


PHARMACY POLICY – 5.01.521

Pharmacologic Treatment of Neuropathy, Fibromyalgia and Seizure Disorders

Effective Date:	Dec. 1, 2017	RELATED POLICIES / GUIDELINES:
Last Revised:	Nov. 21, 2017	5.01.520 Antidepressants: Pharmacy Medical Necessity Criteria for Brands
Replaces:	N/A	5.01.529 Opioid Analgesics
		5.01.550 Pharmacotherapy of Arthropathies
		5.01.605 Medical Necessity Criteria for Pharmacy Edits

Select a hyperlink below to be directed to that section.

[POLICY CRITERIA](#) | [CODING](#) | [RELATED INFORMATION](#)
[EVIDENCE REVIEW](#) | [REFERENCES](#) | [HISTORY](#)

 Clicking this icon returns you to the hyperlinks menu above.

Introduction

Neuropathy is a term that refers to problems with one or more nerves. Neuropathy doesn't always cause symptoms, but usually it does. Depending on the location of the nerve and the type of damage, symptoms can include loss of feeling, numbness, tingling, or pain. Neuropathic nerve pain has been described as feeling like an electric shock, burning, or knifing. Extreme sensitivity to touch may be another symptom. Fibromyalgia is a long-term medical condition that often causes pain in muscles and bones, areas that are tender to the touch, and fatigue. It's believed that fibromyalgia is the result of changes in how the brain and spinal cord process pain signals from the nerves. Seizure disorders are the result of unusual electrical activity in the brain. Uncontrolled electrical signals in the brain produce several symptoms, including seizures. This policy describes specific medications that may be approved for neuropathy, fibromyalgia, and seizure disorders.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria

Drug	Medical Necessity
<p>Savella™ (milnacipran)</p>	<p>Savella™ (milnacipran) may be considered medically necessary for the labeled indication of fibromyalgia.</p> <p>Savella™ (milnacipran) may be covered in the following circumstances:</p> <ul style="list-style-type: none"> • Patients with fibromyalgia when they have failed a reasonable combination of pharmacologic agents, including gabapentin and at least 2 of the following: <ul style="list-style-type: none"> ○ A tricyclic antidepressant (eg, amitriptyline) <p>AND/OR</p> <ul style="list-style-type: none"> ○ A generic SNRI (eg duloxetine, venlafaxine) <p>AND/OR</p> <ul style="list-style-type: none"> ○ Cyclobenzaprine <p>AND/OR</p> <ul style="list-style-type: none"> ○ Tramadol <p>Use of Savella™ (milnacipran) for other indications is considered investigational.</p>
<p>Lyrica® (pregabalin)</p>	<p>Lyrica® (pregabalin) may be considered medically necessary neuropathic pain, fibromyalgia or refractory partial seizures.</p> <p>Lyrica® (pregabalin) may be considered medically necessary for the treatment of Generalized Anxiety Disorder when there have been trials and failure of at least two standard anxiolytic medications*, at least one of which was an SSRI.</p> <p>*SSRI, venlafaxine, benzodiazepines, hydroxyzine</p> <p>Lyrica® (pregabalin) may be covered under the following circumstances:</p> <ul style="list-style-type: none"> • Adult patients with neuropathic pain who have failed trials of gabapentin AND a tricyclic antidepressant (eg, amitriptyline) or a generic SNRI (eg, duloxetine, venlafaxine, desvenlafaxine), unless it is contraindicated



Drug	Medical Necessity
	<ul style="list-style-type: none"> • Patients with a seizure disorder will be considered on an individual case basis • Patients with fibromyalgia when they have failed a reasonable combination of pharmacologic agents, including gabapentin AND at least 2 of the following: <ul style="list-style-type: none"> ○ A tricyclic antidepressant (eg, amitriptyline) AND/OR <ul style="list-style-type: none"> ○ A generic SNRI (eg duloxetine, venlafaxine) AND/OR <ul style="list-style-type: none"> ○ Cyclobenzaprine AND/OR <ul style="list-style-type: none"> ○ Tramadol • Patients with Generalized Anxiety Disorder after a trial and failure of an SSRI (eg, citalopram, fluoxetine) plus one of the following: <ul style="list-style-type: none"> ○ Benzodiazepines (eg, alprazolam, clonazepam) ○ Venlafaxine ○ Hydroxyzine ○ Duloxetine <p>Note: Approved quantities of Lyrica® (pregabalin) should be limited to the maximum dose of 600mg per day in diabetic peripheral neuropathy, post-herpetic neuropathy and fibromyalgia patients. This limit does not apply to seizure patients.</p>

Coding

N/A

Related Information



Benefit Application

This policy is managed through the Pharmacy benefit.

This policy applies to all pharmacy benefit contracts that include Pharmacy Prior Authorization Edits.

Evidence Review

Description

Pathophysiology and Disease Burden of Neuropathy

Neuropathy is a general term for pain or other sensory disturbance resulting from a lesion or dysfunction in the nervous system. Neuropathic pain may be associated with abnormal sensations (dysesthesia) which occur without external stimuli and allodynia, abnormal sensations occurring in response to stimuli. Neuropathic pain may be continuous or episodic. Patients often describe neuropathic pain in terms of familiar sensations such as electric shock, burning or knifing pain. Sensations of coldness, "pins and needles", numbness and itching may also be present, and allodynia may result from normal stimuli, such as bedclothes touching or rubbing the patient's skin.

A general population-based survey in the U.K. published in 2006 estimated neuropathic pain prevalence to be 8%. Neuropathic pain may result from disorders of the peripheral nervous system or the central nervous system and is common in such conditions as stroke, spinal cord injury, multiple sclerosis, diabetes, HIV and cancer, where it may be caused by the tumor compressing nerves, by pathologic fractures in patients with bone metastases or by many of the cytotoxic chemotherapeutic agents employed in cancer treatment. Neuropathic pain may be peripheral or central in origin, and it may be nociceptive (direct result of physical trauma) or nonnociceptive. Diabetic and post-herpetic neuropathy were covered in previous reviews.

