What is levomilnacipran and what does it treat?
Levomilnacipran is an antidepressant medication that works in the brain. It is approved for the treatment of major depressive disorder (MDD).

Symptoms of depression include:

- Depressed mood - feeling sad, empty, or tearful
- Feeling worthless, guilty, hopeless, and helpless
- Loss of interest or pleasure in your usual activities
- Sleep and eat more or less than usual (for most people it is less)
- Low energy, trouble concentrating, or thoughts of death (suicidal thinking)
- Psychomotor agitation ('nervous energy')
- Psychomotor retardation (feeling like you are moving and thinking in slow motion)
- Suicidal thoughts or behaviors

What is the most important information I should know about levomilnacipran?
Do not stop taking levomilnacipran, even when you feel better. Only your healthcare provider can determine the length of treatment that is right for you.

Missing doses of levomilnacipran may increase your risk for relapse in your symptoms.

Stopping levomilnacipran abruptly may result in one or more of the following withdrawal symptoms: irritability, nausea, dizziness, vomiting, nightmares, headache, and/or paresthesias (prickling, tingling sensation on the skin).

Depression is also a part of bipolar illness. People with bipolar disorder who take antidepressants may be at risk for "switching" from depression into mania. Symptoms of mania include "high" or irritable mood, very high self-esteem, decreased need for sleep, pressure to keep talking, racing thoughts, being easily distracted, frequently involved in activities with a large risk for bad consequences (for example, excessive buying sprees).

Medical attention should be sought if serotonin syndrome is suspected. Please refer to serious side effects for signs/symptoms.
Are there specific concerns about levomilnacipran and pregnancy?

If you are planning on becoming pregnant, notify your healthcare provider to best manage your medications. People living with MDD who wish to become pregnant face important decisions. Untreated MDD has risks to the fetus, as well as the mother. It is important to discuss the risks and benefits of treatment with your doctor and caregivers. For women who take antidepressant medications during weeks 13 through the end of their pregnancy (second and third trimesters), there is a risk that the baby can be born before it is fully developed (before 37 weeks).

Regarding breast-feeding, caution is advised since it is not known if levomilnacipran passes into breast milk, so it is important to discuss this with your doctor and caregivers.

What should I discuss with my healthcare provider before taking levomilnacipran?

- Symptoms of your condition that bother you the most
- If you have thoughts of suicide or harming yourself
- Medications you have taken in the past for your condition, whether they were effective or caused any adverse effects
- If you experience side effects from your medications, discuss them with your provider. Some side effects may pass with time, but others may require changes in the medication.
- Any other psychiatric or medical problems you have, including a history of bipolar disorder
- All other medications you are currently taking (including over the counter products, herbal and nutritional supplements) and any medication allergies you have
- Other non-medication treatment you are receiving, such as talk therapy or substance abuse treatment. Your provider can explain how these different treatments work with the medication.
- If you are pregnant, plan to become pregnant, or are breast-feeding
- If you drink alcohol or use drugs

How should I take levomilnacipran?

Levomilnacipran is usually taken one time per day with or without food.

Typically patients begin at a low dose of medicine and the dose is increased after a few days.

The dose usually ranges from 20 mg to 120 mg. Only your healthcare provider can determine the correct dose for you.

Take the capsules whole; do not open, crush, or chew.

Consider using a calendar, pillbox, alarm clock, or cell phone to help you remember to take your medication. You may also ask a family member or friend to remind you or check in with you to be sure you are taking your medication.

What happens if I miss a dose of levomilnacipran?

If you miss a dose of levomilnacipran, take it as soon as you remember, unless it is closer to the time of your next dose. Discuss this with your healthcare provider. Do not double your next dose or take more than what is prescribed.

What should I avoid while taking levomilnacipran?

Avoid drinking alcohol or using illegal drugs while you are taking antidepressant medications. They may decrease the benefits (e.g., worsen your condition) and increase adverse effects (e.g., sedation) of the medication.

What happens if I overdose with levomilnacipran?

If an overdose occurs, call your doctor or 911. You may need urgent medical care. You may also contact the poison control center at 1-800-222-1222.

A specific treatment to reverse the effects of levomilnacipran does not exist.
What are the possible side effects of levomilnacipran?

