MEDICAL MUTUAL®

Drug Policy

Policy: **Impacted Drugs:**	Antidepressants – Serotonin and Norepinephrine Reuptake Inhibitors Step Therapy Policy • Cymbalta® (Duloxetine HCl 40 mg delayed-release capsulesgeneric) • 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) • Venlafaxine HCl extended-release tablets (generic)	**Annual Review Date:** **07/20/2023** **Last Revised Date:** **02/15/2024**

OVERVIEW

All of the serotonin and norepinephrine reuptake inhibitors (SNRIs), with the exception of Savella, are indicated for the treatment of MDD. Some of the SNRIs carry additional indications (Table 1). Table 2 provides the approved indications for the available SSRIs.

Table 1. FDA-Approved Indications for the SNRIs in Adults.[1-11]

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® (venlafaxine immediate-release tablets, generic)	X						
Effexor XR® (venlafaxine extended-release capsules, generic)	X	X	X	X			
Fetzima™ (levomilnacipran extended-release capsules)	X						
Irenka™ (duloxetine 40 mg delayed-release capsules)	X	X^			X	X	
Khedezla™ (desvenlafaxine extended-release tablets)	X						
Pristiq® (desvenlafaxine succinate extended-release tablets, generic)	X						
Savella® (milnacipran tablets)							X

Venlafaxine HCl extended-release tablets (generic)	X		X				
Venlafaxine besylate extended-release tablets (brand product)	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.

Table 2. FDA-Approved Indications for the SSRIs.[13-25]

Brand (generic)	MDD	OCD	Panic Disorder	Bulimia Nervosa	PTSD	SAD	GAD	PMDD	VMS
Celexa® (citalopram tablets and oral solution, generic)	X								
Lexapro® (escitalopram tablets and oral solution, generic)	X$^{\alpha}$						X		
Prozac® (fluoxetine capsules, tablets, and oral solution, generic)	X†	X†	X	X					
fluoxetine delayed-release capsules (generic to Prozac® Weekly™)	X*								
Sarafem® (fluoxetine capsules and tablets, generic only)								X	
Fluvoxamine (generic only)		X†							
fluvoxamine extended-release capsules (generic only)		X†							
Paxil® (paroxetine HCl tablets and oral suspension, generic)	X	X	X		X	X	X		

Table 2 (continued). FDA-Approved Indications for the SSRIs.[13-25]

Brand (generic)	MDD	OCD	Panic Disorder	Bulimia Nervosa	PTSD	SAD	GAD	PMDD	VMS
Paxil CR® (paroxetine HCl controlled-release tablets, generic)	X		X			X		X	
Pexeva® (paroxetine mesylate tablets)	X	X	X				X		
Brisdelle™ (paroxetine 7.5 mg capsules)									X
Zoloft® (sertraline tablets and oral suspension, generic)	X	X†	X		X	X		X	
Viibryd® (vilazodone tablets)	X								
Trintellix™ (formerly Brintellix®) [vortioxetine tablets]	X								

SSRI – Selective serotonin reuptake inhibitor; 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; $^{\alpha}$ FDA-approved indication includes adolescents 12 to 17 years of age; † FDA-approved indication includes children and adolescents; * Approved for the prevention of relapse during the continuation treatment phase of depression; CR – Controlled release; HCl – Hydrochloride.

MEDICAL MUTUAL®

Drug Policy

POLICY STATEMENT

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

Automation: A patient with a history of one Step 1 Product 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: citalopram tablets (Celexa, generic), generic citalopram oral solution, generic duloxetine delayed-release 20 mg, 30 mg, 60 mg capsules, escitalopram tablets (Lexapro, generic), escitalopram oral solution (Lexapro, generic), fluoxetine immediate-release capsules and tablets (Prozac, Sarafem, generic), generic fluoxetine oral solution, generic fluoxetine delayed-release capsules, generic fluvoxamine immediate-release tablets, generic fluvoxamine extended-release capsules, paroxetine HCl immediate- and controlled-release tablets (Paxil, Paxil CR, generic), paroxetine oral suspension (Paxil, generic), Pexeva, sertraline tablets (Zoloft, generic), sertraline oral solution (Zoloft, generic), Trintellix (formerly Brintellix), Viibryd, generic venlafaxine immediate-release tablets, generic venlafaxine extended-release capsules

Step 2: Cymbalta, Desvenlafaxine extended-release tablets (brand product), Drizzalma Sprinkle, Effexor, Effexor XR, Fetzima, Irenka, Khedezla, Savella, generic desvenlafaxine succinate extended-release tablets, generic duloxetine 40 mg delayed-release capsules, generic venlafaxine extended-release tablets, venlafaxine besylate extended-release tablets

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 brand name Desvenlafaxine extended-release tablets, desvenlafaxine succinate extended-release tablets (Pristiq or generics), Khedezla, or Fetzima at any time in the past and discontinued its use, approve the Product that they have used.

3. If the patient has suicidal ideation, approve Desvenlafaxine extended-release tablets, desvenlafaxine succinate extended-release tablets (Pristiq or generics), Khedezla, or Fetzima.

Initial Approval/ Extended Approval.
A) *Initial Approval:* 1 year
B) *Extended Approval:* 1 year

Step Therapy Exception Criteria

MEDICAL MUTUAL®

Drug Policy

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 [documentation required]; **OR**
B. The patient has a contraindication to all preferred agents. If so, please list the contraindications to each preferred agent [documentation required]; **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 [documentation required]. 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 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

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11. Irenka™ capsules [prescribing information]. Baltimore, MD: Lupin Pharma; June 2015.
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18. Lexapro® tablets and oral solution [prescribing information]. Irvine, CA: Allergan; September 2021.
19. Pexeva® tablets [prescribing information]. Roswell, GA: Sebela Pharmaceutical; September 2021.
20. Fluvoxamine maleate tablets [prescribing information]. Baudette, MN: ANI Pharmaceuticals; September 2021.
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22. Luvox CR® extended-release capsules [prescribing information]. Palo Alto, CA: Jazz Pharmaceuticals; January 2017.
23. Viibryd® tablets [prescribing information]. Madison, NJ: Allergan; September 2021.
24. Trintellix™ (formerly Brintellix® tablets) [prescribing information]. Lexington, MA and Deerfield, IL: Takeda and Lundbeck; September 2021.
25. Brisdelle® capsules [prescribing information]. Roswell, GA: Sebela Pharmaceuticals; September 2021.