SELECTIVE SEROTONIN REUPTAKE INHIBITOR

Citalopram

Celexa

Clean, highly selective SSRI with few interactions, now constrained by a hard dose ceiling imposed for dose-dependent QT prolongation.

USUAL ADULT RANGE	HARD CEILING	HALF-LIFE	ONSET
20-40 mg/day PO	40 mg/day; 20 mg if >60 y	35 h; CYP2C19, 3A4, 2D6	1-2 wks; 6-8 wks full

⚠ FDA BOXED WARNING

Suicidal thoughts and behaviors: antidepressants increased the risk of suicidality in pediatric and young adult patients in short-term studies. Closely monitor all treated patients for clinical worsening and emergence of suicidal thoughts and behaviors. Not approved for use in pediatric patients.

INDICATIONS

- FDA-approved only for major depressive disorder in adults, given once daily at **20-40 mg/day** with or without food.
- Off-label but well supported for generalized anxiety disorder, panic disorder, and social anxiety disorder at the same dose range.
- Off-label for obsessive-compulsive disorder, though the QT ceiling prevents the high doses that OCD typically requires for response.
- Off-label for premenstrual dysphoric disorder, given either continuously or restricted to the luteal phase of each menstrual cycle.
- Off-label at **20-30 mg/day** for agitation in Alzheimer disease, where the CitAD trial showed benefit offset by QT and cognitive effects.
- Not approved for any pediatric indication, so all use under age 18 is off-label and requires close suicidality monitoring.

DOSING & TITRATION

- Start **20 mg** PO once daily and increase to a maximum of **40 mg/day** after no less than one week if response is inadequate.
- Doses above **40 mg/day** are not recommended at any age because QT prolongation increases with concentration without added efficacy.
- Cap the dose at **20 mg/day** in patients over 60 years, in hepatic impairment, in CYP2C19 poor metabolizers, and with any CYP2C19 inhibitor.
- Available as 10, 20, and 40 mg tablets and a 10 mg/5 mL oral solution, which is useful for slow tapers and for pediatric off-label use.
- No adjustment is required in mild to moderate renal impairment; use caution and consider slower titration if creatinine clearance is under 20 mL/min.
- Taper gradually over two to four weeks when stopping, since abrupt withdrawal causes dizziness, paresthesia, insomnia, and irritability.

MECHANISM OF ACTION

- The most selective serotonin transporter inhibitor of the SSRIs, with essentially no affinity for norepinephrine or dopamine transporters.
- Racemic mixture of S-citalopram, which carries all the transporter activity, and R-citalopram, which is inactive and may blunt the S-enantiomer.
- Increased synaptic 5-HT gradually desensitizes 5-HT1A autoreceptors, restoring raphe firing over two to six weeks as symptoms improve.
- Mild histamine H1 antagonism explains the modest sedation seen at higher doses relative to fluoxetine or sertraline.
- Blocks the cardiac hERG potassium channel in a concentration-dependent way, which is the pharmacologic basis of its QT ceiling.

PHARMACOKINETICS

- Bioavailability is about 80 percent and is unaffected by food, with peak plasma concentrations reached roughly four hours after a dose.
- Half-life is about **35 hours**, giving once-daily dosing and steady state at approximately one week after initiation or dose change.
- Metabolized by CYP2C19 and CYP3A4 with a minor CYP2D6 contribution; demethylcitalopram is far less potent and clinically unimportant.
- CYP2C19 poor metabolizers reach roughly double the plasma exposure, which is why their maximum dose is capped at **20 mg/day**.
- Only a weak CYP2D6 inhibitor, so citalopram is one of the easiest antidepressants to combine with other psychotropic medication.

ADVERSE EFFECTS

- Nausea, dry mouth, somnolence, insomnia, and increased sweating are the most common early effects and usually settle within two weeks.
- Sexual dysfunction affects roughly **30-40 percent** of patients and includes reduced libido, delayed ejaculation, and anorgasmia.
- Dose-dependent QTc prolongation is the defining safety issue, with mean increases of about 8 msec at 20 mg/day and 19 msec at 60 mg/day.
- Torsades de pointes has been reported in overdose and with concurrent QT-prolonging drugs, hypokalemia, or hypomagnesemia.
- Hyponatremia from SIADH, increased bleeding on NSAIDs or anticoagulants, and treatment-emergent mania are the other prescribing-relevant risks.
- Weight change is close to neutral over the first year, less than paroxetine but slightly more than fluoxetine in comparative cohorts.

MONITORING

- Obtain a baseline ECG in patients with cardiac disease, bradycardia, electrolyte disturbance, or concurrent QT-prolonging drugs.
- Correct hypokalemia and hypomagnesemia before starting, and recheck electrolytes when adding diuretics or during any illness with vomiting.
- Monitor suicidality, activation, and agitation weekly for four weeks and after each dose change, with special attention under age 25.
- Check serum sodium at baseline and within two to four weeks in older adults, diuretic users, and anyone with new confusion or falls.
- Track response with PHQ-9 or GAD-7 every two to four weeks, recognizing that dose escalation beyond 40 mg/day is not an option.

INTERACTIONS & CAUTIONS

- Contraindicated with MAOIs and within **14 days** of stopping one, and with linezolid or intravenous methylene blue.
- Any CYP2C19 inhibitor, including omeprazole, esomeprazole, fluconazole, fluvoxamine, and cimetidine, caps the dose at **20 mg/day**.
- Avoid combining with amiodarone, sotalol, methadone, ondansetron, or antipsychotics that prolong QT unless an ECG is followed closely.
- Additive serotonin syndrome risk with triptans, tramadol, fentanyl, lithium, and St. John's wort; watch for clonus and hyperthermia.
- Increases bleeding risk with aspirin, NSAIDs, and anticoagulants through impaired platelet serotonin uptake.

SPECIAL POPULATIONS

- No consistent teratogenic signal in pregnancy, though late-gestation exposure carries small risks of neonatal adaptation and pulmonary hypertension.
- Compatible with breastfeeding at a relative infant dose near 3 to 5 percent, higher than sertraline but generally considered acceptable.
- Not approved in pediatrics; escitalopram carries the pediatric approval and is preferred when a citalopram-family agent is wanted in youth.
- In patients over 60 the maximum dose is **20 mg/day**, reflecting both reduced clearance and greater vulnerability to QT prolongation.
- Hepatic impairment also caps the dose at 20 mg/day, while renal impairment requires no change unless clearance falls below 20 mL/min.

PRESCRIBING PEARLS

- Hard ceiling: 40 mg/day, and 20 mg/day if over 60, hepatic impairment, or on a 2C19 inhibitor.
- Cleanest SSRI for interactions, so a good choice on complex medical regimens without QT risk.
- Omeprazole is the interaction people miss; it halves clearance and caps citalopram at 20 mg.

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NOTE

References follow APA 7th edition style. Dosing, boxed warnings, and interaction data change; confirm every clinical decision against the current FDA prescribing information (DailyMed) and your institution's formulary. This sheet is an educational quick reference and does not replace the full label or clinical judgment.