Savella®
milnacipran HCl™

# For the management of fibromyalgia

## Stock Savella today

- Delivers simultaneous improvements on 3 measures of fibromyalgia[1,2]
  - **Pain reduction:** ≥30% improvement in 24-hour recall pain from Visual Analog Scale (VAS) baseline
  - **Global or overall fibromyalgia improvement:** Reported 1 ("Very Much Improved") or 2 ("Much Improved") on Patient Global Impression of Change (PGIC)
  - **Physical function improvement:** ≥6 point improvement from baseline on the Short Form-36 Physical Component Summary (SF-36 PCS)
- Decrease in pain as early as week 1 of treatment with a stable dose in patients who reported global improvement[1]
- Low potential for pharmacokinetic drug-drug interactions[1]
  - Clinically important interactions may occur with lithium, epinephrine and norepinephrine, serotonergic drugs, digoxin, clonidine, clomipramine, CNS-active drugs, and MAOIs
- A dual reuptake inhibitor that blocks the uptake of norepinephrine over serotonin with approximately 3 times greater potency in vitro[1]
  - The clinical significance of in vitro data is unknown


## Dosing

- Twice-daily (AM/PM) dosing with or without food, though taking with food may improve tolerability[1]
- The recommended dose of Savella is 100 mg/day (50 mg twice daily); may be increased to 200 mg/day (100 mg twice daily) depending on individual patient response[1]
- Savella is non-narcotic and is not scheduled
- See Full Prescribing Information for complete dosing and administration information

## Savella is available in 12.5 mg, 25 mg, 50 mg, and 100 mg tablets and a 4-week Titration Pack

Savella must be dispensed with Patient Medication Guide.

| Tablet strength | | Package configuration | NDC code |
|---|---|---|---|
| 12.5 mg |  | Bottles of 60 | 0456-1512-60 |
| 25 mg |  | Bottles of 60 | 0456-1525-60 |
| 50 mg<br>Recommended dose is 50 mg twice daily. |  | Bottles of 60 | 0456-1550-60 |
| 100 mg<br>Dose may be increased to 100 mg twice daily based on individual patient response. |  | Bottles of 60 | 0456-1510-60 |
| Titration Pack<br>For patient starts – 1 week of titration and 3 weeks of recommended dose (50 mg twice daily). | | 4-week Titration Pack<br>Contains 55 tablets: 5 x 12.5 mg tablets; 8 x 25 mg tablets; 42 x 50 mg tablets. | 0456-1500-55 |

(tablets shown here are actual size)

**Savella is a selective serotonin and norepinephrine reuptake inhibitor (SNRI), similar to some drugs used for the treatment of depression and other psychiatric disorders. Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of such drugs in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on Savella should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior, especially during the initial few months of drug therapy or at times of dose changes, either increases or decreases. Families and caregivers should be advised of the need for close observation and communication with the prescriber. Savella is not approved for use in the treatment of major depressive disorder. Savella is not approved for use in pediatric patients.**

**Please see additional Important Safety Information on reverse side and accompanying Full Prescribing Information.**

# Savella relieves symptoms of fibromyalgia[1]—stock today

**For more information on Savella, call 1-800-678-1605, ext 66297 or visit www.savella.com.**

## Additional Important Safety Information

### Contraindications

- Savella is contraindicated in patients taking monoamine oxidase inhibitors (MAOIs) concomitantly or within 14 days of discontinuing treatment with an MAOI. There have been reports of serious, sometimes fatal, reactions in patients started on an MAOI who were receiving or had recently discontinued a serotonin reuptake inhibitor. At least 5 days should be allowed after stopping Savella before starting an MAOI.
- Savella is contraindicated in patients with uncontrolled narrow-angle glaucoma and should be used with caution in patients with controlled narrow-angle glaucoma. In clinical trials, Savella was associated with an increased risk of mydriasis.

