# Anafranil (clomipramine hydrochloride) - Drug Summary

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Jump to Section
- BOXED WARNING
- THERAPEUTIC CLASS
- DEA CLASS
- ADULT DOSAGE & INDICATIONS
- PEDIATRIC DOSAGE & INDICATIONS
- ▼ View All Sections...

Related Drug Information ▼

## Anafranil
## (clomipramine hydrochloride)

## BOXED WARNING

Antidepressants increased the risk of suicidal thinking and behavior (suicidality) in short-term studies in children, adolescents, and young adults with major depressive disorder and other psychiatric disorders. Monitor and observe closely for clinical worsening, suicidality, or unusual changes in behavior in patients who are started on antidepressant therapy. Not approved for use in pediatric patients except for patients with obsessive compulsive disorder (OCD).

## THERAPEUTIC CLASS

Tricyclic antidepressant (TCA)

## DEA CLASS

RX

## ADULT DOSAGE & INDICATIONS

### Obsessive Compulsive Disorder

**Initial:** 25mg/day
**Titrate:** Increase gradually (in divided doses w/ meals) as tolerated during the first 2 weeks to approx 100mg/day; thereafter, may increase gradually over several weeks (2-3 weeks between further dose adjustments)
**Max:** 250mg/day

After titration, total daily dose may be given qhs

Maintain on lowest effective dose; periodically reassess long-term usefulness of the drug

### Dosing Considerations with MAOIs

**Switching to/from an MAOI for Psychiatric Disorders:**
Allow at least 14 days between discontinuation of an MAOI and initiation of treatment, and allow at least 14 days between discontinuation of treatment and initiation of an MAOI

**W/ Other MAOIs (eg, Linezolid, IV Methylene Blue):**
Do not start clomipramine in patients being treated w/ linezolid or IV methylene blue
In patients already receiving clomipramine, if acceptable alternatives are not available and benefits outweigh risks, d/c clomipramine and administer linezolid or IV methylene blue; monitor for serotonin syndrome for 2 weeks or until 24 hrs after the last dose of linezolid or IV methylene blue, whichever comes 1st. May resume clomipramine therapy 24 hrs after the last dose of linezolid or IV methylene blue

## PEDIATRIC DOSAGE & INDICATIONS

### Obsessive Compulsive Disorder

**10-17 Years:**
**Initial:** 25mg/day
**Titrate:** Increase gradually (in divided doses w/ meals) as tolerated during the first 2 weeks up to 3mg/kg/day or 100mg/day, whichever is smaller; thereafter, may increase gradually over several weeks (2-3 weeks between further dose adjustments)
**Max:** 3mg/kg/day or 200mg/day, whichever is smaller

After titration, total daily dose may be given qhs

Maintain on lowest effective dose; periodically reassess long-term usefulness of the drug

### Dosing Considerations with MAOIs

**Switching to/from an MAOI for Psychiatric Disorders:**
Allow at least 14 days between discontinuation of an MAOI and initiation of treatment, and allow at least 14 days between discontinuation of treatment and initiation of an MAOI

**W/ Other MAOIs (eg, Linezolid, IV Methylene Blue):**
Do not start clomipramine in patients being treated w/ linezolid or IV methylene blue
In patients already receiving clomipramine, if acceptable alternatives are not available and benefits outweigh risks, d/c clomipramine and administer linezolid or IV methylene blue; monitor for serotonin syndrome for 2 weeks or until 24 hrs after the last dose of linezolid or IV methylene blue, whichever comes 1st. May resume clomipramine therapy 24 hrs after the last dose of linezolid or IV methylene blue

## DOSING CONSIDERATIONS

**Elderly**
Start at lower end of dosing range

## ADMINISTRATION

Oral route

## HOW SUPPLIED

Cap: 25mg, 50mg, 75mg

## CONTRAINDICATIONS

History of hypersensitivity to clomipramine hydrochloride or other TCAs. Use of an MAOI for psychiatric disorders either concomitantly or within 14 days of stopping treatment. Treatment within 14 days of stopping an MAOI for psychiatric disorders. Starting treatment in patients being treated with other MAOIs (eg, linezolid, IV methylene blue). During the acute recovery period after a myocardial infarction (MI).

