

Serotonin-Norepinephrine Reuptake Inhibitors
Effective February 20, 2019

Plan	<input checked="" type="checkbox"/> MassHealth <input checked="" type="checkbox"/> Commercial/Exchange	Program Type	<input type="checkbox"/> Prior Authorization
Benefit	<input checked="" type="checkbox"/> Pharmacy Benefit <input type="checkbox"/> Medical Benefit (NLX)		<input type="checkbox"/> Quantity Limit <input checked="" type="checkbox"/> Step Therapy
Specialty Limitations	N/A		
Contact Information	Specialty Medications		
	All Plans	Phone: 866-814-5506	Fax: 866-249-6155
	Non-Specialty Medications		
	MassHealth	Phone: 877-433-7643	Fax: 866-255-7569
	Commercial	Phone: 800-294-5979	Fax: 888-836-0730
	Exchange	Phone: 855-582-2022	Fax: 855-245-2134
	Medical Specialty Medications (NLX)		
	All Plans	Phone: 844-345-2803	Fax: 844-851-0882
Exceptions	N/A		

Overview

Prescriptions that meet the initial step therapy requirements will adjudicate automatically at the point of sale. If the prescription does not meet the initial step therapy requirements, the prescription will deny with a message indicating that prior authorization (PA) is required. Refer to the criteria below and submit a PA request for the members who do not meet the initial step therapy requirements at the point of sale.

Initial Step-Therapy Requirements:

First-Line: Medications listed on first-line are covered without prior-authorization.

Second-Line: Second-line medications will pay if the member has filled first-line medications as described below or a second-line medication within the past 180 days.

Coverage Guidelines

	FIRST-LINE	SECOND-LINE
Depression	Preferred generic SSRIs [±] Preferred generic SNRIs [*]	desvenlafaxine SR tablet duloxetine (Cymbalta) Fetzima (levomilnacipran SR) capsules Khedeza (desvenlafaxine SR) tablet Pristiq (desvenlafaxine succinate SR) tablet desvenlafaxine fumarate SR tablets
Peripheral Neuropathy & Neuropathic Pain	tricyclic antidepressants gabapentin	duloxetine (Cymbalta)
Fibromyalgia	gabapentin tricyclic antidepressants cyclobenzaprine	duloxetine (Cymbalta)

	FIRST-LINE	SECOND-LINE
	Preferred generic SSRI [±] Preferred generic SNRIs [*]	
Musculoskeletal Pain	acetaminophen (APAP, Tylenol) generic NSAIDs tricyclic antidepressants cyclobenzaprine tramadol Preferred generic SSRI [±] Preferred generic SNRIs [*] opioids	duloxetine (Cymbalta)

[±]Preferred generic SSRIs: citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline

^{*}Preferred generic SNRIs: venlafaxine IR tablets, venlafaxine SR tablets, venlafaxine SR capsules

If a member does not meet the initial step therapy requirements, then approval of a second-line medication will be granted if the member meets the following criteria:

Duloxetine (Cymbalta)

Depression or Generalized Anxiety

1. Member is at risk of harm to self or others
OR
1. Member has been started and stabilized on duloxetine for at least 30 days (excluding the use of samples)
OR
1. Member has a diagnosis of depression or generalized anxiety disorder **AND**
2. Member has had a documented side effect, allergy or treatment failure with at least one of the following:
 - a. fluoxetine
 - b. paroxetine
 - c. citalopram
 - d. escitalopram
 - e. sertraline
 - f. fluvoxamine
- AND**
3. Member has had a documented side effect, allergy or treatment failure with a venlafaxine product

Peripheral Neuropathy/Neuropathic pain

1. Member has been started and stabilized on duloxetine for at least 30 days (excluding the use of samples)
OR
1. Member has a diagnosis of peripheral neuropathy/neuropathic pain **AND**
2. Member has had a documented side effect, allergy or treatment failure with at least one tricyclic antidepressant (e.g., amitriptyline, desipramine, imipramine, etc.) **AND**
3. Member has had a documented side effect, allergy or treatment failure with gabapentin

