Milnacipran hydrochloride (mil-NAY-si-pran HYE-droe-KLOR-ide)

CLASSIFICATION(S):
Antidepressant, serotonin and norepinephrine reuptake inhibitor

PREGNANCY CATEGORY: C

Rx: Savella.

USES
Management of fibromyalgia.

ACTION/KINETICS

Action
The exact mechanism of milnacipran to improve the symptoms of fibromyalgia is not known. The drug is a potent inhibitor of neuronal reuptake of norepinephrine and serotonin.

Pharmacokinetics
Absolute bioavailability is 85–90%.
Maximum concentration: 2–4 hr.
Steady state levels: 36–48 hr. Unchanged drug (55%) and metabolites excreted in the urine. $t_\frac{1}{2}$, terminal: 6–8 hr. AUC and terminal elimination $t_\frac{1}{2}$ increased in impaired renal function.

Plasma protein binding: 13%.

CONTRAINDICATIONS
Concomitant use with MAOIs. Uncontrolled narrow-angle glaucoma, end-stage renal disease, substantial alcohol use or chronic liver disease, lactation.

SPECIAL CONCERNS

• Suicidality and antidepressant drugs. Milnacipran is a selective serotonin and norepinephrine reuptake inhibitor, similar to some drugs used for the treatment of depression and other psychiatric disorders. Antidepressants increased the risk, compared with placebo, of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of major depressive disorder 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 with placebo in adults older than 24 years of age; there was a reduction in risk with antidepressants compared with placebo in adults 65 years of age and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Appropriately monitor clients of all ages who are started on milnacipran and observe closely for clinical worsening, suicidality, or unusual changes in behavior. Advise families and caregivers of the need for close observation and communication with the prescriber. Milnacipran is not approved for use in the treatment of major depressive disorder. Milnacipran is not approved for use in children.

• Contains tartrazine which may cause allergic reactions (including bronchial asthma) in susceptible individuals.

• Use with caution in severe hepatic impairment, in controlled narrow-angle glaucoma, with a history of seizure disorders, with a history of dysuria (e.g., men with prostatic hypertrophy) and when taken in combination with other CNS drugs.

• Safety and efficacy not determined in children younger than 17 years of age with fibromyalgia.

SIDE EFFECTS

Most Common
N&V, constipation, hot flush, headache, dizziness, insomnia, hyperhidrosis, palpitations, ↑ HR, hypertension, dry mouth, URTI.

CNS: Headache, insomnia, dizziness, migraine, anxiety, paresthesia, tension headache, tremor, hypotension, depression, fall, irritability, pyrexia, somnolence, stress, convulsions (including grand mal), delirium, hallucination, loss of consciousness, neuroleptic malignant syndrome, Parkinsonism, worsening of depression and/or emergence of suicidal ideation and suicidality, unusual changes in behavior, withdrawal symptoms. Serotonin syndrome: Agitation, coma, hallucinations, hyperthermia, labile BP, tachycardia, hyperreflexia, incoordination, diarrhea, N&V. GI: N&V, constipation, dry mouth, abdominal pain, decreased appetite, abdominal distension, diarrhea, dysgeusia, dyspepsia, flatulence, GERD, hepatitis. CV: Palpitations, increased HR, hypertension,
tachycardia, flushing, increased BP, hypertensive crisis, SVT, increased risk of bleeding events. **Respiratory:** URTI, dyspnea, chest discomfort, chest pain. **Dermatologic:** Hyperhidrosis, pruritus, rash, erythema multiforme, Stevens-Johnson syndrome. GU: Cystitis, UTI, acute renal failure, galactorrhea. In men: Dysuria, ejaculation disorder/failure, erectile dysfunction, decreased libido, prostatitis, scrotal pain, testicular pain/swelling, urethral pain, urinary hesitation/retention, decreased urine flow. **Metabolic/Nutritional:** Hypercholesterolemia, peripheral edema, decreased/increased weight, anorexia, hypercalcemia. Hematologic: Leukopenia, neutropenia, thrombocytopenia. **Ophthalmic:** Blurred vision, accommodation disorder. **Body as a whole:** Hot flush, fatigue, chills, night sweats.

