**MIANSERIN**

**Therapeutics**

**Brands** • Lerivon  
*see index for additional brand names*

**Generic?** Yes

**Class**
- Neuroscience-based Nomenclature: norepinephrine multi-modal (N-MM)
- Tetracyclic antidepressant
- Noradrenergic agent

**Commonly Prescribed for**  
(italic for FDA approved)
- Depression  
- Anxiety  
- Insomnia  
- Treatment-resistant depression

**How the Drug Works**
- Blocks alpha 2 adrenergic presynaptic receptor, thereby increasing norepinephrine neurotransmission  
- This is a novel mechanism independent of norepinephrine reuptake blockade  
- Blocks alpha 2 adrenergic presynaptic receptors but also alpha 1 adrenergic receptors on serotonin neurons, thereby causing little increase in serotonin neurotransmission  
- Blocks 5HT2A, 5HT2C, and 5HT3 serotonin receptors  
- Blocks H1 histamine receptors

**How Long Until It Works**

*Actions on insomnia and anxiety can start shortly after initiation of dosing*  
- Onset of therapeutic actions in depression, however, is usually not immediate, but often delayed 2–4 weeks  
- If it is not working within 6–8 weeks for depression, it may require a dosage increase or it may not work at all  
- May continue to work for many years to prevent relapse of symptoms

**If It Works**
- The goal of treatment is complete remission of current symptoms as well as prevention of future relapses
- Treatment most often reduces or even eliminates symptoms, but not a cure since symptoms can recur after medicine is stopped  
- Continue treatment until all symptoms are gone (remission)  
- Once symptoms gone, continue treating for 1 year for the first episode of depression  
- For second and subsequent episodes of depression, treatment may need to be indefinite  
- Use in anxiety disorders may also need to be indefinite

**If It Doesn’t Work**
- Many patients have only a partial response where some symptoms are improved but others persist (especially insomnia, fatigue, and problems concentrating)  
- Other patients may be nonresponders, sometimes called treatment-resistant or treatment-refractory  
- Consider increasing dose, switching to another agent or adding an appropriate augmenting agent  
- Consider psychotherapy  
- Consider evaluation for another diagnosis or for a comorbid condition (e.g., medical illness, substance abuse, etc.)  
- Some patients may experience apparent lack of consistent efficacy due to activation of latent or underlying bipolar disorder, and require antidepressant discontinuation and a switch to a mood stabilizer

**Best Augmenting Combos for Partial Response or Treatment Resistance**
- SSRIs, SNRIs, bupropion, reboxetine, atomoxetine (use combinations of antidepressant with caution as this may activate bipolar disorder and suicidal ideation)  
- Modafinil, especially for fatigue, sleepiness, and lack of concentration  
- Mood stabilizers or atypical antipsychotics for bipolar depression, psychotic depression, or treatment-resistant depression  
- Benzodiazepines

**Tests**
- Baseline ECG is recommended for patients over age 50
MIANSERIN (continued)

- May need to monitor blood count during treatment for those with blood dyscrasias, leucopenia, or granulocytopenia
- Since some antidepressants such as mianserin can be associated with weight gain, before starting treatment, weigh all patients and determine if the patient is already overweight (BMI 25.0–29.9) or obese (BMI ≥30)
- Before giving a drug that can cause weight gain to an overweight or obese patient, consider determining whether the patient already has pre-diabetes (fasting plasma glucose 100–125 mg/dL), diabetes (fasting plasma glucose >126 mg/dL), or dyslipidemia (increased total cholesterol, LDL cholesterol, and triglycerides; decreased HDL cholesterol), and treat or refer such patients for treatment, including nutrition and weight management, physical activity counseling, smoking cessation, and medical management

**SIDES EFFECTS**

**How Drug Causes Side Effects**
- Most side effects are immediate but often go away with time
  - Histamine 1 receptor antagonism may explain sedative effects
  - Histamine 1 receptor antagonism plus 5HT2C antagonism may explain some aspects of weight gain

**Notable Side Effects**
- Sedation
- Increased appetite, weight gain

**Life-Threatening or Dangerous Side Effects**
- Rare seizures
- Rare blood dyscrasias
- Rare induction of mania
- Rare activation of suicidal ideation and behavior (suicidality) (short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo beyond age 24)