Pharmacology of Duloxetine

Duloxetine is a potent inhibitor of neuronal serotonin and norepinephrine reuptake and a less potent inhibitor of dopamine reuptake. Duloxetine has no significant affinity for dopaminergic,



adrenergic, cholinergic, histaminergic, opioid, glutamate, and GABA receptors in vitro. Although the exact mechanisms of the antidepressant and central pain inhibitor action of duloxetine are unknown, they are believed to be related to the drug's potentiation of serotonergic and noradrenergic activity in the CNS.

Evidence suggests that pain reduction in response to duloxetine is independent of its antidepressant effect, and can be demonstrated even in non-depressed patients. Analysis suggests that 50-90% of the observed effect is independent of antidepressant activity.

This policy applies to the following medications:

- Lyrica® (pregabalin)
- Savella™ (milnacipran)

Rationale

Therapeutic Alternatives

Prior to the approval of duloxetine and pregabalin, patients with neuropathies were treated with a number of unapproved different medications. While some other agents have shown efficacy in controlled clinical trials the treatment of this condition has frequently been seen as unsatisfactory. One guideline exists for the treatment of neuropathic pain, but it was created prior to the introduction of duloxetine and pregabalin. The neuropathic pain guideline was drafted by members of the faculty of the Fourth International Conference on the Mechanisms and Treatment of Neuropathic Pain. Five first-line medications (gabapentin, the 5% lidocaine patch opioid analgesics, tramadol hydrochloride, and TCAs) are recommended on the basis that their efficacy have been consistently demonstrated in randomized controlled trials.

Tricyclic Antidepressants

These drugs, most specifically amitriptyline and imipramine, are serotonin and norepinephrine reuptake inhibitors (SNRI). They were the first class of drugs proven to be effective in neuropathic pain. The doses used in neuropathic pain are lower than those used for depression. They are usually initiated at 10 to 25 mg at night then titrated up every 3 to 7 days as tolerated. This class of drugs significant adverse effects has limited their usefulness in many patients. Amitriptyline is the most studied agent in this class, but efficacy seems to correlate with the SNRI profile, found mostly in the tertiary amine compounds.



Gabapentin

Gabapentin, an amino acid structurally related to GABA, has been shown in clinical trials to significantly reduce neuropathic pain compared to placebo. Doses up to 3600mg/day were used with long titration phases of up to 3-8 weeks. Some of the studies also demonstrated improvements in sleep, mood, and quality of life scores. The mechanism of gabapentin in analgesia is not fully understood.

5% Lidocaine Patch

Lidocaine patch is a topical anesthetic that works by preventing the generation and conduction of nerve impulses. It is FDA approved for the treatment of post herpetic neuralgia and efficacy for this indication was demonstrated in two published placebo controlled trials. Patients in these studies obtained significantly greater pain relief from the lidocaine patch compared to a vehicle only placebo patch. The patches are dosed as no more than three patches on at a time for no more than 12 hours out of the day. The patch is also limited to patients whose lesions can be covered by three patches.

Opioid Analgesics

Long acting oxycodone, an opioid agonist, has been studied in both PHN and DPN. In PHN, patients on oxycodone CR up to 60mg/day had a significant reduction in pain, disability, and allodynia compared to patients in the placebo group. DPN patients on oxycodone CR up to 120mg/day obtained significantly reduced pain, improvement of daily activities and sleep. However, the value of this class of drugs in neuropathic pain patients is limited by the risk of opioid dependence.

Tramadol

Tramadol, a serotonin and norepinephrine reuptake inhibitor with a μ opioid agonist metabolite, has been shown in two trials to be effective in the treatment of DPN. In these two trials, doses up to a maximum of 400mg/day significantly reduced pain compared to placebo.

Combination therapy is generally more effective than a single agent. Anecdotally, combining an NSAID, an opioid and a pain blocking agent (antidepressant, AED, lidocaine, etc.) seems to be



the most effective strategy. When patients do not have a satisfactory response to treatment with the five first-line medications alone or in combination, several medications may be considered for second-line use. Recommendations for second-line medications are based on positive results from a single randomized controlled trial or inconsistent results from multiple randomized controlled trials. Other medications sometimes used for the treatment of neuropathic pain patients include capsaicin, clonidine, dextromethorphan, and mexiletine. Non-drug therapies (ie, massage, physical therapy, acupuncture, etc.) are also frequently employed for neuropathic pain, as well as a number of other alternative medicine approaches.

The extent to which non-allopathic treatments for neuropathy are resorted to is indicative of the failure of allopathic approaches to adequately manage this all too common problem. Neuropathy patients are often frustrating and can easily become dependent on opioid medications. A combination of two or three drugs is often the best pharmacologic way to manage these patients. Unfortunately, the appropriate combination must be empirically determined, often after repeated trial of alternatives. Referral of these patients to a multidisciplinary pain clinic may be necessary.

Cymbalta® (duloxetine)

Two short-term (12 week) Phase III, pivotal, placebo-controlled trials, and one 52-week, open-label, parallel group extension safety study provided the evidence for FDA approval for diabetic peripheral neuropathy. These unpublished studies consistently indicate that short-term, acute use of duloxetine, at doses of 60-120 mg QD, significantly decreases 24-hour average pain score, and increases the proportion of “responders” (defined as a $\geq 30\%$ reduction in baseline pain severity) compared with placebo. While a dose of 120 mg/day was shown to be safe and effective, there is no evidence that doses > 60 mg/day confer additional significant benefit, and the higher dose is less well tolerated.

