FLUOXETINE (Prozac, Prozac Weekly) Fact Sheet [G]

Bottom Line:

Fluoxetine's wide spectrum of indications and its long track record make it a go-to SSRI, and it is often favored in patients who could use some activation. Its main disadvantage is its high potential for drug interactions.

FDA Indications:

Major depression (8+ years); OCD (7+ years); panic disorder; bulimia; PMDD (as Sarafem).

Off-Label Uses:

PTSD; social anxiety disorder.

Dosage Forms:

- **Capsules (G):** 10 mg, 20 mg, 40 mg.
- **Tablets (G):** 10 mg, 20 mg, 60 mg.
- **Oral solution (G):** 20 mg/5 mL.
- **Delayed-release capsules (G):** 90 mg.

Dosage Guidance:

- Start 10–20 mg QAM; may ↑ by 10–20 mg/day increments after several weeks; max dose 50 mg/day (depression), 60 mg/day (bulimia, panic disorder). Target and max dose in OCD: 80 mg/day.
- Start 5–10 mg QAM in panic disorder to minimize increased anxiety and panic.
- Delayed-release capsules (Prozac Weekly): Start 90 mg Qweek seven days after last dose of 20 mg QAM.
- PMDD (Sarafem): 20 mg QAM continuously or only on cycle days 15–28 (14 days prior to anticipated onset of menstruation).
- In children ages 6–7 (off-label): Start 5 mg QD, increase by 5 mg/day increments weekly; max 30 mg/day. Ages 8–17: Start 10 mg QD, increase by 10 mg/day increments weekly; max 60 mg/day. Many children and adolescents will show good treatment response at 10 mg/day.
- Dose timing: Most respond best to morning dosing given its activating effects.

Monitoring: Sodium in patients at risk.

Cost: $

Side Effects:

- Most common: Nausea, diarrhea, nervousness, insomnia, abnormal dreams, anorexia, sweating, tremor, sexual side effects, headache, rash.
- Serious but rare: Hyponatremia, mainly in the elderly; gastrointestinal bleeding, especially when combined with NSAIDs such as ibuprofen.
- Pregnancy/breastfeeding: Considered relatively safe in pregnancy; avoid in breastfeeding due to long half-life.

Mechanism, Pharmacokinetics, and Drug Interactions:

- Serotonin reuptake inhibitor.
- Metabolized primarily through CYP2D6; potent inhibitor of CYP2C9/2C19 and 2D6; t ½: 4–6 days (fluoxetine), 9 days (norfluoxetine metabolite).
- Avoid use with MAOIs (five-week washout if switching to MAOI); avoid other serotonergic agents (serotonin syndrome). Caution with substrates of 2C9/19 and 2D6.

Clinical Pearls:

- Generally less favored in patients with bipolar disorder, as they may switch to mania due to fluoxetine's long half-life (compared to other antidepressants that can be washed out more quickly).
- Also due to long half-life, effects of dose changes will not be fully reflected for several weeks.
- The benefit of the long half-life is that patients are much less likely to experience serotonin discontinuation symptoms after a missed dose or when discontinuing treatment.
- Of the SSRIs, fluoxetine is most likely to cause rash.
- Fluoxetine/olanzapine combination (Symbyax) is approved for acute depression in bipolar disorder and treatment-resistant depression. See olanzapine fact sheet in Antipsychotics chapter.
- Often considered a first-line agent for kids with depression and anxiety disorders.

Fun Fact:

Eli Lilly was criticized for reformulating fluoxetine in a pink color and calling it "Sarafem" for PMDD. The drug's aggressive marketing campaign included a commercial featuring a harried woman asking herself whether she has PMDD while grocery shopping.