Pharmacy Medical Necessity Guidelines: Antidepressant Medications

Effective: February 1, 2024

Prior Authorization Required	√	Type of Review – Care Management	
Not Covered		Type of Review – Clinical Review	√
Pharmacy (RX) or Medical (MED) Benefit	RX	Department to Review	RXUM
These pharmacy medical necessity guidelines apply to the following: ☒ Tufts Health RITogether – A Rhode Island Medicaid Plan		**Fax Numbers:** RXUM: 617.673.0939	

Note: This guideline does not apply to Medicare Members (includes dual eligible Members).

OVERVIEW

The table below highlights the FDA-approved indications for non-preferred antidepressants on the Tufts Health RITogether formulary.

Generic Name	Brand Name	Major Depressive Disorder	Depression	Generalized Anxiety Disorder	Social Anxiety Disorder	Obsessive-Compulsive Disorder	Panic Disorder	Fibromyalgia	Diabetic Peripheral Neuropathic Pain	Chronic Musculoskeletal Pain	Premenstrual Dysphoric Disorder	Vasomotor Symptoms	Depression w/ Bipolar 1	Treatment-resistant Depression	Postpartum Depression
Bupropion/ dextromethrophan	Auvelity	x													
Desvenlafaxine	Pristiq	X													
Duloxetine delayed-release	Drizalma	X		X				X	X	X					
Fluoxetine Tabs	Sarafem										X				
Fluvoxamine extended-release	Luvox CR					X									
Imipramine Pamoate	Tofranil-PM		X												
Levomilnacipran	Fetzima	X													

Generic Name	Brand Name	Major Depressive Disorder	Depression	Generalized Anxiety Disorder	Social Anxiety Disorder	Obsessive-Compulsive Disorder	Panic Disorder	Fibromyalgia	Diabetic Peripheral Neuropathic Pain	Chronic Musculoskeletal Pain	Premenstrual Dysphoric Disorder	Vasomotor Symptoms	Depression w/ Bipolar 1	Treatment-resistant Depression	Postpartum Depression
Paroxetine 7.5 mg	Brisdelle											X			
Paroxetine extended-release	Paxil CR	X			X		X				X				
Protriptyline	Vivactil		X												
Selegiline Transdermal	Emsam Patch	X													
Trimipramine	Surmontil		X												
Venlafaxine extended-release tablets	Venlafaxine ER Tabs	X			X										
Vilazodone	Viibryd	X													
Vortioxetine	Trintellix	X													
Olanzapine / fluoxetine	Symbyax												X	X	
Zuranolone	Zurzuvae														x

COVERAGE GUIDELINES

The Plan may authorize coverage of a non-preferred antidepressant medication when the following criteria are met:

1. Documentation the Member is stabilized on the requested medication for a duration of at least 2 months

OR

2. The Member recently started on the requested medication in an acute care setting, residential setting, or partial hospital setting

OR

3. One of the following medication-specific criteria:

Bupropion/dextromethorphan (Auvelity)

1. The Member has had an inadequate response, adverse reaction, or contraindication to treatment with two antidepressants from two different classes, such as selective serotonin reuptake inhibitor (SSRI), a selective serotonin-norepinephrine inhibitor (SNRI), a tricyclic antidepressant (TCA), or a monoamine oxidase inhibitor (MAOI)

Desvenlafaxine

1. The Member has had an inadequate response, adverse reaction, or contraindication to treatment with venlafaxine extended-release capsules or tablets

Duloxetine delayed-release sprinkle capsules (Drizalma)

1. Documentation the member has a nasogastric tube or difficulty swallowing

OR

2. The Member meets ALL of the following:
    a) The Member has had an inadequate response, adverse reaction, or contraindication to generic duloxetine (Cymbalta)

    AND

    b) The Member meets ONE of the following:
        i. The Member meets ALL of the following:
            A) The Member has a documented diagnosis of depression or anxiety

            AND

            B) Documentation the Member has had an inadequate response, adverse reaction, or contraindication to treatment with at least two different antidepressants from two different classes, such as a selective serotonin reuptake inhibitor (SSRI), a tricyclic antidepressant (TCA), a monoamine oxidase inhibitor (MAOI), or another serotonin-norepinephrine reuptake inhibitor (SNRI) (e.g., venlafaxine or desvenlafaxine)

        OR

        ii. The Member meets ALL of the following:
            A) The Member has a documented diagnosis of diabetic neuropathic pain

            AND

            B) Documentation the Member has had an inadequate response, adverse reaction, or contraindication to treatment with at least two alternative agents for neuropathic pain (e.g. gabapentin, pregabalin, a TCA, venlafaxine, desvenlafaxine, or another anticonvulsant [carbamazepine or lamotrigine])

        OR

        iii. The Member meets ALL of the following:
            A) The Member has a documented diagnosis of musculoskeletal pain