For fibromyalgia, there are currently no head-to-head trials being conducted to compare duloxetine against any of the other agents recommended for treatment of FM. The three published trials comparing duloxetine versus placebo in treating FM resulted in conclusive evidence of duloxetine’s efficacy in treating FM, albeit the treatment phase for all three trials were relatively short (12 weeks, 12 weeks, and 6 months). Duloxetine, dosed at 60mg to 120mg/d, was shown to be efficacious at significantly reducing painful symptoms of FM, as well as the amount of tender points and interference with various aspects of daily life. Data from two of the three trials suggested better efficacy and improved outcomes are seen in women versus men.



Savella™ (milnacipran)

Milnacipran is an SNRI approved for fibromyalgia. Efficacy studies show milnacipran is more effective than placebo at 3 months for fibromyalgia; however, data at 6 months appears less consistent. No comparative trials with other agents for fibromyalgia are available. Elevated blood pressure, heart rate and LFTs appear to be of concern with milnacipran and use of this agent is not recommended in patients with liver dysfunction, substantial alcohol use, or uncontrolled blood pressure or heart rate.

Lyrica® (pregabalin)

Pregabalin has demonstrated modest efficacy in placebo-controlled trials in neuropathic pain patients. No head-to-head comparison studies with other drugs have been reported. The level of evidence of effectiveness in treating neuropathic pain is greatest for tricyclic antidepressants with mixed serotonin and norepinephrine reuptake inhibition (SNRIs) such as amitriptyline. Pregabalin may be of benefit to a subset of complex partial seizure patients who are refractory to standard first line therapies and is approved to treat fibromyalgia.

Pregabalin is more effective than placebo for symptomatic relief of associated pain and management of symptoms associated with fibromyalgia. Patients were considered responders if they had at least a 30% decrease in pain on the Pain Visual Analog Scale (VAS). The greatest relief of pain and symptoms was seen at a dose of 450mg/day. There was no evidence of greater effect of pain scores for the 600mg daily dose than the 450mg daily dose.

Three studies examining the efficacy have been conducted. Subjects taking pregabalin had a higher percentage of people with a 30% reduction in pain and had overall improvement of symptoms compared to placebo. These results aren't all that clinically relevant. At best, the proportion of subjects experiencing at least a 30% reduction in pain score was 50% for pregabalin vs. 30% for placebo. The data show that pregabalin is statistically better than placebo, but not much better. In many cases, relevant data have been omitted, eg, baseline mean values of the endpoints that would indicate the magnitude of actual improvement with pregabalin.

A 2016 randomized, double-blind, placebo-controlled study evaluated 107 adolescents (12 – 17 years) with fibromyalgia who received pregabalin or placebo. Improvement in the primary endpoint, change from baseline in mean pain score at 15 weeks, was not statistically significant between pregabalin and placebo, with a treatment difference -0.66 (95% CI -1.51 – 0.18);



P=0.121). Of all patients with adverse events (AEs) there were 70.4% in the pregabalin arm and 64.% in the placebo arm. The study noted a post hoc analysis demonstrated there were significant differences in response between subjects from the US and those from other countries, but no explanation was provided. The most common adverse events with pregabalin were dizziness (29.6%) and nausea (22.2%), with 13.2% and 9.4% in the placebo arm. A 6-month open-label extension study with a total of 63 subjects were evaluated from the original study for additional safety information. There were 71.4% of patients who experienced one or more adverse events. The most commonly reported adverse events were dizziness (22.2%), fatigue (12.7%), headache (9.5%), and nausea/abdominal pain/upper abdominal pain (7.9%).

2010 Update

A recent update of the NICE guidelines for drug treatment of neuropathic pain as well as a review newly published in the U.S. (Dworkin, et al.) recommend amitriptyline and gabapentin as first line agents. The importance of evaluating psychosocial factors and use of cognitive behavioral therapy in management was discussed in a recent review by Turk, et al. These and other systematic reviews and expert recommendations continue to support this policy.

2011 Update

Updated to incorporate newly FDA-approved indication for Cymbalta in chronic musculoskeletal pain. No other significant updates to the literature were found.

2012 Update

No information was revealed that would prompt a change in policy.

2014 Update

Policy updated to include generic SNRI trial as a qualifier for coverage.



2015 Update

Policy updated with the addition of duloxetine as a qualifier for Generalized Anxiety Disorder.

2016 Update

A literature search was conducted between June 1, 2015 and December 6, 2016. No new information was found that would prompt a change to the existing policy criteria.

2017 Update

A literature search was conducted between July 1, 2016 and November 2, 2017. No new information was found that would prompt a change to the existing policy criteria.

References

1. Crofford L, Rowbotham MC, Mease PJ, Russell IJ, Dworkin RH, Corbin AE, Young Jr. JP, LaMoreaux LK, Martin SA, Sharma U, Pregabalin 1008-105. Pregabalin for the treatment of fibromyalgia syndrome: results of a randomized, double-blind, placebo-controlled trial. *Arthritis Rheum.* 2005; 52(4):1264-73.
2. Data on file – Pfizer Inc., New York, NY.
3. Data on file – Lilly Pharmaceuticals, Indianapolis, IN.
4. Lyrica® (pregabalin) package insert. Pfizer Inc, New York, NY. Revised June 2007.
5. The National Institute of Diabetes and Digestive and Kidney Diseases (2002) Diabetic Neuropathies: The Nerve Damage of Diabetes. NIH Publication No. 02-3185.
6. DUBY J, Campbell R, Setter S, White J, Rasmussen K. Diabetic neuropathy: an intensive review. *Am J Health Syst Pharm.* 2004;61:103-173.
7. Sumner CJ, Sheth S, Griffin JW, Cornblath DR, Polydefkis M. The spectrum of neuropathy in diabetes and impaired glucose tolerance. *Neurology.* 2003;60:108-111.
8. Schmader KE. Epidemiology and impact on quality of life of post-herpetic neuralgia and painful diabetic neuropathy. *Clin J Pain.* 2002;18:350-354.
9. Backonja MM, Serra S. Pharmacologic management part 1: better-studied neuropathic pain diseases. *Pain Medicine.* 2004;5:S28-S47.
10. Dworkin RH, Backonja MM, Rowbotham MC, Allen RR, et al. Advances in neuropathic pain: diagnosis, mechanisms, and treatment recommendations. *Arch Neurol.* 2003;60:1524-1534.



