MEDICAL MUTUAL®

Drug Policy

Policy: **Impacted Drugs:**	**Antidepressants – Selective Serotonin Reuptake Inhibitors Step Therapy Policy** • escitalopram oral solution (generic) • fluoxetine delayed-release 90 mg capsules (generic to discontinued Prozac® Weekly™) • fluoxetine immediate-release tablets (generic) • fluvoxamine extended-release capsules (generic) • paroxetine HCl controlled-release (CR)/extended-release (ER) tablets (generic) • paroxetine HCl oral suspension (generic) • paroxetine mesylate 7.5 mg capsules (generic) • Trintellix™ (formerly Brintellix®) [vortioxetine tablets – Takeda] • vilazodone hydrochloride tablets (generic) • Duloxetine HCl 40 mg delayed-release capsules, generic • Desvenlafaxine succinate extended-release tablets (generic) • Desvenlafaxine extended-release tablets (Alembic /Ranbaxy [brand product]) • Effexor® (venlafaxine HCl tablets – Wyeth, generic) • Fetzima® (levomilnacipran HCl extended-release capsules – Forest) • Irenka™ (duloxetine 40 mg delayed-release capsules – Lupin, generic) • Khedezla™ (desvenlafaxine extended-release tablets – Osmotica/Macoven) • Savella® (milnacipran HCl tablets – Forest) • Venlafaxine besylate extended-release tablets (Almatica)	**Annual Review Date:** **07/17/2025** **Last Revised Date:** **07/17/2025**

OVERVIEW

Selective Serotonin Reuptake Inhibitor (SSRI) Products

The SSRIs comprise a pharmacologic class of agents with antidepressant action and efficacy in the treatment of a wide range of mood and anxiety disorders (see Table 2).[7-21]

Table 2. FDA-Approved Indications for the SSRIs.[7-21]

Brand (generic)	MDD	OCD	Panic Disorder	Bulimia Nervosa	PTSD	SAD	GAD	PMDD	VMS
Celexa® (citalopram tablets and oral solution, generic) and citalopram capsules	X								
Fluoxetine delayed-release capsules (generic to Prozac® Weekly™)	X*								
Fluoxetine capsules and tablets (generic to Sarafem®)								X	

Fluvoxamine extended-release capsules (generic only)		X†				X			
Fluvoxamine (generic only)		X†							
Lexapro® (escitalopram tablets and oral solution, generic)	Xα						X^		
Paroxetine mesylate 7.5 mg capsules (generic to Brisdelle®)									X
Paxil® (paroxetine HCl tablets and oral suspension, generic)	X	X	X		X	X	X		
Paxil CR® (paroxetine HCl controlled-release tablets, generic)	X		X			X		X	
Pexeva® (paroxetine mesylate tablets)	X	X	X				X		
Prozac® (fluoxetine capsules, tablets, and oral solution, generic)	X†	X†	X	X					
Sertraline capsules	X	X†							
Trintellix™ (vortioxetine tablets)	X								
Viibryd® (vilazodone tablets, generic)	X								
Zoloft® (sertraline tablets and oral suspension, generic)	X	X†	X		X	X		X	

SSRIs – Selective serotonin reuptake inhibitors; MDD – Major depressive disorder; OCD – Obsessive compulsive disorder; PTSD – Posttraumatic stress disorder; SAD – Social anxiety disorder; GAD – Generalized anxiety disorder; PMDD – Premenstrual dysphoric disorder; VMS – Vasomotor symptoms; * Approved for the prevention of relapse during the continuation treatment phase of depression; † FDA-approved indication includes children and adolescents; α FDA-approved indication includes adolescents 12 to 17 years of age; ^ FDA-approved indication includes children and adolescents 7 to 17 years of age; CR – Controlled release; HCl – Hydrochloride.

Serotonin and Norepinephrine Reuptake Inhibitor (SNRI) Products

Desvenlafaxine, duloxetine, Fetzima, and venlafaxine are SNRIs indicated for the **treatment of depression**.[22-31] Additional indications vary by product. Table 3 provides the approved indications for the available SSRIs. While Savella is approved outside the US for major depressive disorder (MDD), it is not in development for this indication in the US.

