



# SWLA

# BEHAVIORAL HEALTH

# UP

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## CLOMIPRAMINE (ANAFRANIL)

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### FOR PATIENTS AND FAMILIES

**Clomipramine** (Anafranil) is one of many antidepressants in the family of tricyclic antidepressants (**tricyclic** refers to their three-ring chemical structure). Clomipramine is primarily used in treating obsessive-compulsive disorder (OCD). Interestingly, the U.S. Drug and Food Administration (FDA) approved clomipramine only for the treatment of OCD, and not depression, although physicians prescribe it for depression. It has been proven effective for treating depression. It is also used to treat agoraphobia (abnormal fear of being in open or public places from which escape might be difficult or embarrassing), panic disorder, and other types of depressive disorders.

It has been hypothesized that the symptoms of OCD may be related to serotonin, a neurotransmitter, in the brain. It is unclear what exact role serotonin plays in OCD, but changes in serotonin levels in the brain effected by medicines like clomipramine are important in mediating treatment-response in OCD. Clomipramine has been the standard in treatment of OCD for over two decades.

Clomipramine is available in generic preparations from different manufacturers, but it is marketed under the brand name of **Anafranil**. It is available in 25-, 50-, and 75-mg capsules.

#### HOW CLOMIPRAMINE IS PRESCRIBED

The usual starting dose for treating OCD is 25–50 mg administered in a single dose at bedtime. The dose is gradually increased during the first 2 weeks in increments of 25 mg/day, depending on clinical response and tolerability to side effects, to about 100 mg/day administered in divided doses. At higher dosages, clomipramine is best taken in two or three divided doses at mealtime to minimize gastrointestinal side effects. The maximum dosage for clomipramine should not exceed 250 mg/day.

#### PROPER USE OF YOUR MEDICATION

##### **Storing Your Medication**

- Keep your medication in a tamper-resistant vial and out of reach of children. Overdosage of clomipramine, a tricyclic antidepressant, is extremely dangerous, especially in infants and young children.
- Store your medication from excessive heat, moisture, and direct light.
- Keep your medication in its original prescription vial with the label intact to prevent others from taking the medication inadvertently.

##### **Taking Your Medication**

- Take your medication as instructed by your physician. Do not abruptly stop taking your medication without telling your physician. Discontinuation of your medication may result in relapse. Abrupt discontinuation of clomipramine may cause unpleasant symptoms. Although not indicative of addiction, the dosage may need to be decreased gradually before discontinuation of clomipramine.

- It may take 4–6 weeks of treatment before the therapeutic benefits of clomipramine are seen, and maximum therapeutic benefits are generally obtained in 8–16 weeks.
- If you miss a dose, take it as soon as possible. However, if it is close to your next dose, skip it and go back to your regular dosing schedule, but do not double-up the dose.
- Clomipramine may be taken with or without food. If it upsets your stomach, take it at mealtime.

### Use of Alcohol and Other Medications

Individuals should refrain from alcohol consumption while taking antidepressants. Alcohol is a depressant and may oppose the action of the medication.

Certain medications, including over-the-counter medicines, may adversely interact with clomipramine. The drug interaction may *lower* the blood level of the affected drug and decrease its effectiveness; or, it may *elevate* the blood level of the affected drug and cause toxicity. There are some drugs that when combined with clomipramine may exacerbate some side effects. Inform your doctor of all the prescription and over-the-counter medications you are taking. If you have questions about your medications, consult your physician or pharmacist.