11. Wolfe F, Ross K, Anderson J, Russell IJ, Hebert L. The prevalence and characteristics of fibromyalgia in the general population. *Arthritis Rheum* 1995; 38: 19-28.
12. Chakrabarty S, Zoorob R. Fibromyalgia. *Am Fam Physician* 2007;76:247-54.
13. Berger A, Dukes E, Martin S, Edelsberg J, Oster G. Characteristics and healthcare costs of patients with fibromyalgia syndrome. *Int J Clin Pract* 2007; 61:1498-1508.
14. White LA, Birnbaum HG, Kaltenboeck A, Tang J, Mallett D, Robinson RL. Employees with fibromyalgia: medical comorbidity, healthcare costs, and work loss. *J Occup Environ Med.* 2008; 50: 13-24.
15. Goldenberg DL, Burckhardt C, Crofford L. Management of fibromyalgia syndrome. *JAMA* 2004; 292: 2388-2395.
16. Goldenberg DL. Pharmacological treatment of fibromyalgia and other chronic musculoskeletal pain. *Best Practice and Research Clinical Rheumatology* 2007; 21:499-511.
17. Cymbalta • (duloxetine hydrochloride) delayed-release capsules prescribing information. Eli Lilly and Company; Indianapolis, IN. August 2008.
18. Prescribing information for Savella™ (milnacipran). Forest Pharmaceuticals, Inc., New York, NY. January, 2009.
19. Mease PJ, Clauw DJ, Gendreau M, et al. The efficacy and safety of milnacipran for treatment of fibromyalgia. A randomized, double blind, placebo controlled trial. *J Rheumatol* 2009;36:398-409.
20. Clauw DJ, Mease P, Palmer RH, Gendreau RM and Wang Y. Milnacipran for the treatment of fibromyalgia in adults: a 15 week, multicenter, randomized, double blind, placebo controlled, multiple dose clinical trial. *Clin Ther* 2008;30(11):1988-2004.
21. Clauw DJ, Palmer RH, Thacker K, et al. Milnacipran efficacy in the treatment of fibromyalgia syndrome: a 15-week, randomized, double blind, placebo-controlled trial. Poster presented at the American College of Rheumatology Annual Scientific Meeting, Boston, Massachusetts, November 6-11, 2007.
22. Gendreau RM, Thorn MD, Gendreau JF, et al. Efficacy of milnacipran in patients with fibromyalgia. *J Rheumatol* 2005;32:1975-1985.
23. Tan T, et al.; Guideline Development Group, Pharmacological management of neuropathic pain in non-specialist settings: summary of NICE guidance. *BMJ* 2010;340:c1079.
24. Turk DC, Audette J, Levy RM, et al. Assessment and treatment of psychosocial comorbidities in patients with neuropathic pain. *Mayo Clin Proc.* 2010 Mar;85(3 Suppl):S42-50.
25. Dworkin RH, O'Connor AB, Audette J, et al. Recommendations for the pharmacological management of neuropathic pain: an overview and literature update. *Mayo Clin Proc.* 2010 Mar;85(3 Suppl):S3-14.
26. Malemud CJ. Focus on pain mechanisms and pharmacotherapy in the treatment of fibromyalgia syndrome. *Clin Exp Rheumatol.* 2009 Sep-Oct;27(5 Suppl 56):S86-91.
27. Arnold LM, Schikler KN, Bateman L, et al. Safety and efficacy of pregabalin in adolescents with fibromyalgia: a randomized, double-blind, placebo-controlled trial and a 6-month open-label extension study. *Pediatr Rheumatol Online J.* 2016;14:46.

History

Date	Comments
12/13/05	Add to Prescription Drug Section - New Policy—effective January 1, 2006.
08/08/06	Replace Policy - Policy reviewed with literature search by Pharmacy and Therapeutic



Date	Comments
	Committee on July 25, 2006. Policy statement updated with exenatide and thiazolidinediones added as medically necessary; Policy Guidelines and Rationale sections updated; references added.
05/08/07	Replace Policy - Policy statement for exenatide updated with additional criteria; Policy Guidelines updated to reflect addition to policy statement. Reviewed by P&T on March 27, 2007.
06/12/07	Replace Policy - Policy statement on coverage criteria for exenatide (Byetta®), sitagliptin and esomeprazole (Nexium®) expanded; medically necessary indications for 5HT3 antagonists, Actiq® and Fentora™ added to policy statement. Policy Guidelines updated and Rationale updated; references added
12/11/07	Replace Policy - Policy reviewed with literature search by Pharmacy and Therapeutic Committee on May 15, 2007. Policy statement updated to include Pregabalin as either medically necessary or investigational under the criteria. Acyclovir, famciclovir and valacyclovir as medically necessary under criteria. References added.
04/08/08	Replace Policy - Policy updated with literature search by Pharmacy. Policy statement was updated to include fibromyalgia as a medically necessary indication under Pregabalin. References added.
12/16/08	Replace Policy - Policy updated with literature search by Pharmacy. Policy statement updated to include the use of leukotriene modifiers for the treatment of allergic rhinitis refractory to nasal corticosteroids under the medically necessary indication.
02/10/09	NEW PR Policy PR.5.01.521 - Policy updated with literature search by Pharmacy. New PR policy. Medically Necessary and Investigational statements added. Policy split from PR.5.01.605
07/14/09	Replace Policy - Policy updated with literature search by Pharmacy. Policy statement updated to include milnacipran (Savella) for the treatment of fibromyalgia under the medically necessary indication. References added.
08/11/09	Minor update to Policy Guidelines section - Added "agents" after pharmacologic for all 3 drugs in the policy guidelines section.
09/15/09	Minor updates - Corrected spelling errors, no other changes.
06/08/10	Minor update to Policy guidelines section - Policy updated with literature search. Removed ": may be approved after a three month trial" from the policy guidelines for each drug. Added references.
05/10/11	Replace Policy - Policy updated with literature review; newly FDA-approved indication for Cymbalta in chronic musculoskeletal pain added to policy statements. No other changes.
06/26/12	Replace policy. Policy updated with literature review; no change in policy statements.
11/13/12	Replace policy. Policy Guidelines section updated with updated to the labeling on Lyrica, which now includes patients with post-herpetic neuropathy or neuropathic pain