**Hematologic:** Leukopenia, neutropenia, thrombocytopenia.

**Laboratory Test Considerations**
- ALT, AST. Hyperprolactinemia, hyponatremia.

**Diagnosis**

**OVD MANAGEMENT**

Symptoms: Increased BP, cardiorespiratory arrest, changes in the level of consciousness (from somnolence to coma), confusion, dizziness, and increased hepatic enzymes. Treatment: There is no specific antidote. Ensure an adequate airway, oxygenation, and ventilation. Monitor cardiac rhythm and vital signs. Gastric lavage with a large-bore orogastric tube with appropriate airway protection may be used if performed soon after ingestion or in symptomatic clients. Activated charcoal may also be used. Induction of emesis is not recommended. Forced diuresis, dialysis, hemoperfusion, and exchange transfusion are not likely to be beneficial.

**Drug Interactions**

- Alcohol / May aggravate preexisting liver disease.
- Aspirin / ↑ Bleeding effects of aspirin; use together with caution.
- Clomipramine / ↑ Euphoria and postural hypotension in those who switched from clomipramine to milnacipran.
- Clonidine / May ↓ antihypertensive effect of clonidine.

**Digoxin** / Possible postural hypotension and tachycardia in combination with IV digoxin; avoid coadministration.

**Epinephrine** / Possible paroxysmal hypertension and arrhythmia.

**Lithium** / Possible serotonin syndrome; see Administration/Storage.

**Norepinephrine** / Possible paroxysmal hypertension and arrhythmia.

**NSAIDs** / ↑ Bleeding effects of NSAIDs; use together with caution.

**Monoamine oxidase inhibitors** / Possible R/T additive serotonergic effects.

**Serotonin drugs** (e.g., SNRIs, SSRIs, tramadol, triptans) / Possible hypertension and coronary artery vasoconstriction.

**HOW SUPPLIED**

Tablets: 12.5 mg, 25 mg, 50 mg, 100 mg.

**DOSAGE**

- TABLETS

Fibromyalgia.

Adults, usual: 50 mg twice a day. **Dose titration:** Give 12.5 mg once on day 1, 12.5 mg twice a day on days 2 and 3, 25 mg twice a day on days 4–7, and 50 mg twice a day after day 7. May increase dose to 100 mg twice a day based on individual response. **Maximum dose:** 200 mg/day (i.e., 100 mg twice a day).

**Nursing Considerations**

**Administration/Storage**

1. Give with or without food, although may improve tolerability if taken with food.

2. After extended use, taper the dose; do not abruptly discontinue.

3. For those with severe renal impairment (i.e., Ccr from 5–29 mL/min), reduce the maintenance dose by 50% to 25 mg twice a day.

4. At least 14 days should elapse between discontinuation of a MAOI and initiation of milnacipran therapy. In addition, at least 5 days should elapse after stopping milnacipran before starting a MAOI.

ASSESSMENT
1. Note reasons for therapy, onset, characteristics of S&S, ROM/mobility, other agents trialed, outcome.
2. Document clinical presentation and assess for any depression; rate pain levels.
3. List drugs prescribed to ensure none interact.
4. Monitor VS, weight, CBC, lytes, renal and LFTs; may need to adjust dose with dysfunction.
5. Note medical history, especially seizures, CAD. Assess ECG for arrhythmia.
6. Drug contains FD&C yellow No. 5 (tartrazine); use caution.

CLIENT/FAMILY TEACHING
1. Take twice a day as directed with or without food to control symptoms of fibromyalgia.
2. Avoid activities that require mental alertness until effects realized; may experience diminished mental and physical capacities.
3. Do not stop taking abruptly, should be tapered if stopping therapy to prevent withdrawal symptoms.
4. Avoid alcohol, NSAIDS, and aspirin during therapy; may affect clotting.
5. Report increased anxiety, agitation, panic attacks, aggressiveness, or other unusual behavioral changes, worsening of depression, and suicidal ideation.
6. Monitor BP and heart rate and report if persistently elevated.
7. Practice reliable contraception and avoid pregnancy.
8. Keep all F/U to assess response, labs, and for adverse SE.

OUTCOMES/Evaluate
↓ Pain and ↑ mobility with fibromyalgia

**Bold Italic** = life threatening side effect  ■ = black box warning  ♦ = Available in Canada