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# CLOMIPRAMINE (Anafranil) Fact Sheet [G]

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**Bottom Line:**

Clomipramine, which has more side effects than SSRIs, is usually considered a second-line medication for OCD.

**FDA Indications:**

OCD.

**Off-Label Uses:**

Cataplexy in narcolepsy; sleep terrors; sleepwalking; major depression; panic disorder; pain.

**Dosage Forms:**

**Capsules (Anafranil, [G]):** 25 mg, 50 mg, 75 mg.

**Dosage Guidance:**

- Start 25 mg QHS and ↑ by 25 mg/day every four to seven days to target dose 150–250 mg/day; max 250 mg/day.
- Using divided doses (BID to TID) may help with tolerability during initiation and titration, but can convert to QHS dosing to minimize daytime sedation.

**Monitoring:** Check clomipramine/norclomipramine levels (trough levels, 12 hours after last dose) in patients on higher doses (150 mg or higher) or in those with significant side effects. Optimal ranges: clomipramine + norclomipramine 220–500 ng/mL. Check ECG if history of cardiac disease.

**Cost:** \$\$

**Side Effects:**

- Most common: Sedation, dry mouth, constipation, weight gain, sexual side effects, urinary hesitation, blurred vision.
- Serious but rare: Seizure (especially at doses greater than 250 mg/day); cardiac effects including orthostasis, arrhythmias, QT prolongation, AV block.
- Pregnancy/breastfeeding: Some evidence of fetal heart defects and neonatal withdrawal; likely safe, but use caution in breastfeeding.

**Mechanism, Pharmacokinetics, and Drug Interactions:**

- As a tricyclic antidepressant, causes both serotonin and norepinephrine reuptake inhibition (more selective for serotonin).
- Metabolized by CYP1A2, 2C19, 2D6, 3A4;  $t_{1/2}$ : 32 hours (69 hours for active metabolite).
- Avoid MAOIs and other serotonergic agents. Caution with other anticholinergic agents or potent CYP inhibitors.

**Clinical Pearls:**

- Clomipramine is the only tricyclic antidepressant that is FDA approved for OCD. Efficacy is likely due to greater selectivity for serotonin reuptake inhibition.
- Used to be considered more effective than SSRIs for OCD, but recent studies show equivalent efficacy.
- Overdose toxicity with potentially serious cardiac effects or fatality with as little as 10-day supply.
- Pharmacokinetics are nonlinear, meaning higher-than-expected levels, longer  $t_{1/2}$ , and drug accumulation in the higher end of dosing range. Full effects of dosage increase in the higher range may not be seen for two weeks or longer.
- Like other serotonergic agents, discontinuation syndrome may occur with abrupt discontinuation; slow taper recommended.

**Fun Fact:**

Clomipramine is on the World Health Organization's Model List of Essential Medicines. This list includes the medications considered to be most effective and safe to meet the most important needs in a health system and is frequently used by countries to help determine local essential medicines.