Lyrica® (pregabalin)
Schedule V Controlled Substance

Indications:
"Lyrica is indicated for: management of neuropathic pain associated with diabetic peripheral neuropathy, management of postherpetic neuralgia, adjunctive therapy for adult patients with partial onset seizures, management of fibromyalgia, management of neuropathic pain associated with spinal cord injury."[1]

Dosage Form/Strength:

•Capsules: 25 mg, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 225 mg, and 300 mg.
•Oral Solution: 20 mg/mL

Criteria for Approval: [1, 2, 3, 4]

- Patient has been using Lyrica with benefit, and the request is for continuation of care;
  OR
  - The patient has one of the following diagnoses:
    - Postherpetic neuralgia (PHN)
    - Fibromyalgia
    - Adjunctive therapy for adult patients with partial onset seizures
    - Neuropathic pain associated with diabetic peripheral neuropathy (DPN)
    - Neuropathic pain associated with spinal cord injury
    - Palliative care for cancer pain; **AND**,
  - The patient meets all of the criteria listed in Table 1 for his/her diagnosis

Table 1: Criteria for Approval for Each Diagnosis[1, 2, 3, 4]		
Postherpetic neuralgia (PHN)	The patient has had a well-documented intolerance, hypersensitivity, contraindication, or insufficient response (despite an adequate trial at maximally tolerated dose) to gabapentin; **AND**	o The patient has tried and failed at least one of the following: OR o Has a contraindication to ALL of the following: ▪ Tricyclic antidepressants, capsaicin cream, lidocaine patch.
Fibromyalgia	The patient has had a well-documented intolerance, hypersensitivity, contraindication, or insufficient response (despite an adequate trial at maximally tolerated dose) to gabapentin; **AND**	o The patient has tried at least one other medication (other than gabapentin) ▪ Labeled for treatment of fibromyalgia, OR ▪ Has published clinical evidence to support the safe and effective use for the diagnosis of fibromyalgia. Clinical evidence must be submitted.
Adjunctive therapy for adult patients with partial onset seizures	The patient is concurrently taking at least one other antiepileptic drug, with insufficient response at maximally tolerated dose	
Neuropathic pain associated with diabetic peripheral neuropathy (DPN)	The patient has had a well-documented intolerance, hypersensitivity, contraindication, or insufficient response (despite an adequate trial at maximally tolerated dose) to gabapentin; **AND**	o The patient has tried and failed at least one of the following: OR o Has a contraindication to ALL of the following: ▪ Tricyclic antidepressants, an opioid, SNRI antidepressants, antiepileptic drugs (carbamazepine, phenytoin, or valproate)
Neuropathic pain associated with spinal cord injury	The patient has had a well-documented intolerance, hypersensitivity, contraindication, or insufficient response (despite an adequate trial at maximally tolerated dose) to gabapentin	
Palliative care for cancer pain	The patient has had a well-documented intolerance, hypersensitivity, contraindication, or insufficient response (despite an adequate trial at maximally tolerated dose) to gabapentin	

Criteria for Reauthorization Approval:

1. Patient meets all of the criteria for the initial authorization; **AND**,
2. There is documented evidence of a positive clinical response to Lyrica therapy.

Criteria for Denial:

- Any diagnosis other than the diagnoses listed in Table 2
  - Unless the patient has already been using Lyrica with benefit for a diagnosis other than those listed above, and the request is for continuation of care; **OR,**
- Concomitant use of Lyrica and gabapentin; **OR**
- The patient meets a denial criterion listed in Table 2 for his/her diagnosis