            AND

            B) Documentation the Member has had an inadequate response, adverse reaction, or contraindication to treatment with at least three alternative therapies from at least two different therapeutic classes (e.g., analgesics, antidepressants, anticonvulsants, skeletal muscle relaxants)

        OR

        iv. The Member meets ALL of the following:
            A) The Member has a documented diagnosis of fibromyalgia

            AND

            B) The Member has had an inadequate response, adverse reaction, or contraindication to treatment with at least two generic agents, such as gabapentin, pregabalin, or antidepressant medications (tricyclic antidepressants, selective serotonin reuptake inhibitors)

Fluoxetine 10 mg, 20 mg tablets

1. Documentation from the provider that treatment with fluoxetine 10 mg or 20 mg capsules is clinically inappropriate

Fluoxetine tablets (Sarafem)

1. Documentation the Member has had an inadequate response, adverse reaction, or contraindication to treatment with two generic alternative agents for premenstrual dysphoric disorder

Fluvoxamine extended-release capsules

1. Documentation the Member has had an inadequate response, adverse reaction, or contraindication to treatment with immediate-release fluvoxamine and at least one alternative SSRI

Imipramine Pamoate

1. Documentation the Member has had an inadequate response, adverse reaction, or contraindication to treatment with imipramine hydrochloride

Levomilnacipran (Fetzima)

1. Documentation the Member has had an inadequate response, adverse reaction, or contraindication to treatment with at least two alternative generic antidepressant agents, one of which must be an SNRI (e.g., venlafaxine, desvenlafaxine, duloxetine)

Olanzapine/Fluoxetine (Symbyax)

1. Documentation the Member has been stabilized on the individual agents, olanzapine and fluoxetine

Paroxetine 7.5 mg capsules (Brisdelle)

1. Documentation the Member has had an inadequate response, adverse reaction, and contraindication to treatment with two alternative agents for vasomotor symptoms of menopause

Paroxetine extended-release tablets

1. Documentation the Member has had an inadequate response, adverse reaction, or contraindication to treatment with immediate-release paroxetine and at least one other alternative SSRI

Selegiline Transdermal (Emsam)

1. The Member meets ONE of the following:
   a) Documentation the Member has had a favorable response to an oral MAOI AND is unable to continue treatment with an oral MAOI agent

   OR

   b) Documentation the Member has had an inadequate response, adverse reaction, or contraindication to treatment with at least one alternative generic agent from at least two alternative therapeutic classes (e.g., alpha-2 antagonists, norepinephrine dopamine receptor inhibitors, SSRIs, SNRIs, TCAs)

Protriptyline and Trimipramine (Surmontil)

1. Documentation the Member has had an inadequate response, adverse reaction, or contraindication to treatment with one alternative tricyclic antidepressant (TCA)

Venlafaxine ER Tablets

1. Documentation the Member has had an inadequate response, adverse reaction, or contraindication to treatment with venlafaxine extended-release capsules

Vilazodone (Viibryd) and Vortioxetine (Trintellix)

1. Documentation the Member has had an inadequate response, adverse reaction, or contraindication to treatment with two alternative generic antidepressants from two different therapeutic classes, one of which must be an SSRI

Zuranolone (Zurzuvae)

1. The Member was recently started on zuranolone in an acute care, residential, or partial hospital setting

OR

2. The Member meets ALL of the following:
    a. Documented diagnosis of moderate to severe postpartum depression (PPD)

    AND

    b. Documentation the Member is postpartum for 12 months or less at the time of the request

    AND

    c. Onset of the depressive episode is between the third trimester and four weeks following delivery and has been documented by standardized rating scales such as the Beck Depression Inventory (BDI), Hamilton Depression Rating Scale (HDRS), Montgomery-Asberg Depression Rating Scale (MADRS), Quick Inventory and Depressive Symptomatology (QIDS, also known as QIDS-SR-16), or the Diagnostic and Statistical Manual of Mental Disorders (DSM 5) criteria

    AND

    d. Documentation that the member has not responded adequately to a trial of an oral antidepressant, or clinical rationale that the trial of an oral antidepressant is not appropriate due to severity of depression (clinical documentation is required)

LIMITATIONS

1. Requests for brand-name products, which have AB-rated generics, will be reviewed according to Non-covered Medications criteria.
2. The Plan will not approve continuation of therapy requests for non-preferred antidepressants if the same active ingredient in a different dosage form is preferred on the formulary. In that instance, the member must meet the specific approval criteria for the non-preferred dosage form.
3. Samples, free goods, or similar offerings of the requested medication do not qualify for an established clinical response or exception, but will be considered on an individual basis for prior authorization.
4. For Zurzuvae (zuranolone), duration of approval is limited to one 14-day course per postpartum period. Approval will not be authorized if the member has previously received Zulresso (brexanolone) or Zurzuvae (zuranolone) for the current postpartum depressive episode from the most recent pregnancy.
5. Quantity limits are as follows:

