescribed doses. This is because gabapentin can be

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absorbed from 3 to 4 times more slowly than pregabalin. Moreover, gabapentin is a nonlinear pharmacokinetic substance, which means that the maximization of its dosage does not intensify its activeness. Pregabalin, on the other hand, is a linear pharmacokinetic, meaning that the dosage volume is directly related to its kick-in level<sup>(4)</sup>. The drugs in the gabapentinoid class have been certified for use by the US Food and Drug Administration (USFDA) for the following applications, consisting of: 1) an antiepileptic drugs (AEDs); 2) an adjunctive therapy for partial seizures with and without secondary generalized seizures in adults and teenagers of at least 12 years old, and it is used for partial seizures for the patients ages 3 to 12 years old<sup>(5)</sup>; 3) a first-line drug for the relief of neuropathic pain<sup>(6)</sup>; 4) a treatment for postherpetic neuralgia (PHN) and diabetic neuropathy<sup>(7,8)</sup>. The drugs in the gabapentinoid class are also certified for off-label use for the following symptoms: bipolar disorder, complex regional pain syndrome, attention deficit disorder, restless leg syndrome, periodic limb movement, sleep disorders, headaches, alcohol withdrawal syndrome, chronic back pain, fibromyalgia, visceral pain, and acute post-operative pain<sup>(9,10)</sup>. It has been noted that gabapentin and pregabalin have been increasingly prescribed for the relief of other acute pains. In 2016, gabapentin was ranked as the 10<sup>th</sup> highest prescription medication in American hospitals with a total of 64 million prescriptions compared to the record of 39 million in 2012. Pregabalin, under the Lyrica® brand, was ranked as the 8<sup>th</sup> highest prescription medication in America in 2016, with an estimation of 4.4 million dollars, which is twice as high as the number recorded in 2012<sup>(11)</sup>. Srinagarind Hospital is a tertiary level hospital that provides multiple medical services. Gabapentin and pregabalin have been used to serve different medical purposes in this hospital. The researcher was tempted to accumulate information on the strengths of these two medicines in order to determine the trends of their usage. The obtained information should provide a baseline for reasonable medical prescriptions.

## Objective

1) To study the trends and consumption of gabapentinoids in both outpatients and hospitalized patients at Srinagarind Hospital, Khon Kaen University.

2) To study the value generated from the use of drugs in gabapentinoid class at Srinagarind Hospital, Khon Kaen University.

## Materials and Methods

### Study design

A retrospective descriptive study.

### Population

The research participants were those with a medical record of being prescribed both the original and the generic types of pregabalin and gabapentin. The Gabapentin used for this research is a generic type having three dosages: 100 mg, 300 mg, and 600 mg. The Pregabalin, used for this research, came from two commercial sources: Lyrica®

(original) and Pregabalin Sandoz (generic). The latter had two dosages. The 75 mg dosage was ordered to the hospital in December 2016 and the 25 mg dosage was ordered in June 2018. The data was collected based on the pharmaceutical records of Srinagarind Hospital from 1 January 2015 to 31 December 2020.

### Data collection

The data was collected based on the pharmaceutical records of Srinagarind Hospital, which included information about the patients' age, gender, types of medical benefits & welfare, and medical information, such as the types and the volume of the prescribed drugs, numbers of prescriptions, and the costs of the drugs.

### Data analysis

Descriptive statistics were used for data analysis and the results were presented with frequencies, percentages, and mean distributions.

## Results

Based on the period of this study, there were 31,379 patients, who had received gabapentinoids, consisting of 12,018 men (38.30%) and 19,361 women (61.70%). The mean age was 57.68 years old, with the youngest patient being 1 year old and the oldest being 100 years old. Most of the patients (19,659 people or 62.65%) used the government medical treatment rights. Meanwhile, the department with the highest number of prescriptions had been the Orthopedic Department (70.86%) as shown in Table 1.

Based on a principal diagnosis, there were 16,708 patients (53.25%), who had been prescribed gabapentinoids. The first three of the most frequent symptoms of those, who had received this medicine, were as follows: 1) spinal stenosis, 2) spondylolysis/spondylolisthesis, and 3) malignant neoplasm, respectively. Only 18 cases were diagnosed either for the treatment of epilepsy.

