STEP THERAPY CRITERIA

BRAND NAME*
(generic)

(desvenlafaxine fumarate extended-release tablets)

FETZIMA
(levomilnacipran)

KHEDEZLA
(desvenlafaxine extended release tablets)

PRISTIQ
(desvenlafaxine succinate extended release tablets)

Status: CVS Caremark Criteria
Type: Initial Step Therapy; Post Step Therapy Prior Authorization Ref # 1888-D

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated*

FDA-APPROVED INDICATIONS

Desvenlafaxine

Desvenlafaxine, a serotonin and norepinephrine reuptake inhibitor (SNRI), is indicated for the treatment of major depressive disorder (MDD). The efficacy of desvenlafaxine has been established in four short-term (8-week, placebo-controlled studies) of outpatients who met DSM-IV criteria for major depressive disorder.

Fetzima

Fetzima, a serotonin and norepinephrine reuptake inhibitor (SNRI) is indicated for the treatment of major depressive disorder (MDD). The efficacy of Fetzima was established in three 8-week, randomized, double-blind, placebo-controlled studies in adult patients with a diagnosis of MDD

Limitation of Use: Fetzima is not approved for the management of fibromyalgia. The efficacy and safety of Fetzima for the management of fibromyalgia have not been established.

Khedezla

Khedezla, a serotonin and norepinephrine reuptake inhibitor (SNRI), is indicated for the treatment of major depressive disorder (MDD). The efficacy of desvenlafaxine has been established in four short-term (8-week, placebo-controlled studies) in adult outpatients who met DSM-IV criteria for major depressive disorder.

Pristiq

Pristiq is indicated for the treatment of adults with major depressive disorder (MDD).

INITIAL STEP THERAPY

If the patient has filled a prescription for at least a 30 day supply of a generic serotonin-norepinephrine reuptake inhibitor (SNRI) OR generic mirtazapine, generic bupropion (IR or generic for Wellbutrin SR/XL), or a generic selective serotonin reuptake inhibitor (SSRI) within the past 120 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has a diagnosis of major depressive disorder

AND

- The patient had an inadequate treatment response or intolerance to a generic serotonin-norepinephrine reuptake inhibitor (SNRI) (e.g., duloxetine, venlafaxine)
  OR
- The patient had an inadequate treatment response or intolerance to mirtazapine, bupropion, or a generic selective serotonin reuptake inhibitor (SSRI) (e.g., citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline)
  OR
- The patient previously demonstrated a response to treatment with desvenlafaxine (e.g., Pristiq, Khedezla) or levomilnacalcipran (Fetzima)

RATIONALE

If the patient has filled a prescription for a 30 day supply of a generic serotonin-norepinephrine reuptake inhibitor (SNRI) OR generic mirtazapine, generic bupropion (IR or generic for Wellbutrin SR/XL), or a generic selective serotonin reuptake inhibitor (SSRI) within the past 120 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.

If the patient does not meet the initial step therapy criteria, then prior authorization is required.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Desvenlafaxine, Khedezla, Pristiq and Fetzima are indicated for the treatment of major depressive disorder (MDD). The efficacy of desvenlafaxine extended-release tablets has been established in four short-term (8-week, placebo-controlled studies) in adult outpatients who met DSM-IV criteria for major depressive disorder. The efficacy of Fetzima was established in three 8-week, randomized, double-blind, placebo-controlled studies in adult patients with a diagnosis of MDD.

For antidepressant medications, the American Psychiatric Association (APA) and the American College of Physicians (ACP) guidelines recommend that adherence to a therapeutic dose and meeting clinical goals are more important than the specific drug selected. The ACP guidelines and AHRQ state that the available evidence does not support clinically significant differences in efficacy, effectiveness, or quality of life among SSRIs, SNRIs, SSNRIs, or other second generation antidepressants for the treatment of MDD. The APA guidelines also state that for most patients, a selective serotonin reuptake inhibitor (SSRI), serotonin norepinephrine reuptake inhibitor (SNRI), mirtazapine, or bupropion is optimal.[6-9]

Therefore, if the patient had an inadequate treatment response, intolerance, or a contraindication to one of the following: a generic serotonin-norepinephrine reuptake inhibitor (SNRI) (e.g., duloxetine, venlafaxine), mirtazapine, bupropion, a generic selective serotonin reuptake inhibitor (SSRI) (e.g., citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline) or previously demonstrated a response to treatment with desvenlafaxine (e.g., Pristiq, Khedezla) or levomilnacalcipran (Fetzima), the requested drug should be approved.