Date	Comments
	resulting from spinal cord injury.
11/26/12	Update Related Policies. Add 5.01.529.
02/11/13	Replace policy. Minor update to policy statement for duloxetine; clarification added to the medically necessary labeled indication for chronic musculoskeletal pain due to chronic osteoarthritis pain and chronic low back pain (previously this stated "including" versus "due to"). The Policy Guidelines were updated to align with this change.
07/08/13	Minor Update – Clarification was added to the policy that it is managed through the member's pharmacy benefit; this is now listed in the header and within the coding section.
12/06/13	Update Related Policies. Change title for 5.01.520.
03/17/14	Replace policy. Policy updated to include generic SNRI trial as a qualifier for coverage.
04/14/14	Interim update. Policy updated with the addition of pregabalin (Lyrica®) as medically necessary for the treatment of Generalized Anxiety Disorder when there have been trials and failure of at least two standard anxiolytic medications. Related policy 5.01.601 replaced with 5.01.550.
09/08/14	Interim update. Policy updated within the Policy Guidelines section only: indication for Pregabalin (Lyrica®) changed to patients with neuropathic pain, with reference of root cause of the neuropathy or neuropathic pain removed, when criteria are met.
03/20/15	Update Related Policies. Change title to 5.01.550.
07/14/15	Annual Review. Added duloxetine as a qualifier for Generalized Anxiety Disorder.
01/01/17	Annual Review, approved December 13, 2016. No new information was found that would prompt a change to the existing policy criteria. Minor grammatical corrections were made to the reference section.
12/01/17	Annual Review, approved November 21, 2017. Clarified criteria for Lyrica®. Added a reference.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). ©2017 Premera All Rights Reserved.

Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.



Discrimination is Against the Law

Premera Blue Cross complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex. Premera does not exclude people or treat them differently because of race, color, national origin, age, disability or sex.

Premera:

- Provides free aids and services to people with disabilities to communicate effectively with us, such as:
 - Qualified sign language interpreters
 - Written information in other formats (large print, audio, accessible electronic formats, other formats)
- Provides free language services to people whose primary language is not English, such as:
 - Qualified interpreters
 - Information written in other languages

If you need these services, contact the Civil Rights Coordinator.

If you believe that Premera has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, you can file a grievance with:

Civil Rights Coordinator - Complaints and Appeals
PO Box 91102, Seattle, WA 98111
Toll free 855-332-4535, Fax 425-918-5592, TTY 800-842-5357
Email AppealsDepartmentInquiries@Premera.com

You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, the Civil Rights Coordinator is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at <https://ocrportal.hhs.gov/ocr/portal/lobby.jsf>, or by mail or phone at: U.S. Department of Health and Human Services
200 Independence Avenue SW, Room 509F, HHH Building
Washington, D.C. 20201, 1-800-368-1019, 800-537-7697 (TDD)
Complaint forms are available at <http://www.hhs.gov/ocr/office/file/index.html>.

Getting Help in Other Languages

This Notice has Important Information. This notice may have important information about your application or coverage through Premera Blue Cross. There may be key dates in this notice. You may need to take action by certain deadlines to keep your health coverage or help with costs. You have the right to get this information and help in your language at no cost. Call 800-722-1471 (TTY: 800-842-5357).

አማርኛ (Amharic):

ይህ ማስታወቂያ አስፈላጊ መረጃ ይዟል። ይህ ማስታወቂያ ስለ ማመልከቻዎ ወይም የ Premera Blue Cross ሽፋን አስፈላጊ መረጃ ሊኖረው ይችላል። በዚህ ማስታወቂያ ውስጥ ቁልፍ ቀዳሾች ሊኖሩ ይችላሉ። የጤና ሽፋንዎን ለመጠበቅና በአስፋፈል እርዳታ ለማግኘት በተውሰኑ የጊዜ ገደቦች እርምጃ መውሰድ ይገባዎት ይሆናል። ይህን መረጃ እንዲያገኙ እና የለምንም ክፍያ በቋንቋዎ እርዳታ እንዲያገኙ መሰታ አለዎት። በስልክ ቁጥር 800-722-1471 (TTY: 800-842-5357) ይደውሉ።

العربية (Arabic):

يحتوي هذا الإشعار على معلومات هامة. قد يحتوي هذا الإشعار على معلومات مهمة بخصوص طلبك أو التغطية التي تزيد الحصول عليها من خلال Premera Blue Cross. قد تكون هناك تواريخ مهمة في هذا الإشعار. وقد تحتاج لاتخاذ إجراء في تاريخ معينه للحفاظ على تغطيتك الصحية أو المساعدة في دفع التكاليف. يحق لك الحصول على هذه المعلومات والمساعدة بلغتك دون تكبد أية تكلفة. اتصل بـ 800-722-1471 (TTY: 800-842-5357)

中文 (Chinese):

本通知有重要的訊息。本通知可能有關於您透過 Premera Blue Cross 提交的申請或保險的重要訊息。本通知內可能有重要日期。您可能需要在截止日期之前採取行動，以保留您的健康保險或者費用補貼。您有權利免費以您的母語得到本訊息和幫助。請撥電話 800-722-1471 (TTY: 800-842-5357)。

Oromoo (Cushite):

Beeksisni kun odeeffannoo barbaachisaa qaba. Beeksisti kun sagantaa yookan karaa Premera Blue Cross tiin tajaajila keessan ilaalchisee odeeffannoo barbaachisaa qabaachuu danda'a. Guyyaawwan murteessaa ta'an beeksisa kana keessatti ilaalaa. Tarii kaffaltiidhaan deeggaramuuf yookan tajaajila fayyaa keessaniif guyyaa dhumaa irratti wanti raawwattan jiraachuu danda'a. Kaffaltii irraa bilisa haala ta'een afaan keessaniin odeeffannoo argachuu fi deeggarsa argachuuf mirga ni qabaattu. Lakkoofsa bilbilaa 800-722-1471 (TTY: 800-842-5357) tii bilbilaa.

