



Therapeutic Class ReviewSM

Neurology – Pregabalin (Lyrica[®])

December 2007

New Product for Review:

pregabalin (Lyrica^{®*}) [Pfizer]

Dossier Provided by Manufacturer: Yes

Dossier Evaluation: 3 (all components present)

- 1 - Dossier missing significant clinical trial(s).
- 2 - Mfg. provided all relevant trials; Missing pharmacoeconomic model.
- 3 - Mfg. provided all relevant trials and information.

Executive Summary

- Pregabalin (Lyrica) is similar in structure and action to gabapentin (Neurontin[®]).
- Although pregabalin (Lyrica) is classified as an anticonvulsant, the majority of its use is in the treatment of pain.
- The FDA approved pregabalin (Lyrica) for treatment of fibromyalgia in June 2007.
 - Treatments for fibromyalgia are seen as an unmet need and receive priority review.
- Other FDA-approved uses include adjunctive treatment of partial onset seizures, neuropathic pain in diabetic peripheral neuropathy (DPN), and postherpetic neuralgia.
- Fibromyalgia pain is central in nature (disturbances in pain processing).
- Although the manufacturer promotes pregabalin (Lyrica) as the only medication approved for fibromyalgia, several generic medications have demonstrated efficacy and are endorsed in fibromyalgia practice guidelines.
 - Tricyclic antidepressants (TCAs), such as amitriptyline, or cyclobenzaprine are considered first-line options.
 - Serotonin reuptake inhibitors (e.g., fluoxetine) or tramadol (with or without acetaminophen) may also be used with or without TCAs or cyclobenzaprine.
 - **The use of gabapentin in fibromyalgia was the focus of a recently published study funded by the NIH.** ^[42] The benefit of gabapentin was similar to pregabalin (Lyrica) based on mean pain scores and proportion of patients responding to therapy.
- Although they have shown benefit in the treatment of fibromyalgia, it is not likely that manufacturers of these generic products will pursue FDA approval for this indication due to the great expense.

Evidence:

Efficacy:

Condition	Reliable evidence?	Uncertain evidence*
Partial onset seizures	√ (NNT = 3 to 6 for ≥ 50% reduction in seizure frequency over 12 weeks)	
Neuropathic pain secondary to DPN		√
Postherpetic neuralgia		√
Generalized anxiety disorder (off-label)		√
Social anxiety disorder (off-label)		√
Fibromyalgia		√
Other pain conditions (off-label)		√

* When evidence is uncertain, caution is urged when making healthcare decisions

- Of the many conditions in which pregabalin (Lyrica) has been studied, there is only reliable evidence for its use as an adjunct therapy for partial onset seizures.^[14]
 - Pregabalin (Lyrica) reduced the seizure frequency when added to an existing anticonvulsant regimen compared to placebo.
 - For every 3 to 6 patients treated with pregabalin (Lyrica) for 12 weeks, one patient will achieve a reduction in seizure frequency by 50% or more.
- There is no evidence to show that pregabalin (Lyrica) is more effective than available treatment options for any condition.
- Trials studying pregabalin (Lyrica) in the treatment of various pain conditions had very high drop-out rates, trial design that often favored pregabalin (Lyrica), and demonstrated only modest benefits in pain reduction.

Decision

Pregabalin (Lyrica) is non-preferred/non-formulary because there is no evidence that it is safer or more effective than preferred/formulary options for the treatment of fibromyalgia syndrome.

