

# Theophylline

**BRAND NAME: THEO-DUR**

AVAILABLE IN  
100 mg, 200 mg, 300 mg, 400 mg, 450 mg and 600 mg  
EXTENDED RELEASE CAPSULES,

## BACKGROUND

Theophylline and its close relatives aminophylline, caffeine and chocolate, are members of the methylxanthine group of chemicals. Caffeine was the first of this group to be found helpful to asthmatic humans but had some unpleasant side effects. Other derivatives were quickly produced in hope of minimizing side effects and maximizing the airway relaxant properties that are so helpful in airway disease.

## HOW THIS MEDICATION WORKS

Theophylline is able to effect several actions which are helpful in a number of respiratory conditions. These beneficial effects are:

- **Increased contraction strength of the diaphragm**

The diaphragm forms the muscular floor of the chest cavity and its contractions correspond to the strength of breathing motions. When breathing becomes difficult, this muscle works harder against the resistance created by disease. The use of theophylline can give new strength to this important respiratory muscle.

- **Increased beat frequency of the respiratory cilia**

The upper respiratory tract is protected by a lining of special cells. These cells secrete a layer of mucus which captures debris we have inhaled and move debris formed by disease lower down in the lungs. This mucus is moved to the throat by microscopic hair-like cells called "cilia" which rhythmically beat, like little oars, to move the mucus and its trapped debris. Once the mucus reaches the throat it is either coughed up or swallowed. Theophylline helps these cilia to beat faster and thereby more rapidly clear respiratory debris.

- **Dilation and relaxation of constricted airways**

This is probably the main reason for using theophylline. By relaxing the airway muscles, airways enlarge. In asthma, a disease involving inappropriate airway constriction, breathing becomes easier. In conditions where fluid or other material has accumulated in airways, dilation of the airways can suppress coughing and increase patient comfort.

- **Central Nervous System stimulation**

Most of us are familiar with this effect with regard to caffeine, a close relative of theophylline. While this can be a negatively perceived side effect, it is very helpful in human infants who suffer from sleep apnea (where the brain simply fails to stimulate the act of breathing during sleep). This same condition is believed to be a problem in the English bulldog and theophylline may be helpful in this regard.

- **Diuretic effects**

This effect amounts to increased need to urinate and is only a problem for some individuals. In most individuals this is a mild effect and helps to dry excessive respiratory secretions thus helping to suppress coughing.

## SIDE EFFECTS

The less serious but still negative side effects of theophylline include: restlessness or caffeine-type jitters (this can be minimized by starting the medication at a lower dose and gradually increasing to the recommended dose), diuretic effect (some individuals only), and upset stomach (which can be mitigated by giving the medication with food).

More serious side effects include increased heart rate which can be a problem for patients with pre-existing heart conditions. Theophylline can increase the secretion of acid in the stomach. This could be a problem for patients with pre-existing ulcers. Theophylline can induce "jitters" or tremors which could exacerbate seizures in patients prone to having seizures.

Humans are sensitive to these side effects and blood levels of theophylline are commonly monitored with blood tests. In dogs, however, no side effects are seen until blood levels are enormously out of range so few problems are observed in pets on theophylline. The problem is that different brands of theophylline may produce inconsistent blood levels. Some brands last too long, some do not last long enough. It is important to use a brand produces consistent therapeutic effects. Unfortunately, the brands that have documented pharmacokinetics in animals are no longer available so the best bet right now is to be sure you have an extended release tablet and see how well it works. If it works well for your pet, try to consistently get the same brand. If it does not work well or has side effects, it is reasonable to try another brand.

## INTERACTIONS WITH OTHER DRUGS

Theophylline is removed from the body by the liver using a system called the cytochrome p450 system. Other drugs that also use this system will influence the way theophylline is metabolized (depending on which drug the enzyme system will preferentially bind to).

Quinolone antibiotics (enrofloxacin, ciprofloxacin, orbifloxacin) will increase blood levels of theophylline dramatically (potentially creating toxicity) and the side effects listed above may actually become a problem. It is worth mentioning that marbofloxacin does not share this interaction unless the patient is also in renal failure. Other medications which can increase the activity of theophylline include cimetidine (Tagamet), clindamycin, erythromycin, lincomycin, corticosteroids, allopurinol and thyroid hormone supplementation.

The effect of theophylline may be reduced when using phenobarbital to control seizures, with ketoconazole, an antifungal medication, or with furosemide, a diuretic.

Theophylline may decrease the effect of beta blockers (heart medicines) such as propranolol and may decrease the effects of benzodiazepine tranquilizers such as alprazolam or diazepam.

## CONCERNS AND CAUTIONS

This medication is typically given twice a day in dogs but only once a day in cats. When this medication is used in the treatment of asthma in cats, we believe it is best to give this medication at bedtime. (Human asthmatics and equine patients with "heaves" have maximum airway constriction between 2 a.m. and 7 a.m. If cats follow this pattern, they will need highest blood levels to be during the early morning. It is not known, however, that cats follow the same pattern as horses and humans but the human and equine diseases are similar to feline asthma in many ways.)

In pregnancy, theophylline crosses the placenta and medicates unborn pups and kittens. It also crosses over into milk and medicates nursing pups and kittens.

**Theophylline is probably best avoided in patients with a tendency to cardiac arrhythmia or patients with liver disease.**

Theophylline may increase a patient's heart rate, exacerbating certain types of heart arrhythmias or interfering with the heart's ability to fill. This could especially be an issue with hyperthyroid cats or cats with hypertrophic cardiomyopathy. Heart failure patients tend to clear theophylline from their bodies more slowly than normal patients.

Patients with insufficient liver function will need a drastic reduction in theophylline dose to avoid toxic side effects but if this is done, theophylline can still be used in such patients.

If a dose is accidentally skipped, do not double up on the next dose. Simply give the dose when it is remembered and time the next dose accordingly..

Last revised: 2/2/2022



# Mar Vista Animal Medical Center

3850 Grand View Blvd., Los Angeles, CA 90066 • (310) 391-6741 • Fax: (310) 391-6744

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

<http://www.marvistavet.com>

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