Français (French):

Cet avis a d'importantes informations. Cet avis peut avoir d'importantes informations sur votre demande ou la couverture par l'intermédiaire de Premera Blue Cross. Le présent avis peut contenir des dates clés. Vous devez peut-être prendre des mesures par certains délais pour maintenir votre couverture de santé ou d'aide avec les coûts. Vous avez le droit d'obtenir cette information et de l'aide dans votre langue à aucun coût. Appelez le 800-722-1471 (TTY: 800-842-5357).

Kreyòl ayisyen (Creole):

Avi sila a gen Enfòmasyon Enpòtan ladann. Avi sila a kapab genyen enfòmasyon enpòtan konsènan aplikasyon w lan oswa konsènan kouvèti asirans lan atravè Premera Blue Cross. Kapab genyen dat ki enpòtan nan avi sila a. Ou ka gen pou pran kèk aksyon avan sèten dat limit pou ka kenbe kouvèti asirans sante w la oswa pou yo ka ede w avèk depans yo. Se dwa w pou resewva enfòmasyon sa a ak asistans nan lang ou pale a, san ou pa gen pou peye pou sa. Rele nan 800-722-1471 (TTY: 800-842-5357).

Deutsche (German):

Diese Benachrichtigung enthält wichtige Informationen. Diese Benachrichtigung enthält unter Umständen wichtige Informationen bezüglich Ihres Antrags auf Krankenversicherungsschutz durch Premera Blue Cross. Suchen Sie nach eventuellen wichtigen Terminen in dieser Benachrichtigung. Sie könnten bis zu bestimmten Stichtagen handeln müssen, um Ihren Krankenversicherungsschutz oder Hilfe mit den Kosten zu behalten. Sie haben das Recht, kostenlose Hilfe und Informationen in Ihrer Sprache zu erhalten. Rufen Sie an unter 800-722-1471 (TTY: 800-842-5357).

Hmoob (Hmong):

Tsawb ntawv tshaj xo no muaj cov ntshiab lus tseem ceeb. Tej zaum tsawb ntawv tshaj xo no muaj cov ntshiab lus tseem ceeb txog koj daim ntawv thov kev pab los yog koj qhov kev pab cuam hnuv ntawm Premera Blue Cross. Tej zaum muaj cov hnuv tseem ceeb uas sau rau hauv daim ntawv no. Tej zaum koj kuj yuav tau ua qee yam uas pab kom koj ua tsis pub dhau cov caij nyoog uas teev tseg rau hauv daim ntawv no mas koj thiaj yuav tau txais kev pab cuam kho mob los yog kev pab them tej nqi kho mob ntawd. Koj muaj cai kom lawv muab cov ntshiab lus no uas tau muab sau ua koj hom lus pub dawb rau koj. Hu rau 800-722-1471 (TTY: 800-842-5357).

Iloko (Ilocano):

Daytoy a Pakdaar ket naglaon iti Napateg nga Impormasion. Daytoy a pakdaar mabalin nga adda ket naglaon iti napateg nga impormasion maipanggep iti aplikasyonyo wenna coverage babaen iti Premera Blue Cross. Daytoy ket mabalin dagiti importante a petsa iti daytoy a pakdaar. Mabalin nga adda rumbeng nga aramidenyo nga addang sakbay dagiti partikular a naituding nga aldaw tapno mapagtalinaedyo ti coverage ti salun-ato wenna tulong kadagiti gastos. Adda karbenganyo a mangala iti daytoy nga impormasion ken tulong iti bukodyo a pagsasao nga awan ti bayadanyo. Tumawag iti numero nga 800-722-1471 (TTY: 800-842-5357).

Italiano (Italian):

Questo avviso contiene informazioni importanti. Questo avviso può contenere informazioni importanti sulla tua domanda o copertura attraverso Premera Blue Cross. Potrebbero esserci date chiave in questo avviso. Potrebbe essere necessario un tuo intervento entro una scadenza determinata per consentirti di mantenere la tua copertura o sovvenzione. Hai il diritto di ottenere queste informazioni e assistenza nella tua lingua gratuitamente. Chiama 800-722-1471 (TTY: 800-842-5357).

日本語 (Japanese):

この通知には重要な情報が含まれています。この通知には、Premera Blue Cross の申請または補償範囲に関する重要な情報が含まれている場合があります。この通知に記載されている可能性がある重要な日付をご確認ください。健康保険や有料サポートを維持するには、特定の期日までに行動を取らなければならない場合があります。ご希望の言語による情報とサポートが無料で提供されます。800-722-1471 (TTY: 800-842-5357)までお電話ください。

한국어 (Korean):

본 통지서에는 중요한 정보가 들어 있습니다. 즉 이 통지서는 귀하의 신청에 관하여 그리고 Premera Blue Cross 를 통한 커버리지에 관한 정보를 포함하고 있을 수 있습니다. 본 통지서에는 핵심이 되는 날짜들이 있을 수 있습니다. 귀하의 건강 커버리지를 계속 유지하거나 비용을 절감하기 위해서 일정한 마감일까지 조치를 취해야 할 필요가 있을 수 있습니다. 귀하의 이러한 정보와 도움을 귀하의 언어로 비용 부담없이 얻을 수 있는 권리가 있습니다. 800-722-1471 (TTY: 800-842-5357) 로 전화하십시오.