Based on the comparison of the type and the dosage volume of gabapentinoid between the years 2015 to 2020, the usage of the medicine was found to have increased with the following specific manner: Lyrica® 150 mg. had increased by 2.7 times, Lyrica® 75 mg had increased by 2 times, and the use of gabapentins with the densities of 100 mg, 300 mg, and 600 mg had been found to increase at the rates of 12.9 times, 1.3 times, and 2.1 times, respectively. The use of Pregabalin Sandoz 75 mg had been found to have increased by 2.8 times between the years 2017 and 2020, while the usage of Pregabalin Sandoz 25 mg had been found to have increased by 1.4 times between the years 2019 and 2020 (Table 3 and Figure 2 and 3).

Based on an analysis of the total usage of gabapentinoid medicines between 2015 and 2020, the top three most prescribed had been: 1) Gabapentin 300 mg, 2) Lyrica® 75 mg, and 3) Gabapentin 100 mg. The total budget used for the medical purchases had been 79,061,537.73 Baht. As sorted by the types and the dosage volumes, gabapentinoid medicines with the three highest purchasing values had been

**Table 1.** The patients' general information

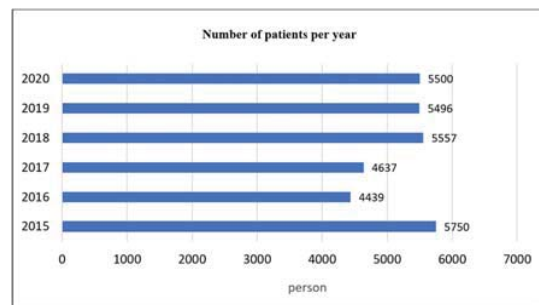
General information	Number of patients (percentages)
Total number of patients	31,379
Gender	
Male	12,018 (38.30)
Female	19,361 (61.70)
Average age	57.68 years
The Oldest	100 years old
The Youngest	1 year old
Medical benefits/rights	
Civil servant	19,659 (62.65)
Self-payment	5,702 (18.17)
Universal healthcare insurance	5,100 (16.25)
Social security	918 (2.93)
Departments	
Orthopedics	22,234 (70.86)
Geriatrics	3,584 (11.42)
Surgery	2,097 (6.68)
Rehabilitation medicine	914 (2.91)
Otolaryngology	343 (1.09)
Anesthesiology	254 (0.81)
Pediatrics	239 (0.76)
Radiology	260 (0.83)
Emergency	258 (0.82)
Obstetrics & Gynecology	231 (0.74)
Psychiatry	182 (0.58)
Ophthalmology	179 (0.57)
Palliative care	74 (0.24)
General practice	26 (0.08)
Others	504 (1.61)

**Table 2.** The first five symptoms observed in the principal diagnoses

Principal diagnoses	Number (cases)
Spinal stenosis	5,041
Spondylolysis/spondylolisthesis	2,116
Malignant neoplasm	651
Neuralgia and neuritis	487
Low back pain	444

as follows: 1) Lyrica® 75 mg, 2) Lyrica® 150 mg, and 3) Gabapentin 300 mg, as shown in Table 4 and Figure 4.

Based on the analysis of the values, which had been generated from annual medical usage and had been sorted

**Figure 1.** Number of patients, who received gabapentinoid medications from 2015 to 2020.

by its types and strengths, the prescription values of gabapentinoid medicines were found to have increased each year, which was directly related to the increasing usage rates of the medicine as shown in Table 5 and Figure 5.

