

# Antiseizure Medications for Cats

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## Background & Pathophysiology

Seizures affect approximately 1% to 2% of cats (author experience). Recurrent seizures (ie, epilepsy) can be classified as structural (ie, caused by an identifiable brain disease such as an infection or tumor) or unknown/idiopathic. Reactive seizures can also be caused by extracranial triggers such as metabolic diseases and toxicities; these seizures are not considered types of epilepsy. In cats, extracranial causes of seizures are not uncommon, and structural epilepsy is more common than idiopathic epilepsy.<sup>1-4</sup> Therefore, blood work, along with a diagnostic investigation to look for a potentially treatable underlying cause, should be performed on any cat presented with seizures. In addition to treating the underlying cause, mainte-

nance antiseizure medications (eg, phenobarbital, zonisamide, levetiracetam; see **Table**, next page) are warranted in many epileptic cats.

## Phenobarbital

Phenobarbital is the most commonly recommended anticonvulsant drug to control epilepsy in cats. It is inexpensive, has an excellent pharmacokinetic profile, and does not appear to cause hepatic enzyme induction or have the same hepatotoxic potential in cats as it does in dogs.<sup>3,5,6</sup> Anticipated adverse effects are usually mild and transient and consist of increased appetite, thirst, sedation, and ataxia. Generalized lymphadenopathy that resolves on withdrawal of the drug has also been reported in a cat receiving phenobarbital.<sup>7</sup> Although q24h dosing

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may be adequate in some cats, q12h dosing is often recommended to ensure a steady serum level.<sup>6,8</sup>

The established therapeutic range of serum phenobarbital levels for dogs (15-45 µg/mL) appears to apply to cats as well.<sup>2</sup> In general, about 40% to 50% of cats become seizure free on phenobarbital, and an additional 30% to 60% are considered well controlled.<sup>3,8</sup>

Because it is difficult for many owners to administer oral medications, an alternative route of administration may be desirable. A recent study provided evidence that therapeutic serum levels of phenobarbital can be achieved via transdermal administration.<sup>9</sup> Two different bases (pluronic lecithin organo-

gel and Lipoderm ActiveMax; pccarx.com) were used, and serum levels between 15 and 26 µg/mL were achieved by administering each at a dose of 9 mg/kg q12h. However, serum levels varied significantly between the different vehicle formulations at the same dosage.<sup>9</sup>

As a general note, transdermal drug absorption depends on the molecule size, chemical nature, and dosage; therefore, not all medications can be absorbed through the skin nor are all medications safe to administer transdermally.<sup>10</sup> Antiseizure medications that have not been shown to be absorbed transdermally should not be prescribed for this route. Serum levels should be monitored at least every 6 months in cats treated with transdermal phenobarbital to ensure safe and effective

**TABLE**

**MEDICATIONS TO TREAT SEIZURES IN CATS**

Medication	Oral Starting Dose & Frequency	Time to Steady State	Parenteral Formulation Available?	Adverse Effects	Efficacy in Cats
Phenobarbital <sup>3,5,6,8</sup>	1.5-2.5 mg/kg q12h	2 weeks	Yes	Polyphagia, polydipsia, sedation, ataxia, lymphadenopathy	>70% of cats well controlled or seizure free
Zonisamide <sup>12</sup>	5-10 mg/kg q24h	1 week	No	Vomiting, diarrhea, anorexia, sedation, ataxia	Unknown
Levetiracetam <sup>10,21</sup>	20 mg/kg q8h	1 day	Yes	Inappetence, lethargy, hypersalivation	Improved seizure control in 7/10 cats poorly controlled on phenobarbital alone; improved seizure control in 100% of cats with audiogenic reflex myoclonic seizures
Gabapentin*	5-10 mg/kg q8-12h	Unknown	No	Sedation, ataxia	Unknown
Pregabalin*	1-2 mg/kg q12h	Unknown	No	Sedation, ataxia	Unknown
Diazepam	Not recommended for oral use in cats because of potential for fatal hepatotoxicity <sup>25</sup>				
Potassium bromide	Not recommended for use in cats because of potential for fatal pneumonitis <sup>26</sup>				

\*Information is anecdotal.

absorption, and cats should be monitored for dermatologic reactions on the ear pinnae.<sup>9</sup>

### Zonisamide

Zonisamide has shown promise as an anti-seizure medication in dogs and in cats with experimentally induced seizures; however, no studies have investigated its efficacy in a clinical population of epileptic cats.<sup>11</sup> One major advantage of zonisamide in cats is its long half-life, which allows q24h dosing.<sup>12</sup> In a pharmacokinetic study in normal cats, adverse effects appeared dose related (seen at 20 mg/kg q24h) and consisted primarily of GI signs, depression, and ataxia.<sup>12</sup> Several reports have shown serious adverse effects, including hepatotoxicity, in dogs receiving zonisamide, possibly because zonisamide is a sulfonamide derivative.<sup>13-15</sup> There are no similar reports in cats, although clinicians should be aware of the possibility of sulfonamide-related adverse effects.<sup>16</sup>

