BlueCross BlueShield of Arizona
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PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 11/17/16**
SECTION: DRUGS	**LAST REVIEW DATE: 11/16/17**
	LAST CRITERIA REVISION DATE: 11/16/17
	ARCHIVE DATE:

FETZIMA® (levomilnacipran hydrochloride extended release) oral capsule

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

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This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

FETZIMA® (levomilnacipran hydrochloride extended release) oral capsule (cont.)

Description:

Fetzima (levomilnacipran) extended release capsule a selective serotonin and norepinephrine reuptake inhibitor (SNRI) is indicated for the treatment of major depressive disorder (MDD). It is not approved for the management of fibromyalgia; the efficacy and safety of Fetzima (levomilnacipran) for the management of fibromyalgia have not been established.

The exact mechanism of the antidepressant action of levomilnacipran is unknown, but is thought to be related to the potentiation of serotonin and norepinephrine in the central nervous system, through inhibition of reuptake at serotonin and norepinephrine transporters. Non-clinical studies have shown that levomilnacipran is a potent and selective serotonin and norepinephrine reuptake inhibitor.

Major depressive disorder (MDD)

- MDD, also known as unipolar depressive disorder, is diagnosed in a patient who has suffered at least one major depressive episode and has no history of mania or hypomania

- A major depressive episode is a period lasting at least two weeks, with five or more of the following symptoms:
    - Depressed mood
    - Anhedonia
    - Insomnia or hypersomnia
    - Change in appetite or weight
    - Psychomotor retardation or agitation
    - Low energy
    - Poor concentration
    - Thoughts of worthlessness or guilt
    - Recurrent thoughts about death or suicide
    - At least one of the symptoms must be depressed mood or anhedonia

- Treatment resistant depression refers to major depressive episodes that do not respond satisfactorily to at least two trials of antidepressant monotherapy; however, the definition has not been standardized

- Treatment refractory depression refers to unipolar major depressive episodes that do not respond satisfactorily to numerous sequential treatment regimens; however, the definition has not been standardized, and there is no clear delineation between treatment resistant and treatment refractory depression

- Unipolar major depression should be treated with medication for 6-12 weeks before deciding whether antidepressant has sufficiently relieved symptoms
    - However, for patients who show little improvement (reduction of baseline symptoms ≤ 25%) after 4-6 weeks, it is reasonable to administer next-step treatment

- Antidepressants such as selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), mirtazapine and bupropion, are recommended by guidelines as first line treatment for patients with MDD

FETZIMA® (levomilnacipran hydrochloride extended release) oral capsule (cont.)

- Efficacy among the various agents is similar and drug selection may be determined by several factors such as previous treatment response, adverse event profile of potential agents, patient preference, route of administration, comorbid medical conditions, and potential for drug-drug interactions

- The standard of care for MDD patients with an inadequate response to monotherapy may include:
  - Optimizing the antidepressant dose for patients who show minimal or no response
  - Transition to another antidepressant
  - The current antidepressant may be augmented with a second antidepressant from a different class, lithium carbonate, thyroid hormone or an atypical antipsychotic
  - Electroconvulsive therapy for treatment resistant patients with severe unipolar major depression or severe unipolar major depression with psychotic features (delusions or hallucinations)

Definitions:

Selective serotonin reuptake inhibitors (SSRI):
Citalopram
Escitalopram
Fluoxetine
Fluvoxamine
Paroxetine
Sertraline
Vilazodone
Vortioxetine

Serotonin-norepinephrine reuptake inhibitors (SNRI):
Desvenlafaxine
Duloxetine
Levomilnacipran
Milnacipran
Venlafaxine

Mono-amine oxidase inhibitors (MAOI):
Isocarboxazid
Phenelzine
Tranylcypromine

Other:
Bupropion
Maprotiline
Mirtazepine
Nefazodone
Trazodone
Tricyclic antidepressants

FETZIMA® (levomilnacipran hydrochloride extended release) oral capsule (cont.)

Fetzima (levomilnacipran)

Medication class:
Antidepressant, Serotonin-Norepinephrine Reuptake Inhibitor (SNRI)

FDA-approved indication(s):
- For the treatment of major depressive disorder (MDD)

Recommended Dose:
- Initiate 20 mg once daily for 2 days, then increase to 40 mg once daily, increase at 40 mg increments at intervals of 2 days or more
- Capsules cannot be opened, must be swallowed whole

Maximum dosage
- 120 mg once daily

Available Dosage Forms:
- 20 mg, 40 mg, 80 mg, and 120 mg extended release capsules
- Titration pack contains 2 x 20 mg capsules and 26 x 40 mg capsules

Limitations 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.