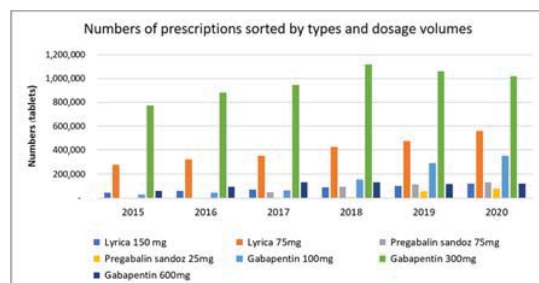
When comparing the prescription value of gabapentinoids by the treatment rights from 2015 to 2020, it was found that the payment via civil servant medical benefits (direct payment/local administration/state enterprises) had been recorded at 70,843,407.74 Baht. It is important to note that the cost was 8.6 times higher than the combination of other treatment rights (Universal health insurance, social security, self-pay) at the cost of 8,218,129.99 Baht. The treatment rights affect the prescribing of drugs because the right of the official government medical treatment is the only health benefit right that allows the withdrawal of the original type of gabapentinoid drugs, which is a non-registered drug on the national list of essential medicines. People, who do not have the aforementioned medical right, must pay for themselves. Moreover, the original type of gabapentinoid is many times more expensive than its counterpart, the generic type drug, which is listed on the national list of essential medicines. (Herein, Gabapentin) (Table 6, Figure 6).

## Discussion

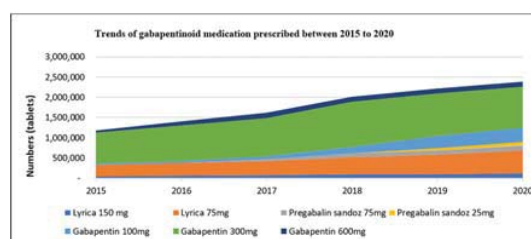
As classified by their commercial names, types, and potencies, the Gabapentinoid medicines being used in Srinagarind Hospital are as follows: Lyrica® 75 mg, Lyrica 150 mg, Pregabalin Sandoz 75 mg, Pregabalin Sandoz 25 mg, Gabapentin 100 mg, Gabapentin 300 mg, and Gabapentin 600 mg. There is a tendency for larger numbers of prescriptions for these medicines every year. The comparison of gabapentinoid usages in 2015 and 2020 showed the following projection of usage across all gabapentinoid entries: Lyrica® 150 mg was found to have increased by 2.7 times and Lyrica® 75 mg was found to have increased by 2 times. For the Gabapentin with the potencies of 100 mg, 300 mg, and 600 mg, the rates of increase were found to be as follows: 12.9 times, 1.3 times, and 2.1 times, respectively. The comparisons of Pregabalin Sandoz 75 mg prescriptions in 2017 and in 2020 showed an increased consumption rate of

**Table 3.** The number of gabapentinoid prescriptions sorted by types and dosage volumes between 2015 to 2020

Types and strengths	The prescribed amounts (tablets)					
	2015	2016	2017	2018	2019	2020
Lyrica 150 mg	45,036	57,688	70,287	90,373	100,312	122,213
Lyrica 75 mg	277,899	322,276	354,208	424,814	475,036	557,238
Pregabalin Sandoz 75 mg	-	1,532	47,562	94,230	111,180	132,349
Pregabalin Sandoz 25 mg	-	-	-	4,770	56,304	80,029
Gabapentin 100 mg	27,488	45,623	61,743	153,705	294,550	355,836
Gabapentin 300 mg	771,037	878,110	946,435	1,118,767	1,059,005	1,018,475
Gabapentin 600 mg	58,840	94,175	133,706	130,844	118,476	122,618

**Figure 2.** The Numbers of gabapentinoid prescriptions sorted by types and dosage volumes between 2015 to 2020.

2.8 times. For the consumption of Pregabalin Sandoz 25 mg in 2019 and 2020, there was an increased rate of 1.4 times. These medicines had been used the most by the Orthopedics Department (70.86 percent). This is consistent with findings studies by Montastruc F, et al<sup>(12)</sup> and Goodman CW and Brett AS<sup>(13)</sup>, to the extent that there has been an increase in the use of these drugs in the treatment of chronic nerve pain, including off-label treatment because it is easy to dispense. The situation was also found to true in England where the prescription of these gabapentinoid drugs have accounted for more than half of all prescriptions in the primary care units in the country. Similarly in the United States, the use of gabapentinoids was found to have increased three-fold between 2009 and 2015<sup>(7)</sup>. The value of the gabapentinoid prescriptions at Srinagarind Hospital from 2015 to 2020 totaled 79,061,537.73 Baht. When sorted by type and drug strength, the top 3 had been: 1) Lyrica® 75 mg, 2) Lyrica® 150 mg, and 3) Gabapentin 300 mg. The prescription values for these medicines had increased every year. This is consistent with an analysis of the prescribing values in the UK, where it was found that Pregabalin had been prescribed 2.7 million times in 2013, and in 2018, the number had risen to 7 million. For the prescription of gabapentin, the dispensing of this drug had increased from 3.5 million to 7 million



Pregabalin Sandoz with the strength of 75 mg was registered to the hospital in December of 2016, and the 25 mg. strength was registered in June of 2018. The comparison of the prescription was conducted after the medicine had been registered for the period of 1 year.

