Savella (milnacipran)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Savella (milnacipran), FDA approved in 2009, is a serotonin norepinephrine reuptake inhibitor (SNRI) used for the management of pain caused by fibromyalgia. Fibromyalgia, the most common cause of generalized musculoskeletal pain, is a multi-symptom condition, commonly presenting as widespread chronic pain, fatigue and sleep issues. Treatment for fibromyalgia usually involves a combination of medications (to relieve pain [e.g., amitriptyline, cyclobenzaprine], improve sleep [e.g., pregabalin,

gabapentin] or mood [e.g., duloxetine, milnacipran]) and non-pharmacological treatments, such as cognitive behavioral therapy, relaxation therapy and aerobic exercise.
NOTE: Although Savella (milnacipran) has been used in the treatment of major depressive disorder and is approved for treating depression in some countries outside the US, this indication is not an FDA-labeled use.

Definitions

"Fibromyalgia" is a multi-symptom condition, commonly presenting as widespread chronic pain, fatigue and sleep issues.

Medical Necessity Criteria for Initial Clinical Review

Initial Indication-Specific Criteria

Fibromyalgia

The Plan considers Savella (milnacipran) medically necessary when ALL of the following criteria are met:

1. The member is 18 years of age or older*; AND*
2. The member has a diagnosis of fibromyalgia*; AND*
3. The member has documented trial and failure of non-pharmacologic therapy (e.g., cognitive behavioral therapy, education, exercise and/or other forms of physical therapy)*; AND*
4. The member is unable to use or has tried and failed a minimum ONE (1) month trial of at least TWO (2) therapies, each from a different drug class:
    a. Cyclobenzaprine*; and/or*
    b. Gabapentinoids (e.g., gabapentin, pregabalin)*; and/or*
    c. Serotonin-norepinephrine reuptake inhibitors (e.g., duloxetine, venlafaxine ER)*; and/or*
    d. Tricyclic Antidepressants (e.g., amitriptyline)*; AND*
5. Clinical chart documentation is provided for review to substantiate the above listed requirements.

Major Depressive Disorder

1. The member is 18 years of age or older; *AND*
2. The member has a diagnosis of major depressive disorder (MDD); *AND*
3. The member is unable to use or has tried and failed TWO (2) therapies, each from a different class for at least six (6) weeks each:
    a. Noradrenergic and dopaminergic antidepressants (bupropion)*; and/or*
    b. Noradrenergic and specific serotonin antidepressants (e.g., mirtazapine)*; and/or*
    c. Selective serotonin reuptake inhibitors (e.g., citalopram, escitalopram, fluoxetine, paroxetine, sertraline)*; and/or*

d. Serotonin-norepinephrine reuptake inhibitors (e.g., duloxetine, venlafaxine IR/ER)*; and/or*
e. Tricyclic antidepressants (e.g., amitriptyline, nortriptyline)*; AND*

4. Clinical chart documentation is provided for review to substantiate the above listed requirements.

If the above prior authorization criteria are met, Savella (milnacipran) will be approved for up to 12 months.

Continued Care

Medical Necessity Criteria for Subsequent Clinical Review

Subsequent Indication-Specific Criteria

Fibromyalgia

The Plan considers Savella (milnacipran) medically necessary when ALL of the following criteria are met:

1. The member still meets the applicable initial criteria*; AND*
2. Recent chart documentation (within the last 3 months) shows the member has experienced therapeutic response to the requested medication as evidenced by ONE (1) of the following:
    a. Clinical improvement in fibromyalgia symptoms (e.g. pain, fatigue, sleep, mood, function) since starting therapy; *or*
    b. Disease stability (e.g., maintenance of pain relief) since starting therapy

Major Depressive Disorder

The Plan considers Savella (milnacipran) medically necessary when ALL of the following criteria are met:

1. Clinical improvement (e.g., reduction in signs and symptoms, including residual symptoms) in symptoms since starting the requested medication; *OR*
2. Stability in condition (e.g., restoration of prior level of psychosocial and occupational function) since starting the requested medication.

If the above reauthorization criteria are met, the requested product will be authorized for up to 12 months

Experimental or Investigational / Not Medically Necessary

Savella (milnacipran) for any other indication is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven. Non-covered indications include, but are not limited to, the following:

- Asperger's Syndrome. There are no high quality studies to support the safety and efficacy of Savella (milnacipran) for the management of Asperger's syndrome.
- Autism Spectrum Disorder. There are no high quality studies to support the safety and efficacy of Savella (milnacipran) for the management of autism spectrum disorder.
- Chronic Migraine (including migraines with and without aura). There are no high quality studies to support the safety and efficacy of Savella (milnacipran) for the management of migraines. In a small (n=45) prospective, open-label study, Savella (milnacipran) reduced headaches and migraine frequency; however there was no comparator group.
- Chronic Pain including back and lower back pain. There are no high quality studies to support the safety and efficacy of Savella (milnacipran) for the management of chronic pain, including back and lower back pain (outside of the use in those with fibromyalgia). Two studies found no benefit in modulating pain in those with burning mouth syndrome and fibromyalgia. One small study (n=32) found significant improvement in pain in those with orofacial region pain (due to burning mouth syndrome and atypical odotalgia). No studies were available to support use of Savella (milnacipran) for back-related pain. A Cochrane review found that Savella (milnacipran) was effective at treating pain due to fibromyalgia in a "minority," and a lack of data to support substantial pain relief.
- Degenerative Joint Disease (DJD). There are no high quality studies to support the safety and efficacy of Savella (milnacipran) for the management of DJD.
- Idiopathic Peripheral Neuropathy or neuropathic pain. There are no high quality studies to support the safety and efficacy of Savella (milnacipran) for the management of idiopathic peripheral neuropathy or neuropathic pain outside of the management of fibromyalgia.
- Irritable Bowel Syndrome (IBS). There are no high quality studies to support the safety and efficacy of Savella (milnacipran) for the management of IBS.
- Osteoarthritis (OA). There are no high quality studies to support the safety and efficacy of Savella (milnacipran) for the management of OA.
- Rheumatoid Arthritis (RA). There are no high quality studies to support the safety and efficacy of Savella (milnacipran) for the management of RA. One one randomized controlled study assess Savella (milnacipran) versus placebo, and found no improvement in RA symptoms.
- Sleep disorders and disturbances. There are no high quality studies to support the safety and efficacy of Savella (milnacipran) for the management of sleep disorders or disturbances outside of the management of fibromyalgia. One small (n=4) randomized controlled study found no improvement in objective measures of obstructive sleep apnea after a single dose. One meta-analysis found Savella (milnacipran) was more effective than placebo in managing sleep disturbances in those with fibromyalgia, and more effective than duloxetine in improving fatigue due to fibromyalgia.
- Systemic Lupus Erythematosus (SLE). There are no high quality studies to support the safety and efficacy of Savella (milnacipran) for the management of SLE.
- Vestibulodynia. There are no high quality studies to support the safety and efficacy of Savella (milnacipran) for the management of vestibulodynia. Only one small (n=22) open-label study

found Savella (milnacipran) significantly reduced pain, coital pain, tampon pain and mean vulvar pain; however, there were no comparator groups.

- Vulvodynia. There are no high quality studies to support the safety and efficacy of Savella (milnacipran) for the management of vulvodynia. There is one small open-label study (n=22) which found improvement in pain and improved mood and sexual function, though there were no comparator groups.

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