**Weight Gain**
- Many experience and/or can be significant in amount

**Sedation**
- Many experience and/or can be significant in amount
- Generally transient

**What to Do About Side Effects**
- Wait
- Wait
- Wait
- Switch to another drug

**Best Augmenting Agents for Side Effects**
- Often best to try another antidepressant monotherapy prior to resorting to augmentation strategies to treat side effects
- Many side effects are dose-dependent (i.e., they increase as dose increases, or they reemerge until tolerance redevelops)
- Many side effects are time-dependent (i.e., they start immediately upon dosing and upon each dose increase, but go away with time)
- Many side effects cannot be improved with an augmenting agent
- Activation and agitation may represent the induction of a bipolar state, especially a mixed dysphoric bipolar II condition sometimes associated with suicidal ideation, and require the addition of lithium, a mood stabilizer or an atypical antipsychotic, and/or discontinuation of mianserin

**DOSING AND USE**

**Usual Dosage Range**
- 30–60 mg/day

**Dosage Forms**
- Tablet 10 mg, 30 mg, 60 mg

**How to Dose**
- Initial 30 mg/day; maximum usually 90 mg/day
**Dosing Tips**
- Can be dosed once or twice daily
- If intolerable anxiety, insomnia, agitation, akathisia, or activation occur either upon dosing initiation or discontinuation, consider the possibility of activated bipolar disorder and switch to a mood stabilizer or an atypical antipsychotic

**Overdose**
- Relatively safe in overdose; sedation, hypertension, or hypotension

**Long-Term Use**
- Safe

**Habit Forming**
- Not expected

**How to Stop**
- Taper is prudent to avoid withdrawal effects, but tolerance, dependence, and withdrawal effects not reliably reported

**Pharmacokinetics**
- Half-life 12–29 hours

**Drug Interactions**
- Tramadol increases the risk of seizures in patients taking an antidepressant
- Carbamazepine and phenytoin may reduce mianserin levels
- Theoretically could cause a fatal “serotonin syndrome” when combined with MAOIs, so do not use with MAOIs or for at least 14 days after MAOIs are stopped unless you are an expert and only for treatment-resistant cases that may justify the risk
- Do not start an MAOI for at least 5 half-lives (5 to 7 days for most drugs) after discontinuing mianserin

**Other Warnings/Precautions**
- Drug may lower white blood cell count (rare; may not be increased compared to other antidepressants but controlled studies lacking)
- Avoid alcohol, which may increase sedation and cognitive and motor effects

**SPECIAL POPULATIONS**

**Renal Impairment**
- Dose adjustment not necessary

**Hepatic Impairment**
- Dose adjustment not necessary

**Cardiac Impairment**
- Baseline ECG is recommended
- Drug should be used with caution

**Elderly**
- Baseline ECG is recommended for patients over age 50
- Some patients may tolerate lower doses better
- Blood dyscrasias, though still rare, may be more common in the elderly

**Children and Adolescents**
- Carefully weigh the risks and benefits of pharmacological treatment against the risks and benefits of nontreatment with antidepressants and make sure to document this in the patient’s chart
- Monitor patients face-to-face regularly, particularly during the first several weeks of treatment

**Do Not Use**
- If patient is taking an MAOI
- If there is a proven allergy to mianserin

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**Potential Advantages**
- Patients particularly concerned about sexual side effects
- Patients with symptoms of anxiety
- As an augmenting agent to boost the efficacy of other antidepressants
- Patients with cardiovascular disease

**Potential Disadvantages**
- Patients particularly concerned about gaining weight
- Patients with low energy

**Primary Target Symptoms**
- Depressed mood
- Sleep disturbance
- Anxiety

**Pearls**
- Adding alpha 2 antagonism to agents that block serotonin and/or norepinephrine reuptake may be synergistic for severe depression
- Adding mianserin to venlafaxine or SSRIs may reverse drug-induced anxiety and insomnia
- Efficacy of mianserin for depression in cancer patients has been shown in small controlled studies
- Only causes sexual dysfunction infrequently
- Generally better tolerated than TCAs, including safer in overdose
- General lack of cardiovascular toxicity

**Pregnancy**
- Controlled studies have not been conducted in pregnant women
- Not generally recommended for use during pregnancy, especially during first trimester
- Must weigh the risk of treatment (first trimester fetal development, third trimester newborn delivery) to the child against the risk of no treatment (recurrence of depression, maternal health, infant bonding) to the mother and child
- For many patients this may mean continuing treatment during pregnancy

**Breast Feeding**
- Some drug is found in mother’s breast milk
- If child becomes irritable or sedated, breast feeding or drug may need to be discontinued
- Immediate postpartum period is a high-risk time for depression, especially in women who have had prior depressive episodes, so drug may need to be reinstituted late in the third trimester or shortly after childbirth to prevent a recurrence during the postpartum period
- Must weigh benefits of breast feeding with risks and benefits of antidepressant treatment versus nontreatment to both the infant and the mother
- For many patients, this may mean continuing treatment during breast feeding
Suggested Reading