**Figure 3.** The Trends of gabapentinoid prescriptions sorted by the types and strengths between 2015 to 2020.

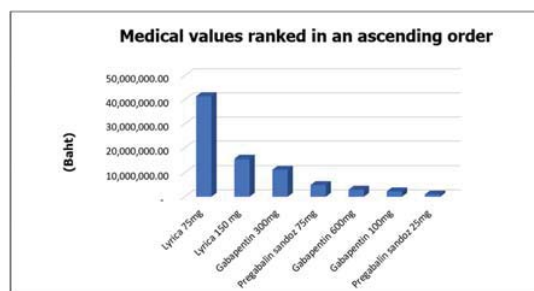
prescriptions<sup>(3,14)</sup>. The prescribing value of the drugs as classified by treatment rights had been found as follows. The right to receive medical treatment for the public servants was at the highest value, which accounted for 89.61 percent of all prescription values and was found to be 8.6 times higher than the combined values of all other payments. The drugs with the highest disbursement value had been Lyrica® 75 mg (40,069,047.69 Baht), followed by Lyrica® 150 mg (15,032,602.80 Baht). The combination of values generated from these two drugs has already accounted for 77.78% of the total payments made through the civil servant medical benefits. Srinagarind Hospital has had to undergo a projected dispensation of gabapentinoids and inevitably needs a higher budget for the disbursement of this drug. Of the gabapentinoids, the drug with the highest value had been Lyrica® 75 mg with a total value of 41,453,186.49 Baht. The researcher has found it reasonable to substitute Lyrica® 75 mg with Pregabalin 75 mg in order to help the hospital save approximately 11,333,913.70 baht (27.34%) of the medical purchasing cost. Another alternative is to change from the original type of drug to the generic one. It has been

**Table 4.** The usage amounts and value of gabapentinoid medicines sorted by the types and strengths between 2015 to 2020 (price per unit of medicine as of 31 December, 2020)

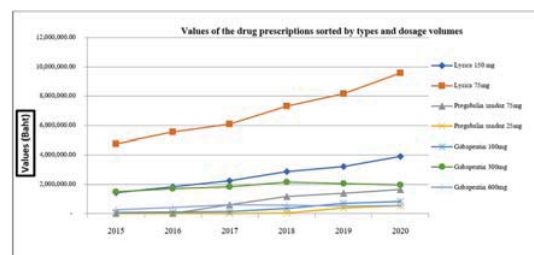
Types and Strengths	Amount (tablets)	Price per tablet (baht)	Values (baht)
Lyrica 150 mg	485,909	31.95	15,524,792.55
Lyrica 75 mg	2,411,471	17.19	41,453,186.49
Pregabalin Sandoz 75 mg	386,853	12.49	4,831,793.97
Pregabalin Sandoz 25 mg	141,103	6.68	942,568.04
Gabapentin 100 mg	938,945	2.35	2,206,520.75
Gabapentin 300 mg	5,791,829	1.93	11,178,229.97
Gabapentin 600 mg	658,659	4.44	2,924,445.96
The total cost of gabapentinoid medicines was 79,061,537.73 baht			

**Table 5.** The values of gabapentinoid medicines classified by types and strengths prescribed between 2015 to 2020

Types and strengths	Medical value (baht)					
	2015	2016	2017	2018	2019	2020
Lyrica 150 mg	1,438,900.20	1,843,131.60	2,245,669.65	2,887,417.35	3,204,968.40	3,904,705.35
Lyrica 75 mg	4,777,083.81	5,539,924.44	6,088,835.52	7,302,552.66	8,165,868.84	9,578,921.22
Pregabalin Sandoz 75 mg	-	19,134.68	594,049.38	1,176,932.70	1,388,638.20	1,653,039.01
Pregabalin Sandoz 25 mg	-	-	-	31,863.60	376,110.72	534,593.72
Gabapentin 100 mg	64,596.80	107,214.05	145,096.05	361,206.75	692,192.50	836,214.60
Gabapentin 300 mg	1,488,101.41	1,694,752.30	1,826,619.55	2,159,220.31	2,043,879.65	1,965,656.75
Gabapentin 600 mg	261,249.60	418,137.00	593,654.64	580,947.36	526,033.44	544,423.92



**Figure 4.** The values of gabapentinoid medicines usage sorted by types and strengths in a descending order between 2015 to 2020.