REFERENCES

1. Desvenlafaxine Fumarate [package insert]. Jacksonville, FL: Ranbaxy Pharmaceuticals Inc.; October 2016.
2. Fetzima [package insert]. Irvine, CA: Allergan Inc.; December 2017
3. Khedezla [package insert]. Marietta, GA: Osmotica Pharmaceutical US LLC; November 2017.
4. Pristiq [package insert]. Philadelphia, PA: Wyeth Pharmaceuticals Inc; April 2018.
5. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.; http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed May 2018.
6. Micromedex Solutions [database online]. Greenwood Village, CO: Truven Health Analytics Inc. Updated periodically. www.micromedexsolutions.com [available with subscription]. Accessed May 2018.
7. Gelenberg A, Freeman M, Markowitz J, et al. American Psychiatric Association. Practice guideline for the treatment of patients with major depressive disorder (3rd Edition). October 2010. Available at https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf. Accessed May 2018.
8. Qaseem A, Vincenza Snow V, Denberg T, et al. Using Second-Generation Antidepressants to Treat Depressive Disorders: A Clinical Practice Guideline from the American College of Physicians. *Ann Intern Me.* 2008;149:725-733.
9. Gartlehner G, Hansen R, Morgan L, et al. Second-Generation Antidepressants in the Pharmacologic Treatment of Adult Depression: An Update of the 2007 Comparative Effectiveness Review. (Prepared by the RTI International–

University of North Carolina Evidence-based Practice Center, Contract No. 290-2007-10056-I.) AHRQ Publication No. 12 EHC012-EF. Rockville, MD: Agency for Healthcare Research and Quality. December 2011. www.effectivehealthcare.ahrq.gov/reports/final.cfm.
10. Qaseem A, Barry M, Kansagara D, et al. Nonpharmacologic Versus Pharmacologic Treatment of Adult Patients With Major Depressive Disorder: A Clinical Practice Guideline From the American College of Physicians. *Ann Intern Med*. 2016;164:350-359.

Written by UM Development (TM)
Date Written: 05/2017
Revised: (TM) 08/2017 (clarify pre-req bup), (ME) 05/2018 (added Fetzima)
Reviewed: Medical Affairs (LS) 06/2017, (DC) 05/2018
External Review: 07/2017, 08/2018

CRITERIA FOR APPROVAL

1	Does the patient have a diagnosis of major depressive disorder?	Yes	No
2	Has the patient had an inadequate treatment response or intolerance to a generic serotonin-norepinephrine reuptake inhibitor (SNRI) (e.g., duloxetine, venlafaxine)? [If yes, then no further questions.]	Yes	No
3	Has the patient had an inadequate treatment response or intolerance to mirtazapine, bupropion, or a generic selective serotonin reuptake inhibitor (SSRI) (e.g., citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline)? [If yes, then no further questions.]	Yes	No
4	Has the patient previously demonstrated a response to treatment with desvenlafaxine (e.g., Pristiq, Khedezla) or levomilnacalcipran (Fetzima)?	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when it is prescribed for major depressive disorder. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Approve, 12 months	Go to 3	
3.	Approve, 12 months	Go to 4	
4.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet one of these conditions: - You tried a generic serotonin-norepinephrine reuptake inhibitor (SNRI) drug, and it did not work for you or you cannot use them (SNRI examples are duloxetine, venlafaxine) - You tried mirtazapine, bupropion, or a generic selective serotonin reuptake inhibitor (SSRI) and it did not work for you or you cannot use them (SSRI examples are citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline) - You had a response to treatment with desvenlafaxine (Pristiq, Khedezla) or levomilnacalcipran (Fetzima) Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance or trial of generic SNRI, SSRI, desvenlafaxine or levomilnacalcipran]