Table 3. FDA-Approved Indications for the SNRIs in Adults.[22-31]

Brand (generic)	MDD	GAD	SAD	Panic Disorder	DPN Pain	Chronic Musculoskeletal Pain	Fibro-myalgia
Cymbalta® (duloxetine delayed-release capsules, generic)	X	X^			X	X	X*
Desvenlafaxine extended-release tablets (Brand product)	X						
Drizalma Sprinkle™ (duloxetine delayed-release capsules)	X	X^			X	X	
Effexor XR® (venlafaxine extended-release capsules, generic)	X	X	X	X			
Fetzima™ (levomilnacipran extended-release capsules)	X						
Pristiq® (desvenlafaxine succinate extended-release tablets, generic)	X						
Savella® (milnacipran tablets)							X
Venlafaxine besylate extended-release tablets (brand product)	X	X					

Venlafaxine HCl immediate-release tablets (generic only)	X						
Venlafaxine HCl extended-release tablets (generic)	X		X				

SNRI – Serotonin norepinephrine reuptake inhibitor; MDD – Major depressive disorder; GAD – Generalized anxiety disorder; SAD – Social anxiety disorder; DPN – Diabetic peripheral neuropathy; ^ Efficacy studied in patients ≥ 7 years of age with GAD; * Approved for use in patients ≥ 13 years of age; HCl – Hydrochloride.

POLICY STATEMENT

This program has been developed to encourage the use of one Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a history of one Step 1 Product (Standard Criteria) within the 130-day look-back period is excluded from Step Therapy. Patients > 18 years of age are targeted in this Step Therapy program.

Step 1: generic bupropion extended-release tablets, generic bupropion sustained-release tablets, generic citalopram oral solution, generic citalopram tablets, generic duloxetine delayed-release (20 mg, 30 mg, 60 mg) capsules, generic escitalopram tablets, generic fluoxetine immediate-release capsules, generic fluoxetine oral solution, generic fluvoxamine immediate-release tablets, generic paroxetine HCl immediate-release tablets, generic sertraline oral solution, generic sertraline tablets, generic venlafaxine extended-release capsules, generic venlafaxine immediate-release tablets

Step 2: generic escitalopram oral solution, generic fluoxetine delayed-release 90 mg capsule, generic fluoxetine immediate-release tablets, generic fluvoxamine extended-release capsules, generic paroxetine HCl controlled-release (CR)/extended-release (ER) tablets, generic paroxetine HCl oral suspension, generic paroxetine mesylate capsules, generic vilazodone hydrochloride tablets, Trintellix, Desvenlafaxine extended-release tablets (brand product), Fetzima, Savella, generic desvenlafaxine succinate extended-release tablets, generic duloxetine 40 mg delayed-release capsules, venlafaxine besylate extended-release tablets

STANDARD CRITERIA

1. If the patient has tried one Step 1 Product, approve a Step 2 Product.

2. If the patient is currently taking or has taken Desvenlafaxine extended-release tablets (brand product), desvenlafaxine succinate extended-release tablets (Pristiq or generics), Fetzima, vilazodone hydrochloride tablets (Viibryd or generics), or Trintellix at any time in the past and discontinued its use, approve the Product that they have used.

3. If the patient cannot swallow or has difficulty swallowing tablets or capsules, approve generic escitalopram oral solution or generic paroxetine HCl oral suspension.

4. If the patient has suicidal ideation, approve Desvenlafaxine extended-release tablets (brand product), desvenlafaxine succinate extended-release tablets (generics), Fetzima, vilazodone hydrochloride tablets (generics), or Trintellix.