Drug Name	Quantity Limit
Trintellix (vortioxetine)	1 tablet per day
Drizalma (duloxetine delayed-release sprinkle capsule) 20 mg, 60 mg	2 capsules per day
Drizalma (duloxetine delayed-release sprinkle capsule) 30 mg, 40 mg	3 capsules per day
Emsam (selegiline)	1 patch per day
Fetzima (levomilnacipran)	1 tablet per day
Viibryd (vilazodone)	1 tablet per day30 tablets per 30 days
Zurzuvae (zuranolone) 20 mg, 25 mg	2 capsules per day
Zurzuvae (zuranolone) 30 mg	1 capsule per day

CODES

None

REFERENCES

1. American Psychiatric Association. Practice guideline for the treatment of patients with major depressive disorder, 3rd edition. 2010 November. URL: http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf. Available from Internet. Accessed 2016 February 19.
2. American Psychiatric Association (APA). Practice guideline for the treatment of patients with obsessive-compulsive disorder. 2007 July. URL: http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/ocd.pdf. Available from Internet. Accessed 2016 February 19.
3. American Psychiatric Association (APA). Guideline watch (2013): practice guideline for the treatment of patients with obsessive compulsive disorder. URL:

https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/ocd-watch.pdf. Available from Internet. Accessed 2020 June 26.
4. American Psychiatric Association (APA). Practice guideline for the treatment of patients with panic disorder. 2009 January. URL: http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/panicdisorder.pdf. Available from Internet. Accessed 2016 February 19.
5. Anderson IM. Meta-analytical studies on new antidepressants. *Br Med Bull*. 2001;57:161-78.
6. Anderson IM. Selective serotonin reuptake inhibitors versus tricyclic antidepressants: a meta-analysis of efficacy and tolerability. *J Affect Disord*. 2000;58(1):19-36.
7. Asnis GM, Bose E, Gommoll CP, et al. Efficacy and safety of levomilnacipran sustained release 40 mg, 80 mg, or 120 mg in major depressive disorder: a phase 3, randomized, double-blind, placebo-controlled study. *J Clin Psychiatry*. 2013;74(3):242-8.
8. Auvelity (bupropion/dextromethorphan) [prescribing information]. New York, NY: Axsome Therapeutics, Inc; December 2022.
9. Bandelow B, Zohar J, Hollander E, et al. World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for the pharmacological treatment of anxiety, obsessive–compulsive and post-traumatic stress disorders—first revisions. *World J Bioil Psychiatry.* 2008,9(4):248-312.
10. Cymbalta (duloxetine) [prescribing information]. Indianapolis, IN: Eli Lilly and Company; August 2023.
11. Donohue JM, Pincus HA. Reducing the societal burden of depression: a review of economic costs, quality of care and effects of treatment. *Pharmacoeconomics.* 2007;25:7.
12. Drizalma (duloxetine delayed-release) [prescribing information]. Cranbury, NJ: Sun Pharmaceutical Industries, Inc.; July 2021.
13. Dunn JD, Tierney JG. A step therapy algorithm for the treatment and management of chronic depression. *Am J Manag Care.* 2006 Oct;12(12 Suppl):S335-44.
14. Emsam (selegiline) [prescribing information]. Madison, NJ: Allergan USA, Inc; September 2021.
15. Fantino B, Moore N. The self-reported Montgomery-Asberg depression rating scale is a useful evaluative tool in major depressive disorder. *BMC Psychiatry*. 2009;9(26):1-6.
16. Fetzima (levomilnacipran) [prescribing information]. North Chicago, IL: AbbVie, Inc; August 2023.
17. Fluvoxamine extended-release [prescribing information]. Parsippany, NJ: Teva Pharmaceuticals; August 2023.
18. Hansen RA, Gartlehner G, Lohr KN, et al. Efficacy and safety of second-generation antidepressants in the treatment of major depressive disorder. *Ann Intern Med*. 2005;143(6):415-26.
19. Imipramine HCl [prescribing information]. Birmingham, AL: Oxford Pharmaceuticals, LLC; January 2022.
20. Imipramine pamoate [prescribing information]. Berkeley Heights, NJ: Hikma Pharmaceuticals USA, Inc.; October 2021.
21. Iranikah M, Wensel TM, Thomason AR. Vilazodone for the treatment of major depressive disorder. *Pharmacotherapy*. 2012;32(10):958-65.
22. Kessler RC, Berglund P, Demler O, et al. The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). *JAMA*. 2003;289(23):3095.
23. Montgomery SA, Asberg M. A new depression scale designed to be sensitive to change. *Br J Psychiatry*. 1979;134:382-9.
24. National Institute for Health and Care Excellence. Depression in adults: recognition and management. 2009 October. URL: http://www.nice.org.uk/guidance/cg90. Available from Internet. Accessed 2016 February 19.
25. National Institute for Health and Care Excellence. Depression in children and young people: identification and management. 2015 March. URL: http://www.nice.org.uk/guidance/published?type=cg. Available from Internet. Accessed 2016 February 19.
26. Paroxetine capsule [prescribing information]. Somerset, NJ: Solco Healthcare US, LLC; April 2021.
27. Paxil CR (paroxetine) [prescribing information]. Weston, FL: Apotex Corp.; August 2023.
28. Pristiq (desvenlafaxine succinate ER) [prescribing information]. Philadelphia, PA: Wyeth Pharmaceuticals; August 2023.
29. Protriptyline [prescribing information]. Laurelton, NY: Epic Pharma, LLC; May 2020.
30. Rickels K, Athanaisiou M, Robinson D, et al. Evidence for efficacy and tolerability of vilazodone in the treatment of major depressive disorder: a randomized, double-blind, placebo-controlled, trial. *Journal of Clinical Psychiatry.* 2009:70(3);326-33.
31. Sarafem (fluoxetine) [prescribing information]. Irvine, CA: Allergan USA, Inc; January 2017.