Common side effects
Nausea, vomiting, orthostatic hypotension, constipation, increased sweating, increased heart rate, palpitations, difficulty urinating, decreased appetite. These will often improve over the first week or two as you continue to take the medication.

Sexual side effects, such as problems with orgasm or ejaculatory delay, often do not diminish over time.

Rare/serious side effects
Serotonin syndrome (symptoms may include shivering, diarrhea, confusion, severe muscle tightness, fever, seizures, and death), increased blood pressure, low sodium (symptoms of low sodium levels may include headache, weakness, difficulty concentrating and remembering), angle closure glaucoma (symptoms of angle closure glaucoma may include eye pain, changes in vision, swelling or redness in or around eye).

Levomilnacipran may increase the risk of bleeding events. Combined use of aspirin, nonsteroidal anti-inflammatory drugs (e.g. ibuprofen, naproxen), warfarin, and other anti-coagulants may increase this risk. This may include gums that bleed more easily, nose bleed, or gastrointestinal bleeding. Some cases have been life threatening.

Are there any risks for taking levomilnacipran for long periods of time?
To date, there are no known problems associated with long term use of levomilnacipran. It is a safe and effective medication when used as directed.

What other medications may interact with levomilnacipran?
Levomilnacipran should not be taken with or within 2 weeks of taking monoamine oxidase inhibitors (MAOIs). These include phenelzine (Nardil®), tranylcypromine (Parnate®), isocarboxazid (Marplan®), and selegiline (Emsam®).

Although rare, there is an increased risk of serotonin syndrome when levomilnacipran is used with other medications that increase serotonin, such as other antidepressants, migraine medications called “triptans” (e.g., Imitrex®), some pain medications (e.g., tramadol (Ultram®)), and the antibiotic linezolid (Zyvox®).

Levomilnacipran may increase the effects of other medications that can cause bleeding (e.g., ibuprofen (Advil®, Motrin®), warfarin (Coumadin®), and aspirin).

The following medications may increase the levels and effects of levomilnacipran:

- Antibiotics, such as clarithromycin (Biaxin®) and azithromycin (Zithromax®)
- Antidepressants, such as fluoxetine (Prozac®), paroxetine (Paxil®), and nefazodone
- Antifungals, such as fluconazole (Diflucan®), ketoconazole (Nizoral®), and itraconazole (Sporanox®)
- The antiarrhythmia agent quinidine
- HIV medications, such as the protease inhibitors indinavir (Crixivan®), ritonavir (Norvir®), saquinavir (Fortovase®, Invirase®), and lopinavir/ritonavir (Kaletra®)

How long does it take for levomilnacipran to work?
Sleep, energy, or appetite may show some improvement within the first 1-2 weeks. Improvement in these physical symptoms can be an important early signal that the medication is working. Depressed mood and lack of interest in activities may need up to 6-8 weeks to fully improve.
Summary of Black Box Warnings

Suicidal Thoughts or Actions in Children and Adults

Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients with major depressive disorder (MDD), both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality) or unusual changes in behavior, whether or not they are taking antidepressant medications. This risk may persist until significant remission occurs.

In short-term studies, antidepressants increased the risk of suicidality in children, adolescents, and young adults when compared to placebo. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24. Adults age 65 and older taking antidepressants have a decreased risk of suicidality. Patients, their families, and caregivers should be alert to the emergence of anxiety, restlessness, irritability, aggressiveness and insomnia. If these symptoms emerge, they should be reported to the patient’s prescriber or healthcare professional. All patients being treated with antidepressants for any indication should watch for and notify their healthcare provider for worsening symptoms, suicidality and unusual changes in behavior, especially during the first few months of treatment.

Important Disclosure: This information is being provided as a community outreach effort of the College of Psychiatric and Neurologic Pharmacists. This information is for educational and informational purposes only and is not medical advice. This information contains a summary of important points and is not an exhaustive review of information about the medication. Always seek the advice of a physician or other qualified medical professional with any questions you may have regarding medications or medical conditions. Never delay seeking professional medical advice or disregard medical professional advice as a result of any information provided herein. The College of Psychiatric and Neurologic Pharmacists disclaims any and all liability alleged as a result of the information provided herein.