MEDICAL MUTUAL®

Drug Policy

Initial Approval/ Extended Approval.
A) *Initial Approval:* 2 years
B) *Extended Approval:* 2 years

Step Therapy Exception Criteria

In certain situations, the patient is not required to trial preferred agents. Approve for 1 year if the patient meets the following (A, B, or C):

A. The patient has an atypical diagnosis and/or unique patient characteristics which prevent use of all preferred agents. If so, please list diagnosis and/or patient characteristics*; **OR**
B. The patient has a contraindication to all preferred agents. If so, please list the contraindications to each preferred agent*; **OR**
C. The patient is continuing therapy with the requested non-preferred agent after being stable for at least 90 days [verification in prescription claims history required] or, if not available, [verification by prescribing physician required] AND meets ONE of the following:
    1. The patient has at least 130 days of prescription claims history on file and claims history supports that the patient has received the requested non-preferred agent for 90 days within a 130-day look-back period AND there is no generic equivalent available for the requested nonpreferred product (i.e. AA-rated or AB-rated to the requested nonpreferred product); OR
    2. When 130 days of the patient's prescription claims history file is unavailable for verification, the prescriber must verify that the patient has been receiving the requested non-preferred agent for 90 days AND that the patient has been receiving the requested non-preferred agent via paid claims (i.e. the patient has NOT been receiving samples or coupons or other types of waivers in order to obtain access to the requested non-preferred agent) AND there is no generic equivalent available for the requested nonpreferred product (i.e. AA-rated or AB-rated to the requested nonpreferred product).

***Documentation Required:** When documentation is required, the prescriber must provide written documentation supporting the trials of these other agents, noted in the criteria as an asterisk (*). Documentation should include chart notes, prescription claims records, and/or prescription receipts.

Approval Duration: All approvals for continuation of therapy are provided for 1 year unless noted otherwise below. In cases where the initial approval is authorized in months, 1 month is equal to 30 days.

Documentation Requirements:
The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or

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performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Prozac® capsules [prescribing information]. Indianapolis, IN: Lilly; August 2023.
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3. Zoloft® tablets, oral concentrate [prescribing information]. Morgantown, WV: Viatris; August 2023.
4. Celexa® tablets and oral solution [prescribing information]. North Chicago, IL: AbbVie; October 2023.
5. Paxil CR® controlled-release tablets [prescribing information]. Weston, FL: Apotex; February 2024.
6. Lexapro® tablets/oral solution [prescribing information]. North Chicago, IL: AbbVie; October 2023.
7. Pexeva® paroxetine mesylate tablets [prescribing information]. Roswell, GA: Sebela; August 2023.
8. Fluvoxamine maleate tablets [prescribing information]. Baudette, MN: ANI: August 2023.
9. Fluvoxamine extended-release capsules [prescribing information]. Malvern, PA: Endo; October 2023.
10. Sarafem® capsules [prescribing information]. Indianapolis, IN: Lilly; August 2023.
11. Viibryd® tablets [prescribing information]. North Chicago, IL: AbbVie; October 2023.
12. Trintellix® tablets [prescribing information]. Lexington, MA and Deerfield, IL: Takeda and Lundbeck; August 2023.
13. Brisdelle® capsules [prescribing information]. Georgetown, Grand Cayman: Legacy Pharma; February 2025.
14. Sertraline capsules [prescribing information]. Morristown, NJ: Almatica; August 2023.
15. Citalopram capsules [prescribing information]. Morristown, NJ: Almatica; August 2023.
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17. Effexor XR® extended-release capsules [prescribing information]. Morgantown, WV: Viatris; August 2023.
18. Venlafaxine hydrochloride tablets [prescribing information]. Parsippany, NJ: Teva; August 2023.
19. Pristiq® extended-release tablets [prescribing information]. Philadelphia, PA: Wyeth; August 2023.
20. Venlafaxine extended-release tablets [prescribing information]. Cranbury, NJ: Sun; September 2023.
21. Venlafaxine besylate extended-release tablets [prescribing information]. Morristown, NJ: Almatica; August 2023.
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23. Desvenlafaxine extended-release tablets [prescribing information]. Cranbury, NJ: Sun; August 2023.
24. Drizalma Sprinkle™ delayed-release capsules [prescribing information]. Cranbury, NJ: Sun; August 2023.
25. Savella® tablets [prescribing information]. Madison, NJ: Allergan; May 2024.