ລາວ (Lao):

ແຈ້ງການນີ້ມີຂໍ້ມູນສໍາຄັນ. ແຈ້ງການນີ້ອາດຈະມີຂໍ້ມູນສໍາຄັນກ່ຽວກັບຄໍາຮ້ອງສະໝັກ ຫຼື ຄວາມຄົມຄອງປະກັນໄພຂອງທ່ານຜ່ານ Premera Blue Cross. ອາດຈະມີວັນທີ່ສໍາຄັນໃນແຈ້ງການນີ້. ທ່ານອາດຈະຈຳເປັນຕ້ອງດໍາເນີນການຕາມກຳນົດ ເວລາສະເພາະເພື່ອຮັກສາຄວາມຄົມຄອງປະກັນສະພາບ ຫຼື ຄວາມຊ່ວຍເຫຼືອເວັ້ນເວີ້ ຄ່າໃຊ້ຈ່າຍຂອງທ່ານໄດ້. ທ່ານມີສິດໄດ້ຮັບຂໍ້ມູນນີ້ ແລະ ຄວາມຊ່ວຍເຫຼືອເປັນພາສາຂອງທ່ານໂດຍບໍ່ເສຍຄ່າ. ໃຫ້ໃບທາ 800-722-1471 (TTY: 800-842-5357).

ភាសាខ្មែរ (Khmer):

សេចក្តីជូនដំណឹងនេះមានព័ត៌មានយ៉ាងសំខាន់។ សេចក្តីជូនដំណឹងនេះប្រហែលជាមានព័ត៌មានយ៉ាងសំខាន់អំពីទម្រង់បែបបទ ឬការរៀបចំរបស់អ្នកតាមរយៈ Premera Blue Cross ។ ប្រហែលជាមាន កាលបរិច្ឆេទសំខាន់នៅក្នុងសេចក្តីជូនដំណឹងនេះ។ អ្នកប្រហែលជាត្រូវការបញ្ជាក់សមត្ថភាព ដល់កិច្ចការផ្ទៃក្នុងដូចជា ធានា ដើម្បីនឹងរក្សាទុកការធានារ៉ាប់រងអនាគតរបស់អ្នក ឬប្រាក់ជំនួយចេញថ្លៃ។ អ្នកមានសិទ្ធិទទួលបានព័ត៌មាននេះ និងជំនួយនៅក្នុងភាសារបស់អ្នកដោយមិនអស់លុយឡើយ។ សូមទូរស័ព្ទ 800-722-1471 (TTY: 800-842-5357)។

ਪੰਜਾਬੀ (Punjabi):

ਇਸ ਨੋਟਿਸ ਵਿਚ ਖਾਸ ਜਾਣਕਾਰੀ ਹੈ. ਇਸ ਨੋਟਿਸ ਵਿਚ Premera Blue Cross ਵਲੋਂ ਤੁਹਾਡੀ ਕਵਰੇਜ ਅਤੇ ਅਰਜੀ ਬਾਰੇ ਮਹੱਤਵਪੂਰਨ ਜਾਣਕਾਰੀ ਹੋ ਸਕਦੀ ਹੈ . ਇਸ ਨੋਟਿਸ ਨਵ ਖਾਸ ਤਾਰੀਖਾਂ ਹੋ ਸਕਦੀਆਂ ਹਨ. ਜੇਕਰ ਤੁਸੀਂ ਜਸਰਤ ਕਵਰੇਜ ਰਿੱਖਣੀ ਹੋਵੇ ਜਾਂ ਓਸ ਦੀ ਲਾਗਤ ਜਵਿੱਚ ਮਦਦ ਦੇ ਇਛੁੱਕ ਹੋ ਤਾਂ ਤੁਹਾਨੂੰ ਅੰਤਮ ਤਾਰੀਖ ਤੋਂ ਪਹਿਲਾਂ ਢੁੱਝ ਖਾਸ ਕਦਮ ਚੁੱਕਣ ਦੀ ਲੋੜ ਹੋ ਸਕਦੀ ਹੈ ,ਤੁਹਾਨੂੰ ਮੁਫਤ ਵਿੱਚ ਤੋਂ ਅਪਣੀ ਭਾਸ਼ਾ ਵਿੱਚ ਜਾਣਕਾਰੀ ਅਤੇ ਮਦਦ ਪ੍ਰਾਪਤ ਕਰਨ ਦਾ ਅਧਿਕਾਰ ਹੈ ,ਕਾਲ 800-722-1471 (TTY: 800-842-5357).

فارسی (Farsi):

این اعلامیه حاوی اطلاعات مهم میباشد. این اعلامیه ممکن است حاوی اطلاعات مهم درباره فرم تقاضا و یا پوشش بیمه ای شما از طریق Premera Blue Cross باشد. به تاریخ های مهم در این اعلامیه توجه نمایید. شما ممکن است برای حفظ پوشش بیمه تان یا کمک در پرداخت هزینه های درمانی تان، به تاریخ های مشخصی برای انجام کارهای خاصی احتیاج داشته باشید. شما حق این را دارید که این اطلاعات و کمک را به زبان خود به طور رایگان دریافت نمایید. برای کسب اطلاعات با شماره 800-722-1471 (کلیران TTY تماس باشماره 800-842-5357) تماس برقرار نمایید.

Polskie (Polish):

To ogłoszenie może zawierać ważne informacje. To ogłoszenie może zawierać ważne informacje odnośnie Państwa wniosku lub zakresu świadczeń poprzez Premera Blue Cross. Prosimy zwrócić uwagę na kluczowe daty, które mogą być zawarte w tym ogłoszeniu aby nie przekroczyć terminów w przypadku utrzymania polisy ubezpieczeniowej lub pomocy związanej z kosztami. Macie Państwo prawo do bezpłatnej informacji we własnym języku. Zadzwońcie pod 800-722-1471 (TTY: 800-842-5357).