## WARNINGS/PRECAUTIONS

Not approved for the treatment of bipolar depression. May precipitate mixed/manic episode in patients at risk for bipolar disorder. Serotonin syndrome reported; d/c immediately and initiate supportive symptomatic treatment. Pupillary dilation that occurs following use may trigger an angle closure attack in a patient with anatomically narrow angles who does not have a patent iridectomy. Caution with history of narrow-angle glaucoma. May cause seizures; caution with history of seizure disorder or other predisposing factors (eg, brain damage, alcoholism). May impair mental/physical abilities. May cause orthostatic hypotension and tachycardia. Psychosis, confusion, and other neuropsychiatric phenomena reported. May precipitate acute psychotic episode in patients with unrecognized schizophrenia and hypomania/mania in patients with affective disorder. Leukopenia, agranulocytosis, thrombocytopenia, anemia, and pancytopenia reported; obtain leukocyte and differential blood counts if fever and sore throat develop. Elevated liver enzymes, hyperthermia, sexual dysfunction in males, and weight changes reported. Caution with liver disease, hyperthyroidism, increased intraocular pressure (IOP), urinary retention, adrenal medulla tumors (eg, pheochromocytoma, neuroblastoma), significant renal dysfunction, and in elderly. Withdrawal symptoms may occur; taper dose gradually upon discontinuation. D/C use prior to elective surgery with general anesthetics.

## ADVERSE REACTIONS

Dry mouth, constipation, nausea, dyspepsia, anorexia, somnolence, tremor, dizziness, nervousness, libido change, impotence, sweating, increased appetite, weight gain, insomnia.

## DRUG INTERACTIONS

See Contraindications. Caution with anticholinergics, sympathomimetics, drugs that lower seizure threshold, or CNS-active drugs. Caution in patients on thyroid medication. May block effects of guanethidine, clonidine, or similar agents. Increased levels with haloperidol, methylphenidate, and hepatic enzyme inhibitors (eg, cimetidine, fluoxetine). Decreased levels with hepatic enzyme inducers (eg, barbiturates, phenytoin). Drugs that inhibit CYP2D6 (eg, quinidine, cimetidine, many CYP2D6 substrates [other antidepressants, phenothiazines, propafenone, flecainide]) may increase plasma concentrations; may require lower doses for either TCA or the other drug, and monitoring of TCA plasma levels. Caution with SSRI coadministration and when switching between TCAs and SSRIs (eg, fluoxetine, sertraline, paroxetine, fluvoxamine); sufficient time must elapse before starting therapy when switching from fluoxetine (at least 5 weeks may be necessary). Neuroleptic malignant syndrome may occur with neuroleptics. May increase levels of phenobarbital and highly protein-bound drugs (eg, warfarin, digoxin). May cause serotonin syndrome with other serotonergic drugs (eg, triptans, TCAs, fentanyl, lithium, tramadol) and with drugs that impair metabolism of serotonin; d/c immediately if serotonin syndrome occurs. Coadministration with electroconvulsive therapy may increase the risks.

## PREGNANCY AND LACTATION

Category C, not for use in nursing.

## MECHANISM OF ACTION

TCA; has not been established. Presumed to influence obsessive and compulsive behaviors through its effects on serotonergic neuronal transmission, which includes the capacity to inhibit reuptake of serotonin.

## PHARMACOKINETICS

**Absorption:** Administration of variable doses resulted in different pharmacokinetic parameters. **Distribution:** Plasma protein binding (97%); found in breast milk. **Metabolism:** Hepatic (extensive biotransformation); desmethylclomipramine (major active metabolite). **Elimination:** Feces (24-32%), urine (51-60%); $T_{1/2}$=32 hrs (clomipramine), 69 hrs (desmethylclomipramine).

## ASSESSMENT

Assess for history of hypersensitivity to the drug or other TCAs, recent MI, presence/risk for bipolar disorder, affective disorder, unrecognized schizophrenia, CVD, history of seizures or predisposing factors, hyperthyroidism, increased IOP, history of narrow-angle glaucoma, susceptibility to angle closure glaucoma, urinary retention, tumors of the adrenal medulla, hepatic/renal impairment, pregnancy/nursing status, and possible drug interactions.

## MONITORING

Monitor for clinical worsening, suicidality, unusual changes in behavior, orthostatic hypotension, tachycardia, precipitation of psychotic episode, hypomania/mania, weight changes, sexual dysfunction, serotonin syndrome, angle closure glaucoma, and other adverse reactions. Periodically monitor LFTs. Monitor hematologic changes and obtain leukocyte and differential blood counts if fever and sore throat develop. Periodically reassess need for continued treatment.

## PATIENT COUNSELING

Inform about benefits, risks, and appropriate use of therapy. Encourage patients, families, and caregivers to be alert for the emergence of unusual changes in behavior, worsening of depression, and suicidal ideation, especially early during treatment and when dose is adjusted; advise to report such symptoms to physician, especially if severe, abrupt in onset, or not part of presenting symptoms. Inform about the risk of seizure and high incidence of sexual dysfunction among males. Inform that therapy may impair physical/mental abilities; caution against performing hazardous tasks (eg, operating machinery/driving). Caution about using alcohol, barbiturates, or other CNS depressants. Instruct to notify physician if pregnant/intend to become pregnant, or breastfeeding. Caution about the risk of angle closure glaucoma.

## STORAGE

20-25°C (68-77°F). Protect from moisture.

Back to top