Table 2: Criteria for Denial for Each Diagnosis		
Postherpetic neuralgia (PHN)	Patient has not had a well-documented intolerance, hypersensitivity, contraindication, or insufficient response to gabapentin; **OR**	o The patient has not tried and failed at least one of the following: OR o Does not have a contraindication to ALL of the following: ▪ Tricyclic antidepressants, capsaicin cream, lidocaine patch.
Fibromyalgia	Patient has not had a well-documented intolerance, hypersensitivity, contraindication, or insufficient response to gabapentin; **OR**	o The patient has not tried at least one other medication (other than gabapentin) ▪ Labeled for treatment of fibromyalgia, OR ▪ Has published clinical evidence to support the safe and effective use for fibromyalgia (OR clinical evidence was not submitted).
Adjunctive therapy for adult patients with partial onset seizures	Patient is not concurrently taking at least one other antiepileptic drug, with insufficient response at maximally tolerated dose	
Neuropathic pain associated with diabetic peripheral neuropathy (DPN)	Patient has not had a well-documented intolerance, hypersensitivity, contraindication, or insufficient response to gabapentin; **OR**	o The patient has not tried and failed at least one of the following: OR o The patient does not have a contraindication to ALL of the following: ▪ Tricyclic antidepressants, an opioid, SNRI antidepressants, antiepileptic drugs (carbamazepine, phenytoin, or valproate)
Neuropathic pain associated with spinal cord injury	Patient has not had a well-documented intolerance, hypersensitivity, contraindication, or insufficient response to gabapentin	
Palliative care for cancer pain	Patient has not had a well-documented intolerance, hypersensitivity, contraindication, or insufficient response to gabapentin	

Criteria for Reauthorization Denial:

1. Patient does not meet all of the criteria for the initial authorization; **OR**
2. There is no documented evidence of a positive clinical response to Lyrica therapy.

Length of Authorization – Initial coverage:

- May be authorized for up to 6 months

Length of Authorization – Reauthorization:

- May be reauthorized for up to 1 year

Quantity Limit:

- Lyrica 50mg, 75 mg, 100 mg, 150 mg, 200mg capsules: Limit is 3 capsules per day
- Lyrica 225mg, 300mg capsules: Limit is 2 capsules per day
- Lyrica 20mg/mL solution: Limit is 30mL/day

Mechanism of Action:

"Lyrica (pregabalin) binds with high affinity to the alpha2-delta site (an auxiliary subunit of voltage-gated calcium channels) in central nervous system tissues. Although the mechanism of action of pregabalin has not been fully elucidated, results with genetically modified mice and with compounds structurally related to pregabalin (such as gabapentin) suggest that binding to the alpha2-delta subunit may be involved in pregabalin's anti-nociceptive and antiseizure effects in animals. In animal models of nerve damage, pregabalin has been shown to reduce calcium-dependent release of pro-nociceptive neurotransmitters in the spinal cord, possibly by disrupting alpha2-delta containing-calcium channel trafficking and/or reducing calcium currents. Evidence from other animal models of nerve damage and persistent pain suggest the anti-nociceptive activities of pregabalin may also be mediated through interactions with descending noradrenergic and serotonergic pathways originating from the brainstem that modulate pain transmission in the spinal cord.

While pregabalin is a structural derivative of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA), it does not bind directly to GABAA, GABAB, or benzodiazepine receptors, does not augment GABAA responses in cultured neurons, does not alter rat brain GABA concentration or have acute effects on GABA uptake or degradation. However, in cultured neurons prolonged application of pregabalin increases the density of GABA transporter protein and increases the rate of functional GABA transport. Pregabalin does not block sodium channels, is not active at opiate receptors, and does not alter cyclooxygenase enzyme activity. It is inactive at serotonin and dopamine receptors and does not inhibit dopamine, serotonin, or noradrenaline reuptake." [1]

References / Footnotes:

[1]Lyrica® package insert: Pfizer, Inc. NY, NY. March 2016. http://labeling.pfizer.com/ShowLabeling.aspx?id=561#section-12.1. Accessed 4/6/2016.

[2] F. Goodman. "Criteria for nonformulary use of pregabalin." VHA Pharmacy Benefits Management Service and the Medical Advisory Panel. 2008. https://view.officeapps.live.com/op/view.aspx?src=http%3A%2F%2Fwww.pbm.va.gov%2FPBM%2Fclinic

alguidance%2Fcriteriaforuse%2FPregabalinCriteriaforNonformularyUseRev20080310.doc. Accessed 4/6/2016.

[3] van den Beuken-van Everdingen MH, de Graeff A, Jongen JL, Dijkstra D, Mostovaya I, Vissers KC. "Pharmacological Treatment of Pain in Cancer Patients: The Role of Adjuvant Analgesics, a Systematic Review." Pain Pract. 2016 May 21.

[4] Sanderson C, Quinn SJ, Agar M, Chye R, Clark K, Doogue M, Fazekas B, Lee J, Lovell MR, Rowett D, Spruyt O, Currow DC. "Pharmacovigilance in hospice/palliative care: net effect of pregabalin for neuropathic pain." BMJ Support Palliat Care. 2016 Feb 23.