Clinical Policy: Levomilnacipran (Fetzima)

Reference Number: HIM.PA.125
Effective Date: 12.01.17
Last Review Date: 08.21
Line of Business: HIM

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Levomilnacipran (Fetzima®) is a serotonin and norepinephrine reuptake inhibitor (SNRI).

FDA Approved Indication(s)

Fetzima is indicated for the treatment of major depressive disorder.

Limitation(s) 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.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Fetzima is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Major Depressive Disorder (must meet all)**:**

1. Diagnosis of major depressive disorder;
2. Age ≥ 18 years;
3. Failure of TWO of the following, each tried for ≥ 4 weeks at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated: SSRI, SNRI, bupropion, mirtazapine;
4. Dose does not exceed 120 mg (1 capsule) per day.

Approval duration: 12 months

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PA.154 for health insurance marketplace.

II. Continued Therapy

A. Major Depressive Disorder (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;

3. If request is for a dose increase, new dose does not exceed 120 mg (1 capsule) per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PA.154 for health insurance marketplace.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – HIM.PA.154 or evidence of coverage documents;

B. Fibromyalgia.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
MAOI: monoamine oxidase inhibitor
SNRI: serotonin and norepinephrine reuptake inhibitor
SSRI: selective serotonin reuptake inhibitor

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
bupropion (Wellbutrin® XL)	150 to 450 mg PO QAM	450 mg/day
mirtazapine (Remeron®)	15 to 45 mg PO QHS	45 mg/day
SSRIs		
citalopram (Celexa®)	20 mg PO QD	40 mg/day
escitalopram (Lexapro®)	10-20 mg PO QD	20 mg/day
Fluvoxamine® (Luvox CR®)	50-300 mg PO QD	300 mg/day
fluoxetine (Prozac®)	20 mg PO QD	80 mg/day
paroxetine (Paxil®)	20 mg PO QD	50 mg/day
paroxetine controlled release (Paxil CR®)	25 mg PO QD	62.5 mg/day
sertraline (Zoloft®)	50 mg PO QD	200 mg/day
SNRIs		
desvenlafaxine (Pristiq®)	50 mg PO QD	400 mg/day
duloxetine (Cymbalta®)	20 mg PO BID, 30 mg BID, or 60 mg PO QD	120 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
venlafaxine (Effexor®)	75 mg PO BID to TID	225 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Hypersensitivity to levomilnacipran, milnacipran HCl, or any excipient;
  - Serotonin Syndrome and MAOIs: Do not use MAOIs with Fetzima or within 7 days of stopping treatment with Fetzima. Do not use Fetzima within 14 days of stopping an MAOI. In addition, do not start Fetzima in a patient who is being treated with linezolid or intravenous methylene blue.
- Boxed warning(s): Increased risk of suicidal thinking and behavior in children, adolescents and young adults taking antidepressants; monitor for worsening and emergence of suicidal thoughts and behaviors; not approved for use in pediatric patients.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Major depressive disorder	40 mg to 120 mg PO QD	120 mg QD

VI. Product Availability

Extended-release capsules: 20 mg, 40 mg, 80 mg and 120 mg

VII. References

1. Fetzima Prescribing Information. Irvine, CA: Allergan USA, Inc.; October 2019. Available at: www.fetzima.com. Accessed July 29, 2020.
2. Gelenberg AJ, Freeman MP, Markowitz JC, et al. Practice guideline for the treatment of patients with major depressive disorder, third edition. Arlington, VA: American Psychiatric Association; May 2010. Available online at http://www.psychiatryonline.org/guidelines. Accessed July 29, 2020.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	08.23.17	11.17
4Q 2018 annual review: no significant changes; references reviewed and updated.	08.10.18	11.18
4Q 2019 annual review: no significant changes; references reviewed and updated.	08.26.19	11.19
4Q 2020 annual review: no significant changes; references reviewed and updated.	07.29.20	11.20
3Q 2021 annual review: shortened the trial durations of alternative agents from 8 weeks to 4 weeks; added bupropion and mirtazapine as additional options for trial; combined trial requirements by providing an option to try any two among SSRI, SNRI, bupropion,	07.20.21	08.21

Reviews, Revisions, and Approvals	Date	P&T Approval Date
and mirtazapine; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.		
Clarified SNRI agents in Appendix B.	12.13.21	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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