Português (Portuguese):

Este aviso contém informações importantes. Este aviso poderá conter informações importantes a respeito de sua aplicação ou cobertura por meio do Premera Blue Cross. Poderão existir datas importantes neste aviso. Talvez seja necessário que você tome providências dentro de determinados prazos para manter sua cobertura de saúde ou ajuda de custos. Você tem o direito de obter esta informação e ajuda em seu idioma e sem custos. Ligue para 800-722-1471 (TTY: 800-842-5357).

Română (Romanian):

Prezenta notificare conține informații importante. Această notificare poate conține informații importante privind cererea sau acoperirea asigurării dumneavoastră de sănătate prin Premera Blue Cross. Pot exista date cheie în această notificare. Este posibil să fie nevoie să acționați până la anumite termene limită pentru a vă menține acoperirea asigurării de sănătate sau asistența provizorie la costuri. Aveți dreptul de a obține gratuit aceste informații și ajutor în limba dumneavoastră. Sunați la 800-722-1471 (TTY: 800-842-5357).

Русский (Russian):

Настоящее уведомление содержит важную информацию. Это уведомление может содержать важную информацию о вашем заявлении или страховом покрытии через Premera Blue Cross. В настоящем уведомлении могут быть указаны ключевые даты. Вам, возможно, потребуется принять меры к определенным предельным срокам для сохранения страхового покрытия или помощи с расходами. Вы имеете право на бесплатное получение этой информации и помощь на вашем языке. Звоните по телефону 800-722-1471 (TTY: 800-842-5357).

Fa'asamoa (Samoan):

Atonu ua iai i lenei fa'asilasilaga ni fa'amatalaga e sili ona taua e tatau ona e malamalama i ai. O lenei fa'asilasilaga o se fesoasoani e fa'amatala atili i ai i le tulaga o le polokalame, Premera Blue Cross, ua e tau fia maua atu i ai. Fa'amolemole, ia e iloilo fa'alelei i aso fa'apitoa olo'o iai i lenei fa'asilasilaga taua. Masalo o le'a iai ni feau e tatau ona e faia ao le'i aulia le aso ua ta'ua i lenei fa'asilasilaga ina ia e iai pea ma maua fesoasoani mai ai i le polokalame a le Malo olo'o e iai i ai. Olo'o iai iate oe le aia tatau e maua atu i lenei fa'asilasilaga ma lenei fa'matalaga i legagana e te malamalama i ai aunoa ma se togiga tupe. Vili atu i le telefoni 800-722-1471 (TTY: 800-842-5357).

Español (Spanish):

Este Aviso contiene información importante. Es posible que este aviso contenga información importante acerca de su solicitud o cobertura a través de Premera Blue Cross. Es posible que haya fechas clave en este aviso. Es posible que deba tomar alguna medida antes de determinadas fechas para mantener su cobertura médica o ayuda con los costos. Usted tiene derecho a recibir esta información y ayuda en su idioma sin costo alguno. Llame al 800-722-1471 (TTY: 800-842-5357).

Tagalog (Tagalog):

Ang Paunawa na ito ay naglalaman ng mahalagang impormasyon tungkol sa iyong aplikasyon o pagsakop sa pamamagitan ng Premera Blue Cross. Maaaring may mga mahalagang petsa dito sa paunawa. Maaring mangailangan ka na magsagawa ng hakbang sa ilang mga itinakdang panahon upang mapanatili ang iyong pagsakop sa kalusugan o tulong na walang gastos. May karapatan ka na makakuha ng ganiitong impormasyon at tulong sa iyong wika ng walang gastos. Tumawag sa 800-722-1471 (TTY: 800-842-5357).

ไทย (Thai):

ประกาศนี้มีข้อมูลสำคัญ ประกาศนี้อาจมีข้อมูลที่สำคัญเกี่ยวกับกาการสมัครหรือขอบเขตประกันสุขภาพของคุณผ่าน Premera Blue Cross และอาจมีกำหนดการในประกาศนี้ คุณอาจจะต้องดำเนินการภายในกำหนดระยะเวลาที่แน่นอนเพื่อจะรักษาการประกันสุขภาพของคุณหรือการช่วยเหลือที่มีค่าใช้จ่าย คุณมีสิทธิที่จะได้รับข้อมูลและความช่วยเหลือในภาษาของคุณโดยไม่มีค่าใช้จ่าย โทร 800-722-1471 (TTY: 800-842-5357)

Український (Ukrainian):

Це повідомлення містить важливу інформацію. Це повідомлення може містити важливу інформацію про Ваше звернення щодо страховального покриття через Premera Blue Cross. Зверніть увагу на ключові дати, які можуть бути вказані у цьому повідомленні. Існує імовірність того, що Вам треба буде здійснити певні кроки у конкретні кінцеві строки для того, щоб зберегти Ваше медичне страхування або отримати фінансову допомогу. У Вас є право на отримання цієї інформації та допомоги безкоштовно на Вашій рідній мові. Дзвоніть за номером телефону 800-722-1471 (TTY: 800-842-5357).

Tiếng Việt (Vietnamese):

Thông báo này cung cấp thông tin quan trọng. Thông báo này có thông tin quan trọng về đơn xin tham gia hoặc hợp đồng bảo hiểm của quý vị qua chương trình Premera Blue Cross. Xin xem ngày quan trọng trong thông báo này. Quý vị có thể phải thực hiện theo thông báo đúng trong thời hạn để duy trì bảo hiểm sức khỏe hoặc được trợ giúp thêm về chi phí. Quý vị có quyền được biết thông tin này và được trợ giúp bằng ngôn ngữ của mình miễn phí. Xin gọi số 800-722-1471 (TTY: 800-842-5357).