DULOXETINE (Cymbalta, Drizalma Sprinkle) Fact Sheet [G]

Bottom Line:
Duloxetine is the main SNRI alternative to venlafaxine/desvenlafaxine. It has a niche for depressed patients with various comorbid pain syndromes. However, you should balance this advantage against its potentially serious (though rare) hepatic side effects.

FDA Indications:
Major depression; generalized anxiety disorder (GAD) (children ages 7+ and adults); diabetic peripheral neuropathic pain; fibromyalgia; chronic musculoskeletal pain (including osteoarthritis and chronic low back pain).

Off-Label Uses:
Other neuropathic or chronic pain disorders; other anxiety disorders; stress urinary incontinence.

Dosage Forms:
Delayed-release capsules (Drizalma Sprinkle, [G]): 20 mg, 30 mg, 40 mg, 60 mg.

Dosage Guidance:
- Depression and GAD: Start 40–60 mg/day; may be divided (20 or 30 mg BID) or given as a single daily dose; target dose 60 mg QD; for doses >60 mg/day, titrate in increments of 30 mg/day over one week to max 120 mg/day, although doses >60 mg/day not shown to be more effective.
- Fibromyalgia and chronic pain: Start 30 mg QD, increase to target 60 mg QD; max dose 60 mg/day.
- Diabetic neuropathy: Start, target, and maximum dose of 60 mg QD.
- Dose timing: Depends on patient preference, since it causes drowsiness in some but insomnia in others. Let patients experiment until they get it right.

Monitoring: LFTs if suspect liver disease; periodic blood pressure.

Cost: $; Drizalma Sprinkle: $

Side Effects:
- Most common: Nausea, dry mouth, constipation, diarrhea, decreased appetite, vomiting, fatigue, insomnia, dizziness, agitation, sweating, headache, urinary hesitation, and sexual side effects.
- Serious but rare: Rare cases of hepatic failure (including fatalities) have been reported (too rare to require routine LFTs in all patients). Hepatitis with abdominal pain, hepatomegaly, elevated transaminases >20 times normal, with and without jaundice observed. May cause orthostatic hypotension or syncope, especially in first week of therapy and after dose increases. Urinary retention reported; hospitalization and/or catheterization were necessary in some cases.
- Pregnancy/breastfeeding: Not enough data to recommend.

Mechanism, Pharmacokinetics, and Drug Interactions:
- Serotonin and norepinephrine reuptake inhibitor.
- Metabolized primarily through CYP1A2 and 2D6; inhibitor of CYP2D6; t ½: 12 hours.
- Avoid use with MAOIs, other serotonergic medications. Caution with drugs metabolized by CYP2D6 (eg, paroxetine, fluoxetine, aripiprazole, iloperidone, risperidone, atomoxetine, beta blockers) as their levels may be increased. Potent inhibitors of CYP2D6 (eg, paroxetine, fluoxetine, quinidine) and CYP1A2 (eg, fluvoxamine, ciprofloxacin) may increase duloxetine levels.

Clinical Pearls:
- Duloxetine advantages vs venlafaxine: milder discontinuation symptoms; less hypertension; less toxic in overdose; FDA indications for pain syndromes. Duloxetine disadvantages vs venlafaxine: potential hepatic toxicity; greater potential for drug interactions.
- Since capsules are delayed release, they should be swallowed whole; do not chew or crush. Although the manufacturer does not recommend opening the capsules, their contents may be sprinkled on applesauce or in apple juice and swallowed immediately.
- Avoid in patients with a history of heavy alcohol use or chronic hepatic disease because of the possibility that duloxetine and alcohol may interact, causing hepatic injury, or the possibility that duloxetine may aggravate preexisting hepatic disease.
- Drizalma Sprinkle is a new formulation for use in patients with swallowing difficulty, either by sprinkling over applesauce or administering via nasogastric tube.

Fun Fact:
Duloxetine is approved in Europe for stress urinary incontinence, but the FDA refused this indication in the US because of concerns regarding liver toxicity and potential suicidal ideation.