Warnings and Precautions:
- Fetzima is not approved for use in treating bipolar depression
- The efficacy of Fetzima has not been established beyond 8 weeks
- With moderate renal impairment (CrCl 30-59 mL/min), do not exceed 80 mg once daily
- With severe renal impairment (CrCl 15-29 mL/min), do not exceed 40 mg once daily
- It is not recommended in individuals with end stage renal disease
- When used with strong CYP3A4 inhibitors, do not exceed 80 mg once daily
- Must be tapered when decision is made to stop Fetzima
- Discontinue if serotonin syndrome develops
- Discontinue if urinary hesitation or retention occurs
- Patients who experience sustained increase in blood pressure should discontinue Fetzima or consider another appropriate medical intervention
- Patients who experience sustained increase in heart rate should discontinue Fetzima or consider another appropriate medical intervention
- Fetzima should be discontinued in patients who develop signs and symptoms of hyponatremia
- It should not be taken with alcohol

FETZIMA® (levomilnacipran hydrochloride extended release) oral capsule (cont.)

Criteria:

- **Criteria for initial therapy:** Fetzima (levomilnacipran) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual is 18 years of age or older

  2. A confirmed diagnosis of Major Depressive Disorder (MDD)

  3. Individual has failure, contraindication or intolerance to **TWO** preferred SSRI step therapy **and TWO** preferred SNRI step therapy agents:
     - Preferred SSRI step therapy agents include:
       - Citalopram
       - Escitalopram
       - Fluoxetine
       - Fluvoxamine
       - Paroxetine
       - Sertraline
     - Preferred SNRI step therapy agents include:
       - Desvenlafaxine
       - Duloxetine
       - Venlafaxine HCl ER
       - Venlafaxine HCl

  4. There are **NO** contraindications:
     - Contraindications include:
       - Hypersensitivity to levomilnacipran, milnacipran HCl, or any excipient in the Fetzima formulation
       - Simultaneous use with or within 14 days of stopping an mono-amine oxidase inhibitor (MAOI)
       - Use of MAOI within 7 days of stopping Fetzima
       - Starting Fetzima in an individual on Linezolid

  Initial approval duration: 12 months

- **Criteria for continuation of coverage (renewal request):** Fetzima (levomilnacipran) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual's condition responded while on therapy
     - Response is defined as:
       - Improved mood, behavior, interest in daily activities, sleep, energy, sense of worthiness, no thoughts of suicide and no attempts, no aggression or violent behavior, no hospitalizations

  2. Individual has been adherent with the medication

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3. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use
    - Contraindications as listed in the criteria for initial therapy section
    - Adverse effect such as:
        - Serotonin syndrome, signs and symptoms may include: agitation, hallucinations, delirium, tachycardia, labile blood pressure, dizziness, diaphoresis, flushing, hyperthermia, tremor, rigidity, myoclonus, hyperreflexia, incoordination, seizures, nausea, vomiting, and diarrhea
        - Urinary hesitation or retention

4. There are no significant interacting drugs

Renewal duration: 12 months

Resources:

Fetzima. Package Insert. Revised by manufacturer 7/2014. Accessed 9/16/16.

UpToDate: Unipolar major depression in adults: Choosing initial treatment. Current through Sep 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/unipolar-major-depression-in-adults-choosing-initial-treatment?source=search_result&search=major%20depressive%20disorder&selectedTitle=1~150

UpToDate: Unipolar major depression in adults: Treatment of resistant depression. Current through Sep 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/unipolar-depression-in-adults-treatment-of-resistant-depression?source=see_link

UpToDate: Unipolar major depression in adults: Management of highly resistant (refractory) depression. Current through Sep 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/unipolar-depression-in-adults-management-of-highly-resistant-refractory-depression?source=see_link

UpToDate: Overview of prevention and treatment for pediatric depression. Current through Sep 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/overview-of-prevention-and-treatment-for-pediatric-depression?source=search_result&search=major%20depressive%20disorder&selectedTitle=3~150

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:	Dosage Form:
Directions for Use:	Quantity: / Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

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