PAROXETINE (Brisdelle, Paxil, Paxil CR, Pexeva) Fact Sheet [G]

Bottom Line:
Paroxetine is the least favored SSRI due to its side effect profile (greatest sexual side effects, weight gain, sedation, constipation), drug interaction profile, and risk for discontinuation syndrome. However, its wide range of FDA anxiety indications leads some clinicians to favor it for patients with significant anxiety.

FDA Indications:
Major depression; OCD; panic disorder; social anxiety disorder; generalized anxiety disorder (GAD); PTSD; PMDD; vasomotor symptoms associated with menopause (Brisdelle).

Off-Label Uses:
Premature ejaculation.

Dosage Forms:
- **Tablets (Paxil, Pexeva, [G]):** 10 mg, 20 mg, 30 mg, 40 mg.
- **Capsules (Brisdelle, [G]):** 7.5 mg.
- **Oral suspension (Paxil, [G]):** 10 mg/5 mL.
- **ER tablets (Paxil CR, [G]):** 12.5 mg, 25 mg, 37.5 mg.

Dosage Guidance:
- Start 10–20 mg QD in evening or bedtime; may ↑ by 10 mg/day increments weekly.
- ER: Start 12.5–25 mg QD; may ↑ by 12.5 mg/day increments weekly.
- Max dose: 50 mg/day (depression, GAD, PTSD); 60 mg/day (OCD, panic disorder, social anxiety disorder); 75 mg/day (ER). Max dose in elderly: 40 mg/day (IR); 50 mg/day (ER).
- PMDD: Start 12.5 mg ER QD; may ↑ to max 25 mg/day after one week. Or, 12.5–25 mg ER QD on cycle days 15–28 (14 days prior to anticipated onset of menstruation).
- Vasomotor menopausal symptoms: 7.5 mg QHS.
- Dose timing: Usually best given at bedtime due to sedation.

Monitoring: Sodium in patients at risk; ECG in patients on citalopram >40 mg/day or if cardiac disease.

Cost: IR/ER: $; capsule, oral suspension: $$

Side Effects:
- Most common: Nausea, constipation, dry mouth, somnolence, sedation, sexual side effects, weight gain, sweating, tremor, headache.
- Serious but rare: Hyponatremia, mainly in the elderly; gastrointestinal bleeding, especially when combined with NSAIDs such as ibuprofen.
- Pregnancy/breastfeeding: Mixed data, less favored than others, and should generally be avoided in pregnancy; safe in breastfeeding.

Mechanism, Pharmacokinetics, and Drug Interactions:
- Serotonin reuptake inhibitor.
- Metabolized primarily through 2D6; potent inhibitor of 2D6; t ½: 21 hours.
- Avoid use with MAOIs (two-week washout if switching to MAOI); avoid other serotonergic agents (serotonin syndrome). Caution with substrates of 2D6.

Clinical Pearls:
- Paroxetine has the widest range of FDA-approved indications; however, it is not approved for any use in children or adolescents.
- Ideal medication for thin patients with insomnia and significant anxiety who are not very sexually active.
- Caution with medications that require CYP2D6 to convert into active drug or active metabolite (eg, tamoxifen, tramadol, hydrocodone, codeine) as therapeutic effects will be lowered by paroxetine's potent inhibition of CYP2D6. This is the opposite effect of the majority of 2D6 substrates, which will have their levels increased when combined with paroxetine.
- Paroxetine seems to pose the greatest risk to a fetus in terms of cardiovascular malformation. Unless the benefits of paroxetine outweigh discontinuation or alternative antidepressants, a switch to another antidepressant should be considered.

Fun Fact:
In 2012, paroxetine manufacturer GlaxoSmithKline was fined $3 billion by the U.S. Department of Justice for unlawfully promoting paroxetine's use in kids based on misleading data from its infamous Study 329. *New Scientist* wrote in 2015: "You may never have heard of it, but Study 329 changed medicine."