32. Sheehan DV, Harnett-Sheehan K, Raj BA. The measurement of disability. *Int Clin Psychopharmacol*. 1996;11(Suppl3):89-95.
33. Soleimani L, Lapidus KAB, Iosifescu DV. Diagnosis and treatment of major depressive disorder. *Neurol Clin*. 2011;29:177-93.
34. Symbyax (olanzapine/fluoxetine) [prescribing information]. Indianapolis, IN: Eli Lilly and Company; August 2023.
35. Trimipramine [prescribing information]. Berlin, CT: Breckenridge Pharmaceuticals, Inc; May 2020.
36. Thomas KL, Ellingrod VL. Pharmacogenetics of selective serotonin reuptake inhibitors and associated adverse drug reactions. *Pharmacotherapy*. 2009;29(7):822-31.
37. Tofranil-PM (imipramine pamoate) [prescribing information]. Webster Groves, MO: Mallinckrodt, Inc; June 2014.
38. Trintellix (vortioxetine) [prescribing information]. Deerfield, IL: Lundbeck; August 2023.
39. Venlafaxine extended-release tablets [prescribing information]. Parsippany, NJ: Edenbridge Pharmaceuticals, LLC; March 2023.
40. Viibryd (vilazodone) [prescribing information]. Madison, NJ: Allergan USA, Inc.; August 2023.
41. Zurzuvae (zuranolone) [prescribing information]. Cambridge, MA: Sage Therapeutics, Inc and Biogen; November 2023.

APPROVAL HISTORY

September 13, 2022: Reviewed by Pharmacy & Therapeutics Committee.

Subsequent endorsement date(s) and changes made:

1. November 8, 2022: Added criteria for Auvelity to the MNG. Updated Emsam criteria to reduce number of previous trials from three to two.
2. October 10, 2023: Effective January 1, 2024, updated the previous trial language to align with other MNGs. Updated Drizalma criteria to allow approval if the member has a nasogastric tube or difficulty swallowing and added criteria for the diagnosis of fibromyalgia. Updated Auvelity, Emsam, Trintellix, and Viibryd criteria to remove diagnosis requirement. Also updated Trintellix and Viibryd criteria to remove age requirement. Updated limitations section to remove statement that continuation of therapy requests for non-preferred antidepressants if the same active ingredient in a different dosage form is preferred on the formulary.
3. January 9, 2024: Effective February 1, 2024, added criteria for Zurzuvae to the MNG. Updated the fax number for RxUM.

BACKGROUND, PRODUCT AND DISCLAIMER INFORMATION

Pharmacy Medical Necessity Guidelines have been developed for determining coverage for plan benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. The plan makes coverage decisions on a case-by-case basis considering the individual member's health care needs. Pharmacy Medical Necessity Guidelines are developed for selected therapeutic classes or drugs found to be safe, but proven to be effective in a limited, defined population of patients or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. The plan revises and updates Pharmacy Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests needed revisions.

For self-insured plans, coverage may vary depending on the terms of the benefit document. If a discrepancy exists between a Pharmacy Medical Necessity Guideline and a self-insured Member's benefit document, the provisions of the benefit document will govern.

Treating providers are solely responsible for the medical advice and treatment of members. The use of this policy is not a guarantee of payment or a final prediction of how specific claim(s) will be adjudicated. Claims payment is subject to member eligibility and benefits on the date of service, coordination of benefits, referral/authorization and utilization management guidelines when applicable, and adherence to plan policies and procedures and claims editing logic.

Provider Services