Depression and Peripheral Neuropathy/Neuropathic pain



1. Member has a diagnosis of depression AND peripheral neuropathy/neuropathic pain

Fibromyalgia

1. Member has been started and stabilized on duloxetine for at least 30 days (excluding the use of samples)
OR
1. Member has a diagnosis of fibromyalgia **AND**
2. Member has had a documented side effect, allergy or treatment failure at least one (1) agent from three different categories (total of 3 required trials):
 - a. tricyclic antidepressants (e.g., amitriptyline, desipramine, imipramine, etc.)
 - b. SSRI's (e.g., citalopram, fluoxetine, paroxetine, sertraline, etc.)
 - c. cyclobenzaprine
 - d. gabapentin**AND**
3. Member has had a documented side effect, allergy or treatment failure with a venlafaxine product

Musculoskeletal Pain (Osteoarthritis or Low Back Pain)

1. Member has been started and stabilized on duloxetine for at least 30 days (excluding the use of samples)
OR
1. Member has a diagnosis of musculoskeletal pain (osteoarthritis or low back pain) **AND**
2. Member has had a documented side effect, allergy, or treatment failure with at least two (2) preferred, generic NSAID products **AND**
3. Member has had a documented side effect, allergy or treatment failure with at least two (2) additional agents from different classes including:
 - a. tricyclic antidepressants (e.g., amitriptyline, desipramine, imipramine, etc.)
 - b. tramadol (Ultram)
 - c. cyclobenzaprine
 - d. SSRI's (e.g., citalopram, fluoxetine, paroxetine, sertraline, etc.)
 - e. SNRI's (venlafaxine IR tabs, venlafaxine SR tablets, venlafaxine SR capsules, desvenlafaxine, etc.)

Pristiq (desvenlafaxine succinate SR), Khedezla (desvenlafaxine SR), desvenlafaxine SR tablets, Fetzima (levomilnacipran) capsules, & desvenlafaxine fumarate SR tablets

1. Member is at risk of harm to self or others
OR
1. Member has been started and stabilized on the requested medication for at least 30 days (excluding the use of samples)
OR
1. Member has a diagnosis of depression **AND**
2. Member has had a documented side effect, allergy or treatment failure with at least one of the following:
 - a. fluoxetine
 - b. paroxetine



- c. citalopram
- d. escitalopram
- e. sertraline
- f. fluvoxamine

AND

- 3. Member has had a documented side effect, allergy or treatment failure with a venlafaxine product

Pharmacist note: Patients being treated with tamoxifen should not be concomitantly treated with fluoxetine, paroxetine, sertraline, etc. due to the potential decrease in plasma concentrations of the active metabolites of tamoxifen. Citalopram & fluvoxamine do not appear to have this interaction. Step therapy rules would still require a trial through venlafaxine prior to a non-preferred SNRI.

Limitations

- 1. Musculoskeletal Pain (Osteoarthritis or Low Back Pain) may be approved for up to 12 months
- 2. All other diagnosis/indication may be approved up to 36 months
- 3. The following quantity limits apply:

DESVENLAFAX TAB 100MG ER	30 tablets per month
DESVENLAFAX TAB 25MG ER	30 tablets per month
DESVENLAFAX TAB 50MG ER	30 tablets per month
DULOXETINE CAP 20MG	60 capsules per month
DULOXETINE CAP 30MG	30 capsules per month
DULOXETINE CAP 60MG	30 capsules per month
FETZIMA CAP 120MG	30 capsules per month
FETZIMA CAP 20MG	30 capsules per month
FETZIMA CAP 40MG	30 capsules per month
FETZIMA CAP 80MG	30 capsules per month
FETZIMA CAP TITRATIO	1-time fill

