

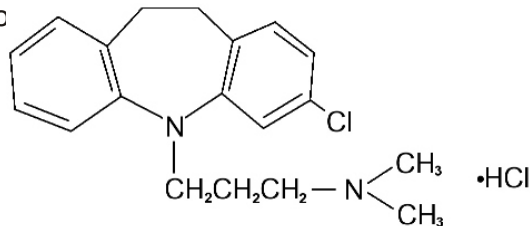
# Clomipramine

## BRAND NAMES: ANAFRANIL, CANIQUELL, CLOMICALM

AVAILABLE IN  
5 mg, 20 mg, 40 mg, 80 mg  
TABLETS  
approved for veterinary use  
25 mg, 50 mg, 75 mg  
CAPSULES  
for human use

## BACKGROUND

Not surprisingly, there is a very large market for medications used in the treatment of anxiety disorders in people. People want to be free from worry and stress without suffering drowsiness, addiction, or any other untoward side effects. In earlier times, the benzodiazepine family of drugs (of which Valium® is a member) were the predominant anxiety medications but their use was complicated by sedative side effects and chemical dependence. These unacceptable side effects drove researchers to seek a better solution. The tricyclic antidepressants, so named for their results of these efforts.



*Chemical structure of clomipramine. Note the 3 carbon rings that make it a "tricyclic" antidepressant.*

Of course, anxiety is not a problem exclusive to humans. Many pets have anxiety about separation from their owner, about aggressive pets with whom they share their home, about loud noises such as thunderstorms, and about other issues. The medications used to help animals with these issues are the same of the same medications that humans use. Clomipramine is the first to achieve FDA approval for use in dogs as well as humans.

The precise mechanism of action (i.e., exactly how these drugs work) is not known fully but it is believed that they act by increasing the activity of the neurotransmitter serotonin in the brain. Clomipramine is classified as a "tricyclic" antidepressant (because of its 3 ring chemical structure as shown above) and affects several neurotransmitters including **serotonin**. Serotonin, in simple terms, is associated with the cozy, happy feelings of comfort. Clomipramine inhibits the removal of serotonin in the brain so that the serotonin present is present for a longer time.

## HOW THIS MEDICATION IS USED

While clomipramine is only approved for use in humans and dogs, it is also widely used in cats. It is helpful in treating:

- Separation anxiety or other forms of anxiety
- Feline inappropriate urination (house soiling)
- Obsessive compulsive disorders
- Conflict aggression (aggression over possessions and resources)

Clomipramine is given once or twice daily and may be given with or without food. If nausea is felt to be an issue, a small amount of food given with the medication may be all that is needed to relieve this problem.

If a dose is accidentally skipped, do not double up on the next dose; simply pick up where the dose was left off and time the next dose accordingly.

Store clomipramine capsules and tablets at room temperature, protected from light.

## **SIDE EFFECTS**

The most common side effect one is likely to see is sedation. This is generally managed by adjusting the dose of the medication.

Clomipramine has potential to produce what are called **anticholinergic** side effects. This means that clomipramine inhibits the involuntary functions mediated by the neurotransmitter acetylcholine. These are not usually significant but the list of anticholinergic side effects that could become of concern includes:

- Retention of urine/difficulty passing urine (Watch for straining to urinate)
- Reduced intestinal motility (Watch for vomiting, drooling, appetite loss)
- Increased eye pressure (Watch for eye pain, dilated pupils)
- Heart rhythm disturbance (especially in patients with unregulated hyperthyroidism or taking thyroid supplementation)

Other side effects reported include: vomiting, diarrhea, and dry mouth (which might manifest as increased water consumption).

Side effects generally considered to be minor include: mild constipation, narrow urine stream, mild upset stomach (vomiting, diarrhea, reduced appetite), and drowsiness.

Side effects considered to be potentially serious include: heart rhythm disturbance (generally only an issue if there is a pre-existing rhythm problem or concurrent use of one of the medications listed below), increased eye pressure/glaucoma (not usually a problem unless there is a pre-existing predisposition).

## **INTERACTIONS WITH OTHER DRUGS**

Clomipramine is incompatible with monoamine oxidase inhibitors. Monoamine oxidase inhibitors have very few veterinary uses where this is likely to be an issue but there are two situations where this drug interaction might be relevant. Clomipramine could pose a problem with amitraz-containing tick or mite control products as amitraz is a monoamine oxidase inhibitor.

The other monoamine oxidase inhibitor used for animals is selegiline which is used to treat cognitive dysfunction (senility) and sometimes is used for in the treatment of Cushing's disease. The drug interaction with clomipramine could result in a condition called "serotonin syndrome" which features extreme high blood pressure. Other medications that can increase the risk for serotonin syndrome include: meperidine (pain reliever), pentazocine (pain reliever), tramadol (pain reliever), fluoxetine (another anxiety medication), buspirone (another anxiety medication), trazodone (another anxiety medication), mirtazapine (appetite stimulant), and dextromethorphan (cough suppressant).

Anti-thyroid medications such as methimazole carry a risk of blood dyscrasias meaning that some blood cell lines may be suppressed. When these drugs are used in combination with clomipramine the risk of this side effect is increased.

Cimetidine (Tagamet®) may slow the removal of clomipramine, effectively increasing the potential to reach a toxic blood level.

Using clomipramine with other drugs that have anticholinergic side effects (as reviewed above) increase the chances of seeing those side effects. Such other drugs include most antihistamines.

Heart rhythm disturbance is made more significant with concurrent use of: cisapride (a constipation drug), any of the azole antifungal agents (such as itraconazole, ketoconazole, or fluconazole), the quinolone class of antibiotics (such as enrofloxacin, pradofloxacin, marbofloxacin, or orbifloxacin), the macrolide class of antibiotics (azithromycin, erythromycin).

The potential for neurologic side effects of metoclopramide (for nausea) are made worse with concurrent use of clomipramine.

## CONCERNS AND CAUTIONS

- Several weeks of use are needed before one may expect to see a therapeutic effect. Up to 2 months may be needed to determine if clomipramine is helpful to a given patient.
- Clomipramine should not be used in patients with seizure disorders as it may facilitate seizures.
- Clomipramine may affect male fertility but does not seem to cause trouble when used during pregnancy.
- Clomipramine may exacerbate glaucoma and may exacerbate heart rhythm abnormalities though its anticholinergic side effects described above.
- It does not matter if this medication is taken with food or not. It is well absorbed from the intestinal tract either way.
- Clomipramine definitely crosses into the milk of nursing mothers.
- An overdose of approximately 12 times the recommended dose is often lethal.
- Tricyclic antidepressants may alter blood glucose levels.
- Clomipramine is activated in the liver. It is removed from the body via the kidneys as well as the liver. Patients with liver disease may not metabolize this drug predictably.
- If clomipramine is to be discontinued, this is best done in a tapering dose rather than suddenly. See your veterinarian for instructions.

In a 2003 study published in the Journal of Veterinary Internal Medicine, it was found that clomipramine lowered thyroid test values in at least 35% of patients. These dogs were not believed to actually have hypothyroidism; results were interpreted to mean that a dog on clomipramine could be erroneously diagnosed as hypothyroid.

The chief brand name canine version of clomipramine (Clomicalm<sup>®</sup>) is manufactured by Virbac. Their web page detailing this product and including the actual product insert is at:

<https://vetlabel.com/lib/vet/meds/clomicalm-1>

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Additional drug and general pet care information can be found on our world wide web site:

<http://www.marvistavet.com>