Products

Drug Products	FDA approval ^a	FDA approved indications	Usual Dose/Route	Potential Off-label Uses ^c
Serotonin/Norepinephrine Reuptake Inhibitors (SNRIs)				
duloxetine (Cymbalta [®]) ^[1]	8/2004	Major depressive disorder, Pain associated with diabetic peripheral neuropathy, and Generalized anxiety disorder	60mg po QD to BID	Pain management Stress urinary incontinence Fibromyalgia
venlafaxine (Effexor [®]) ^[2] (Effexor XR [®]) ^[3]	12/2003 10/1997	Major depressive disorder, Generalized anxiety disorder, Social anxiety disorder, and Panic disorder	75mg po BID 150mg XR po QD	Atypical facial pain, Post-mastectomy pain syndrome, Colonic sensorimotor functions, Obsessive-compulsive disorder, Diabetic peripheral neuropathy, Painful polyneuropathy ¹ , Bipolar depression, Premenstrual dysphoric disorder, Management of hot flushes, diabetic neuropathic pain ⁴¹ , fibromyalgia, migraine HA
Tricyclic Antidepressants (TCAs)				
amitriptyline ^[4]	4/1961	Depression w/ anxiety	25mg po TID	polyneuropathy, diabetic neuropathic pain
desipramine ^[4]	10/1964	Depression	150mg po daily	Attention deficit disorder, Diabetic neuropathic pain
imipramine ^[4]	5/1984	Depression Enuresis (children)	100mg po daily	Panic disorder, diabetic neuropathic pain, urinary incontinence
Antiepileptics				
carbamazepine ^[4]	3/1968	Bipolar disorder, epilepsy, trigeminal neuralgia	200mg po BID	Antidiuretic (diabetes insipidus), psychotic disorders
gabapentin ^[4]	10/1998	Epilepsy, post herpetic neuralgia	1200mg/day – 3600mg/day (divided doses TID)	diabetic neuropathic pain, migraine prophylaxis, social phobia
phenytoin ^[4]	8/1976	Generalized tonic-clonic/complex partial seizures, seizures s/p neurosurgery	100mg po TID	Antiarrhythmic, antineuralgic, seizures from eclampsia or preeclampsia, skeletal muscle relaxant
divalproex (Depakote [®]) ^[5]	3/1983	Mania associated w/ bipolar disorder, adjunctive and monotherapy for partial complex seizures, adjunctive and monotherapy for simple and complex absence seizures, migraine prophylaxis	500mg po BID - TID	Alcohol withdrawal syndrome, cluster headache, post traumatic headache, intractable hiccoughs, myoclonus, cancer-related neuropathic pain, panic disorder, schizoaffective disorder, social phobia, West syndrome
lamotrigine (Lamictal [®]) ^[6]	12/1994	Adjunctive and monotherapy for partial seizures, Bipolar disorder	100 - 200mg po BID	Migraine headache with aura, trigeminal neuralgia
levetiracetam (Keppra [®]) ^[7]	11/1999	Adjunctive therapy for partial onset seizures, or myoclonic sz; Generalized seizures (± T-C)	750 - 1500mg po BID	Manic bipolar 1 disorder, migraine prophylaxis, neuropathic pain, post-herpetic neuralgia
oxcarbazepine (Trileptal [®]) ^[8]	1/2000	Adjunctive and monotherapy for partial seizures	600mg po BID	Bipolar disorder, panic disorder, trigeminal neuralgia
pregabalin (Lyrica [®]) ^[9] (Available strengths: 25mg, 50mg, 75mg, 100mg, 150mg, 200mg, 225mg and 300mg)	12/2004	Adjunctive therapy for adult patients with partial onset seizures, pain associated with diabetic peripheral neuropathy (PDN), postherpetic neuralgia (PHN) pain, Fibromyalgia	150 - 600mg/day (divide 2-3 times/day) PDN: 100mg po TID PHN: 150-300mg/day (divide 2-3 times/day)	Generalized anxiety disorder, social anxiety disorder, fibromyalgia, other pain conditions
tiagabine (Gabitril [®]) ^[10]	9/1997	Adjunctive therapy for partial onset seizures	16 mg po BID 12 mg po QID	Painful spasms 2° to multiple sclerosis, post traumatic stress disorder, spasticity
topiramate (Topamax [®]) ^[11]	12/1996	Epilepsy, migraine	200mg po BID	Diabetic neuropathic pain ³⁷⁻³⁸
zonisamide (Zonegran [®]) ^[12]	3/2000	Adjunctive therapy for partial onset seizures	200 - 400mg po QD	Binge eating
Opioids				
tramadol ^[4]	3/1995	Moderate-severe pain	50mg po Q6hrs	Diabetic neuropathic pain ⁴²⁻⁴³
oxycodone ^[4]	10/1998	Moderate-severe pain	5mg po Q4-6 hrs	Diabetic neuropathic pain ⁴⁴⁻⁴⁵
Others				
levocarnitine ^[4]	12/1985	Carnitine deficiency	330mg po BID to TID	Diabetic neuropathic pain ⁴⁷⁻⁴⁸
capsaicin ^[4]	OTC	Arthritis pain, diabetic peripheral neuropathy, postherpetic neuralgia,	Apply thin layer 3-5x/day	Psoriasis
lidocaine topical patch (Lidoderm [®]) ^[13]	3/1999	Pain associated with post-herpetic neuralgia	Apply over affected area with up to 3 patches for 12 hours daily.	Other neuropathic pain syndromes

^a Date applies to approval date for the original brand name medication where there are now generics available.

^c As listed in © 1974 - 2007 Thomson MICROMEDEX database or as referenced.

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