References

- 1. Cymbalta (duloxetine) [prescribing information]. Indianapolis, IN: Eli Lilly and Company; January 2017
- 2. Fetzima (levomilnacipran) [prescribing information]. Irvine, CA: Allergan USA Inc; December 2017
- 3. Venlafaxine hydrochloride extended-release tablets [prescribing information]. Bridgewater, NJ: Trigen Laboratories; October 2017.
- 4. Neurontin (gabapentin) [prescribing information]. New York, NY: Pfizer; February 2018
- 5. Pristiq (desvenlafaxine) [prescribing information]. Philadelphia, PA: Wyeth Pharmaceuticals; March 2018
- 6. Khedezla (desvenlafaxine) [prescribing information]. Morristown, NJ: Pernix Therapeutics, LLC; January 2017.
- 7. Cyclobenzaprine [prescribing information]. Boca Raton, FL: Virtue Rx LLC; December 2017
- 8. Amitriptyline hydrochloride [prescribing information]. Chestnut Ridge, NY: Par Pharmaceutical; August 2017.[PubMed 22376048]
- 9. Walitt B, Urrútia G, Nishishinya MB, et al. Selective serotonin reuptake inhibitors for fibromyalgia syndrome. Cochrane Database Syst Rev 2015: CD011735.

10. Aiyer R, Barkin RL, Bhatia A. Treatment of Neuropathic Pain with Venlafaxine: A Systematic Review. *Pain Med* 2017; 18:1999.
11. Nielsen S, Lintzeris N, Bruno R, et al. Benzodiazepine use among chronic pain patients prescribed opioids: associations with pain, physical and mental health, and health service utilization. *Pain Med* 2015; 16:356.
12. von Wolff A, Hölzel LP, Westphal A, et al. Selective serotonin reuptake inhibitors and tricyclic antidepressants in the acute treatment of chronic depression and dysthymia: a systematic review and meta-analysis. *J Affect Disord* 2013; 144:7.
13. Lunn MP, Hughes RA, Wiffen PJ. Duloxetine for treating painful neuropathy, chronic pain or fibromyalgia. *Cochrane Database Syst Rev* 2014: CD007115.
14. Arnold I, Rosen A, Pritchett Y, et al. A randomized double-blind placebo-controlled trial of duloxetine in treatment of women with fibromyalgia with or without major depressive disorder. *Pain* 2005; 119:5-15.
15. Wang ZY, Shi SY, Li SJ, et al. Efficacy and Safety of Duloxetine on Osteoarthritis Knee Pain: A Meta-Analysis of Randomized Controlled Trials. *Pain Med* 2015; 16:1373.
16. Sullivan M, Bentley S, Fan MY, Gardner G. A single-blind placebo run-in study of venlafaxine XR for activity-limiting osteoarthritis pain. *Pain Med.* 2009 Jul-Aug;10(5):806-12.
17. Mazza M, Mazza O, Pazzaglia C, et al. Escitalopram 20 mg versus duloxetine 60 mg for the treatment of chronic low back pain. *Expert Opin Pharmacother.*2010; 11(7):1049.
18. Skljarevski V, Desai D, Liu-Seifert H, et al. Efficacy and safety of duloxetine in patients with chronic low back pain. *Spine.* 2010; 35:E578-585.
19. Lambert M. ICSI releases guideline on chronic pain assessment and management. *Am Fam Physician.* 2010 Aug 15;82(4):434-9.

Review History

06/27/05 – Reviewed
 02/27/06 – Reviewed
 03/05/07 – Reviewed
 07/2007 – Change look-back to 360 days
 02/25/08 – Updated
 09/22/08 – Fibro
 10/23/08 – Venlafaxine SR
 11/24/08 – Pristiq
 02/23/09 – Reviewed
 02/22/10 – Updated
 07/19/10 – Gen. Effexor XR & gen venlafax tabs
 02/28/11 – Cymbalta MuscSkel pain
 02/27/12 – Updated
 02/25/13 – Updated
 06/03/13 – Venlafaxine SR caps to preferred
 01/13/14 – Khedezla & desvenlafaxine ER tabs
 04/07/14 – Feb 2014 P&T updates & Fetzima; 12/2/13 file);
 08/04/14 – Duloxetine generic
 02/23/15 – Reviewed
 02/26/18 – Reviewed
 02/20/19 – Updated

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