

Savella (milnacipran) FDA-Approved for Fibro

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The Food and Drug Administration (FDA) on Jan. 14, approved Savella as the first drug specifically for the treatment of fibromyalgia ... and not just the pain. During clinical trials, the Fibromyalgia Network has been referring to Savella as its study name "milnacipran" in Fibromyalgia Network Journal articles. While two other medications have been given FDA approval for treating fibromyalgia pain, they were already available on the U.S. market for other medical uses.

Given the FDA's track record of okaying less than 20 new drugs per year, the approval of Savella represents a major milestone for people with invisible body-wide pain and the multiple symptoms of fibromyalgia. It's a sign that the pharmaceutical industry is finally waking up to the fact that their shareholders and patients with fibromyalgia can both benefit from new drug developments.

U.S. pharmacies are expected to stock Savella by April, but patients living in several countries throughout Europe and Asia already have access to the drug under the brand name Ixel. Although Ixel is marketed as an antidepressant in these countries (not as a treatment for fibromyalgia), this drug has a good safety record that dates back to 1997.

Savella is believed to work in the central nervous system to increase norepinephrine (NE) and serotonin.¹ These two transmitting substances are part of the pain inhibitory system that helps filter out pain signals in the spinal cord so that fewer travel all the way up to the brain. One study showed that serotonin and NE are both low in the spinal fluid of people with fibromyalgia, which could explain why Savella is particularly useful for treating this condition.² The drug is in the class of dual reuptake inhibitors, the same as Cymbalta (duloxetine), but it exerts a much stronger effect on NE than serotonin. When NE and serotonin are released at the nerve endings, Savella latches on to these molecules and carries them back across the nerve junction so that they can be reused again to fight pain. In a way, the drug acts to recycle both NE and serotonin.

The FDA's approval of Savella for the treatment of fibromyalgia was based on a combined response to three different measures: (1) at least a 30 percent reduction in pain, (2) a patient overall rating of either "very much improved" or "much improved," and (3) significant progress in physical functioning. Although patients taking 100 mg or 200 mg of Savella per day showed greater improvement on these three measures than the patients in the placebo group (i.e., they took a sugar pill), individual responses are impossible to predict.³

Relief of fibromyalgia symptoms were noticeable after one week in the group of patient responders. In addition, Savella exerted a favorable effect on reducing daytime fatigue and memory/concentration difficulties. One of the desirable side effects of the drug is weight loss of about one to two pounds per month. However, the same reason that the drug helps people lose weight (e.g., its more potent effect on NE) also tends to cause a slight increase in both blood pressure and heart rate.

Other common side effects are nausea, headache, constipation, profuse sweating, dizziness, hot flush, insomnia, dry mouth, and palpitations. The nausea typically goes away after one to two weeks of continued therapy and may be minimized by taking the medication with food. Savella has little chance of interfering with the action of other medications, it takes about two hours to be fully absorbed by the digestive system, and half of it will end up in the urine after six-to-eight hours (e.g., its half-life). Due to this short half-life, it's recommended that the drug be taken twice a day.

Many fibromyalgia patients are chemically sensitive, so trying a new drug can be both frightening and exciting. There is no way to predict if you will respond favorably to Savella or if you will experience intolerable side effects. Then again, the drug may not do much of anything. Based on the drug's research studies and what is known about Savella, here are a few useful tips:

- If Effexor (venlafaxine) or Cymbalta provided you with pain relief but they caused you to gain weight, Savella could be the drug for you.
- Savella is also similar in action to many tricyclic antidepressants, such as amitriptyline, but unlike the tricyclics, it does not affect other transmitter substances that cause severe dry "cotton ball" mouth, next-day hangover sedation, and weight gain. If a tricyclic medication worked for you but the side effects turned you off, then you may find Savella to be just as effective but with minimal side effects.
- People with restless legs syndrome may discover that Savella makes their sleep worse. However, a smaller dose taken only in the morning may offer pain relief as long as you have appropriate treatment for your sleep disorder in the evening. Beware, however, if your daytime fatigue starts to get worse, it could be that your sleep disorder is being adversely affected (sometimes it is hard to know if sleep is being altered when one becomes overwhelmingly exhausted day and night).
- If you have difficult-to-control hypertension, the cardiovascular side effects of Savella could pose a problem. Then again, it is essential that your pain be treated too, so perhaps your doctor can re-evaluate your hypertension medications.
- If you require other medications that raise the level of serotonin in your body (e.g., tramadol for pain, sumatriptan for migraines, cyclobenzaprine for relaxing muscles, trazodone for aiding sleep, Lexapro or MAO inhibitors for depression, 5-HTP as an over-the-counter supplement, etc.), then you may not be a candidate for Savella. The combination of Savella with other serotonin boosting drugs could cause serotonin syndrome, a serious toxic consequence of too much serotonin in the body.
- If for any reason you feel that you need to go off of Savella, it is recommended that you taper your dose slowly to minimize the side effects of the drug's withdrawal from your body.

If you and your doctor think that you might be a candidate for Savella, it is best to begin at the lowest possible dose of 12.5 mg per day (taken in the morning with breakfast). If the drug is well-tolerated, the prescribing instructions say to take Savella twice a day, slowly working up to the recommended dose of 100 mg per day after a week. Some patients may prefer dosing up slower while charting their progress as well as possible side effects. If it becomes harder to fall asleep at night, talk to your doctor about reducing the evening dose or taking it earlier in the day. Depending upon your response, you may go up as high as 200 mg per day. If you are prescribed this medication, please review all precautions with your doctor and pharmacist. You may also visit www.savella.com for more details.

1. Obata H, et al. *Anesth Analg* 100:1406-10, 2005.
2. Russell IJ, et al. *Arthritis Rheum* 35:550-6, 1992.
3. Mease PJ, et al. *J Rheumatol* 36:2 8-12, 2009.