**Figure 5.** The values of gabapentinoid prescriptions sorted by types and dosage volumes between 2015 to 2020.

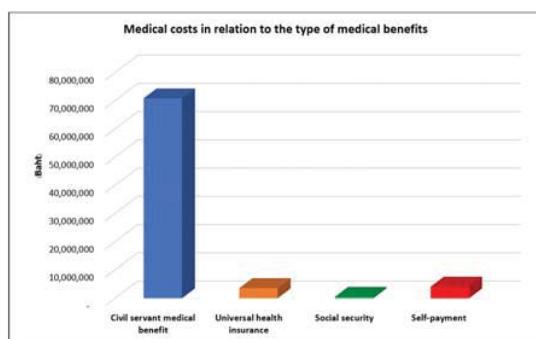
suggested, however, that a clinical efficiency analysis be conducted in order to verify the potential of the generic alternative. In 2019, an announcement was made by the USFDA, which warned about the dangers of respiratory depression caused by gabapentin or pregabalin in people with existing respiratory risk factors, such as the elderly,

those with Opioid analgesics, people taking other drugs that depress the central nervous system, and individuals with reduced lung function, such as those with chronic obstructive pulmonary disease. The agency had reviewed data on the application of gabapentinoids (a combination of gabapentin and pregabalin) in different publications, including observational studies, clinical trials, human studies or animal



**Table 6.** Medication costs for gabapentinoids based on the types of health care benefits from 2015 to 2020

Types and strengths	Medication costs based on the type of health care benefits (baht)			
	Civil servant medical benefits	Universal health insurance	Social security	Self-payment
Lyrica 150 mg	15,032,602.80	-	-	492,189.75
Lyrica 75 mg	40,069,047.69	-	-	1,384,138.80
Pregabalin Sandoz 75 mg	4,096,270.36	-	-	735,523.61
Pregabalin Sandoz 25 mg	868,486.84	-	-	74,081.20
Gabapentin 100 mg	1,634,511.95	341,861.55	61,797.95	168,349.30
Gabapentin 300 mg	7,488,064.18	2,384,603.78	387,250.64	918,311.37
Gabapentin 600 mg	1,654,423.92	882,623.16	78,445.92	308,952.96
Total	70,843,407.74	3,609,088.49	527,494.51	4,081,546.99

**Figure 6.** Medication costs for gabapentinoid based on the types of health care benefits from 2015 to 2020.

studies, and case reports, which had been directed to the USFDA. Results of the review revealed that gabapentinoids had often been prescribed in combination with other drugs that have a depressant effect on the central nervous system, such as opioid analgesics, anti-anxiety drugs, anti-depressants, and antihistamine drugs. This dual dispensing increases the risk of life-threatening respiratory depression<sup>(15)</sup>. It is critically important for the dispensing of this drug to be performed more conscientiously. It is recommended that gabapentinoid prescriptions in Srigarind Hospital should be further investigated in order to promote the most cost-effective strategies for the administration of this drug.

### Conclusion

Trends in the use of gabapentinoid at Srinagarind Hospital were found to be increasing with higher drug value rates every year. In order to assess the drug supply with the goal of helping to supervise drug administration in the hospital in a more reasonable way, the information presented in this research study should be considered and should help to reduce

the hospital's expenses.

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### What is already known on this topic?

Gabapentinoid are useful in neuropathic pain, partial epilepsy, fibromyalgia, diabetic polyneuropathy and post herpetic neuralgia.

### What this study adds?

Trends in the use of gabapentinoid at university hospital were found to be increasing with higher drug value rates every year.

### Potential conflicts of interest

The authors declare no conflict of interest.

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