### Warnings and Precautions

- Prescriptions for Savella should be written for the smallest quantity of tablets, consistent with good patient management, in order to reduce the risk of overdose.
- Development of a potentially life-threatening serotonin syndrome or neuroleptic malignant syndrome (NMS)-like reactions have been reported with SSRIs and SNRIs alone, including Savella, but particularly with concomitant use of serotonergic drugs (including triptans), drugs that impair metabolism of serotonin (including MAOIs), or antipsychotics or other dopamine antagonists. The management of these reactions should include immediate discontinuation of Savella and the concomitant agent and supportive symptomatic treatment. The concomitant use of Savella with serotonin precursors is not recommended.
- SNRIs, including Savella, have been associated with cardiovascular effects, including cases of elevated blood pressure, requiring immediate treatment. In clinical trials, sustained increases in systolic and diastolic blood pressure occurred more frequently in Savella-treated patients compared to placebo. Among patients who were non-hypertensive at baseline, approximately twice as many patients receiving Savella, vs placebo, became hypertensive at the end of the study. Clinically significant increases in pulse (≥20 bpm) occurred more frequently in Savella-treated than placebo-treated patients. Blood pressure and heart rate should be monitored prior to initiating treatment with Savella and periodically throughout treatment. Pre-existing hypertension, tachyarrhythmias, and other cardiac diseases should be treated before starting therapy with Savella. Savella should be used with caution in patients with significant hypertension or cardiac disease. Concomitant use of Savella with drugs that increase blood pressure and pulse has not been evaluated, and such combinations should be used with caution. For patients who experience a sustained increase in blood pressure or heart rate while receiving Savella, either dose reduction or discontinuation should be considered.
- Savella should be prescribed with caution in patients with a history of seizure disorder or mania.
- Savella has been associated with mild elevations of ALT and AST (1 to 3 times the upper limit of normal). Rarely, reports of serious liver injury, including fulminant hepatitis, have been reported in patients treated with milnacipran. Savella should be discontinued in patients who develop jaundice or other evidence of liver dysfunction and should not be resumed unless another cause can be established.
- As with other SNRIs and SSRIs, withdrawal symptoms have been observed following discontinuation of milnacipran. A gradual dose reduction is recommended.
- Hyponatremia may occur as a result of treatment with SSRIs and SNRIs, including Savella. Elderly patients may be at greater risk. Discontinuation should be considered for patients with symptomatic hyponatremia.
- SSRIs and SNRIs, including Savella, may increase the risk of bleeding events. Patients should be cautioned regarding the risk of bleeding associated with concomitant use of Savella and NSAIDs, aspirin, warfarin, or other drugs that affect coagulation.
- Savella can affect urethral resistance and micturition. Caution is advised in the use of Savella in patients with a history of dysuria, notably in male patients with a history of obstructive uropathies as these patients may experience higher rates of genitourinary adverse events.
- Savella should ordinarily not be prescribed to patients with substantial alcohol use or evidence of chronic liver disease.

### Use in Specific Populations

- There are no adequate and well-controlled studies in pregnant women. Savella should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

### Adverse Reactions

- In clinical trials, the most frequently occurring adverse reaction was nausea (37% vs 20% for placebo). The most commonly occurring adverse reactions (≥5% and greater than placebo) were headache (18% vs 14%), constipation (16% vs 4%), dizziness (10% vs 6%), insomnia (12% vs 10%), hot flush (12% vs 2%), hyperhidrosis (9% vs 2%), vomiting (7% vs 2%), palpitations (7% vs 2%), heart rate increased (6% vs 1%), dry mouth (5% vs 2%), and hypertension (5% vs 2%).

**References: 1.** Savella (milnacipran HCl) prescribing information. Forest Pharmaceuticals, Inc. St. Louis, MO. **2.** Clauw DJ, Mease P, Palmer RH, Gendreau RM, Wang Y. Milnacipran for the treatment of fibromyalgia in adults: a 15-week, multicenter, randomized, double-blind, placebo-controlled, multiple-dose clinical trial. *Clin Ther.* 2008;30(11):1988-2004.

**Please see Boxed Warning on front and accompanying Full Prescribing Information.**

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Savella® milnacipran HCl ™

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