Original Effective Date: 4/1/2012
Current Effective Date: 03/07/2024
Last P&T Approval/Version: 01/31/2024
Next Review Due By: 01/2025
Policy Number: C4731-A

Savella (milnacipran)

PRODUCTS AFFECTED

Savella (milnacipran)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This 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 Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Fibromyalgia, Major depressive disorder

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case- by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. FIBROMYALGIA:
1. Documented diagnosis of fibromyalgia
AND
2. Documentation of treatment failure, serious side effects or clinical contraindication to ALL

of the following:
(a) One formulary/preferred tricyclic antidepressant (TCA) at up to maximally indicated doses OR cyclobenzaprine AND
(b) An adequate trial of a therapeutic dose of gabapentin (1200-2400mg daily) AND
(c) Duloxetine
AND

3. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Savella (milnacipran) include: use with Monoamine Oxidase Inhibitor (MAOI) intended to treat psychiatric disorders, starting Savella (milnacipran) in a member being treated with linezolid or methylene blue,]

B. DEPRESSION:
1. Documented diagnosis of major depressive disorder
AND
2. Documentation of trial and failure or intolerance to a majority (not more than 3) of the preferred formulary alternatives for the given diagnosis. Submit documentation including medication(s) tried, dates of trial(s) and reason for treatment failure(s).
AND
3. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Savella (milnacipran) include: use with Monoamine Oxidase Inhibitor (MAOI) intended to treat psychiatric disorders, starting Savella (milnacipran) in a member being treated with linezolid or methylene blue]

CONTINUATION OF THERAPY:

A. FIBROMYALGIA/DEPRESSION:
1. Adherence to therapy at least 85% of the time as verified by Prescriber and member's medication fill history (review Rx history for compliance)
AND
2. Documentation of positive clinical response as demonstrated by low disease activity and/or improvements in the condition's signs and symptoms
AND
3. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity

DURATION OF APPROVAL:

Initial authorization: 12 months, Continuation of therapy: 12 months

PRESCRIBER REQUIREMENTS:

FIBROMYALGIA: Prescribed by or in consultation with a rheumatologist, neurologist or practitioner specializing in the treatment of fibromyalgia.
DEPRESSION: None
[If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:

18 years of age and older

QUANTITY:

Max dose of 100mg BID (200mg daily)

PLACE OF ADMINISTRATION:

The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and

patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:
Fibromyalgia Agents - SNRI

FDA-APPROVED USES:
Indicated for the management of fibromyalgia. Savella is not approved for use in pediatric patients.

COMPENDIAL APPROVED OFF-LABELED USES:
Major Depressive Disorder

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Savella (milnacipran) is indicated for the management of fibromyalgia. Savella (milnacipran) is not approved for use in pediatric patients. Savella (milnacipran) is a selective norepinephrine and serotonin reuptake inhibitor that works in the management of fibromyalgia by inhibiting norepinephrine uptake with greater potency than serotonin. Savella (milnacipran) is not labeled for the treatment of depression.
Compared to placebo, treatment with Savella (milnacipran) resulted in improvements in pain, member global fibromyalgia assessment, and physical function scores in patients with fibromyalgia.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Savella (milnacipran) are considered experimental/investigational and therefore will follow the Molina Healthcare, Inc. off-label policy. Savella (milnacipran) is contraindicated in members with using monoamine oxidase inhibitors concomitantly or in close temporal proximity and use in patients with uncontrolled narrow-angle glaucoma.
Savella (milnacipran) can increase blood pressure and heart rate. Antidepressants may worsen depression and induce suicidality in certain patients during the early phases of treatment. serotonin syndrome has been reported with SNRIs and SSRIs. Concomitant use of serotonergic drugs such as triptans, tramadol, and drugs that inhibit serotonin reuptake, including Savella, is not recommended. Seizures have been reported in patients treated with Savella. Prescribe with caution in patients with a history of seizures. Savella is not recommended for patients with end-stage renal disease.

OTHER SPECIAL CONSIDERATIONS:
Savella (milnacipran) has a black box warning for suicidality and antidepressant drugs due to its mechanism of action as a serotonin and norepinephrine reuptake inhibitor.

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Savella TABS 12.5mg, 25mg, 50mg, 100mg,
Savella Titration Pack MISC 12.5 & 25 & 50MG

REFERENCES

1. Savella (milnacipran HCl) [package insert]. Irvine, CA: Allergan USA, Inc.; September 2023.
2. Arnold LM, et al. Gabapentin in the treatment of fibromyalgia: a randomized, double- blind, placebo-controlled, multicenter trial. Arthritis Rheum. 2007;56(4):1336-44.
3. Arnold LM, Gendreau RM, Palmer RH, et al. Efficacy and safety of milnacipran 100mg/day in patients with fibromyalgia: results of a randomized, double-blind, placebo-controlled trial. Arthritis Rheum. 2010Sep;62(9):2745-56.
4. Clauw DJ, Mease P, Palmer RH, et al. Milnacipran for the treatment of fibromyalgia in adults: a15-week, multicenter, randomized, double-blind, placebo-controlled, multiple-dose clinical trial. Clin Ther. 2008Nov;30(11):1988-2004.
5. Kranzler JD, Gendreau RM. Role and rationale for the use of milnacipran in the management of fibromyalgia. Neuropsychiatr Dis Treat. 2010 May;25(6):197-208.
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7. Macfarlane, G. J., Kronisch, C., Dean, L. E., Atzeni, F., Häuser, W., Fluß, E., Choy, E., Kosek, E., Amris, K., Branco, J., Dincer, F., Leino-Arjas, P., Longley, K., McCarthy, G. M., Makri, S., Perrot, S., Sarzi-Puttini, P., Taylor, A., & Jones, G. T. (2017). EULAR revised recommendations for the management of fibromyalgia. Annals of the rheumatic diseases, 76(2), 318–328. https://doi.org/10.1136/annrheumdis-2016-209724
8. Abrahamian, H., Hofmann, P., Kinzl, J., & Toplak, H. (2012). Diabetes mellitus and comorbid depression: improvement of both diseases with milnacipran. A replication study (results of the Austrian Major Depression Diabetes Mellitus study group). Neuropsychiatric disease and treatment, 8, 355–360. https://doi.org/10.2147/NDT.S33679

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information FDA-Approved Uses Available Dosage Forms References	Q1 2024
REVISION- Notable revisions: Diagnosis Required Medical Information Continuation of Therapy Contraindications/Exclusions/Discontinuation Other Special Considerations References	Q1 2023
Q2 2022 Established tracking in new format	Historical changes on file