### POSSIBLE SIDE EFFECTS

- *Drowsiness and sedation.* Patients taking clomipramine frequently report side effects of drowsiness and sedation. For this reason, the medication is initiated at a low dose and administered at bedtime to minimize daytime sedation. As the dosage is increased, clomipramine is administered in divided doses. A larger portion of the divided dose may be taken at bedtime to reduce daytime sedation.
- *Anticholinergic side effects.* When clomipramine interferes with the part of the nervous system—the cholinergic system—that regulates those particular body functions, it produces unwanted side effects. Drugs that inhibit the function of the cholinergic nervous system produce **anticholinergic side effects**. These side effects include dry mouth, blurred vision, disturbance of **accommodation** (failure of the eye to adjust when looking at nearby objects), constipation, urinary retention and hesitation, and palpitations. Furthermore, excessive anticholinergic action may produce confusion, especially in elderly patients.
- *Gastrointestinal (GI) side effects.* Nausea, dry mouth, loss of appetite, constipation, and heartburn are common GI complaints from taking clomipramine. As discussed above, dry mouth and constipation are anticholinergic side effects of the medication. Taking clomipramine at mealtime may reduce nausea. Using a bulk laxative, such as Metamucil, or a stool softener, increasing exercise, and drinking adequate liquid may prevent constipation.
- *Weight changes.* Weight gain was reported in 18% of patients receiving clomipramine. If weight gain is problematic, and a program of reducing caloric intake and increasing exercise does not control the weight, the physician may switch the patient to another antidepressant without this side effect.
- *Orthostatic hypotension.* Low blood pressure due to a postural change is known as **orthostatic hypotension**. Clomipramine may oppose the action of the body to elevate blood pressure when there is a change in position. When blood pressure cannot be elevated rapidly to compensate for a postural change as the patient rises from bed or stands up, orthostatic hypotension results. A drop in blood pressure can cause the individual to feel light-headed and dizzy, and sometimes faint and fall. By learning to rise slowly to allow the blood pressure to adjust, the patient can avoid or minimize orthostatic hypotension. Orthostatic hypotension from clomipramine is usually mild. Elderly patients and those taking larger doses may be more susceptible to this side effect.
- *Sexual dysfunction.* Clomipramine may cause sexual dysfunction, including impotence, delayed ejaculation, diminished libido, and anorgasmia (inability to achieve orgasm). Although some patients may be hesitant to discuss their sexual problems, they are encouraged to do so with their doctor. The physician may suggest switching to another antidepressant with a lower incidence of sexual problems.

**Warning:** Clomipramine may cause drowsiness and dizziness. Patients must exercise caution when engaging in daily activities that require mental alertness, such as operating a motor vehicle. It is recommended that the patients do not engage in hazardous tasks until they are reasonably certain that their medication does not adversely affect their performance or impair their judgment.

## POSSIBLE ADVERSE REACTIONS

- *Seizures.* Clomipramine, as with other tricyclic antidepressants, may lower the seizure threshold and increase the risk of seizures in susceptible individuals. The risk may be further enhanced when clomipramine is combined with other medicines that also lower seizure threshold. Albeit seizures are rare with clomipramine, patients with a history of seizure disorder should be monitored closely during treatment.
- *Mania and hypomania.* In patients diagnosed with bipolar disorder, taking clomipramine may precipitate mania or hypomania (less severe form of mania). Although the incidence of triggering mania or hypomania is very low, individuals with a history of bipolar illness should be aware of this adverse reaction while taking clomipramine.
- *Drug interactions.* Patients taking clomipramine should *never* take **monoamine oxidase inhibitor** (MAOI) antidepressants, such as **phenelzine** (Nardil), **tranylcypromine** (Parnate), and **isocarboxazid** (Marplan). This combination may result in severe elevation of blood pressure, fever, and possible seizures. If medical intervention and discontinuation the medications are not immediate, the reaction may be fatal. Clomipramine must be used cautiously in combination with selective serotonin reuptake inhibitor (SSRI) antidepressants, such as **fluoxetine** (Prozac) and **paroxetine** (Paxil). The combination may precipitate an adverse reaction known as **serotonin syndrome**, with symptoms that include confusion, restlessness, tremors, sweating, diarrhea, and fever.

## PREGNANCY AND BREAST FEEDING

Clomipramine is classified in **Category C** of the U.S. Food and Drug Administration (FDA) Pregnancy Risk Categories. It is given this classification because there are no clinical studies in women, nor is there adequate information, to determine the risk of clomipramine during pregnancy. Animal studies have found some abnormalities in the fetus of animals during maternal exposure to clomipramine. Interpretation of the animal studies to human risks, however, is unclear. Therefore, clomipramine should be prescribed during pregnancy only if the benefits outweigh the potential risks.

Clomipramine is excreted in breastmilk. It is recommended that women who breastfeed not take clomipramine.

**If you have any questions about this handout, please consult your physician.**