### Levetiracetam

Levetiracetam has a novel mechanism of action and may also be neuroprotective.<sup>17,18</sup> In cats, it has a short half-life ( $\approx$ 3 hours), which necessitates q8h administration,<sup>18</sup> which may be a drawback for many owners. An extended-release tablet exists but is not available in a tablet size appropriate for patients that weigh less than 35 pounds and cannot be split.<sup>19</sup>

Recently, the pharmacokinetics of single-dose administration of 500 mg extended release levetiracetam in cats were investigated. The results suggested that q24h dosing of this formulation may be possible in many cats.<sup>20</sup> No adverse effects were observed in any of the 7 cats.

Levetiracetam has an excellent safety profile, and there are no reports of serious adverse effects associated with its use in veterinary patients. Reported adverse effects in cats are mild and can include inappetence, lethargy, and transient hypersalivation.<sup>18,21</sup>

One study evaluated levetiracetam as an add-on therapy in 10 cats with epilepsy that were poorly managed with phenobarbital; 7 cats experienced more than 50% reduction in seizure frequency during the 3-month follow-up period.<sup>21</sup> In a recent randomized clinical trial, levetiracetam was found to be more effective than phenobarbital in controlling a specific type of epilepsy recently described in geriatric cats.<sup>22</sup> These cats suffer from seizures triggered by auditory stimuli that usually start with myoclonic jerks but may progress to generalized tonic-clonic seizures.<sup>23</sup> Of the newer generation of antiseizure medications, levetiracetam has the best side effect profile and is the only drug with documented efficacy in cats.

### Other Antiseizure Medications

Gabapentin and pregabalin are similar medications used in dogs to treat neuropathic pain and, less commonly, seizures. Neither the pharmacokinetics nor the antiseizure efficacy of these medications have been investigated in cats, although there are anecdotal reports of their use for seizure management in this species.<sup>24</sup> Use of gabapentin as a sedative in fractious cats and for analgesia in cats with musculoskeletal pain has been reported.<sup>25,26</sup>

Use of potassium bromide and oral diazepam is not recommended in cats, as these drugs have been associated with potentially fatal adverse allergic pneumonitis and hepatitis, respectively.<sup>27,28</sup>

Imepitoin was recently approved in Europe to treat dogs with epilepsy. Its efficacy in dogs was comparable to that of phenobarbital in a large randomized blinded study, and its adverse effects appeared to be more tolerable than those of phenobarbital.<sup>29</sup> This drug is not available in the United States, and there is no information available regarding its safety or efficacy in cats. ■

See next page for references.



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## Brief Summary of Prescribing Information

# CLAVAMOX® CHEWABLE

(amoxicillin and clavulanate potassium tablets)

## Chewable Tablets

### Antimicrobial For Oral Use In Dogs And Cats

**CAUTION:** Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

**INDICATIONS:** CLAVAMOX CHEWABLE Tablets are indicated in the treatment of:

**Dogs:** Skin and soft tissue infections such as wounds, abscesses, cellulitis, superficial/juvenile and deep pyoderma due to susceptible strains of the following organisms:  $\beta$ -lactamase-producing *Staphylococcus aureus*, non- $\beta$ -lactamase-producing *Staphylococcus aureus*, *Staphylococcus* spp., *Streptococcus* spp., and *E. coli*.

Periodontal infections due to susceptible strains of both aerobic and anaerobic bacteria. CLAVAMOX CHEWABLE has been shown to be clinically effective for treating cases of canine periodontal disease.

**Cats:** Skin and soft tissue infections such as wounds, abscesses, and cellulitis/dermatitis due to susceptible strains of the following organisms:  $\beta$ -lactamase-producing *Staphylococcus aureus*, non- $\beta$ -lactamase-producing *Staphylococcus aureus*, *Staphylococcus* spp., *Streptococcus* spp., *E. coli*, and *Pasteurella* spp.

Urinary tract infections (cystitis) due to susceptible strains of *E. coli*.

Therapy may be initiated with CLAVAMOX CHEWABLE prior to obtaining results from bacteriological and susceptibility studies. A culture should be obtained prior to treatment to determine susceptibility of the organisms to CLAVAMOX. Following determination of susceptibility results and clinical response to medication, therapy may be reevaluated.

### DOSE AND ADMINISTRATION:

The dose should be prescribed using a combination of whole tablet strengths (62.5 mg, 125 mg, 250 mg, 375 mg). Do not remove from foil strip until ready to use. Even if the tablet is broken, the entire tablet should be consumed.

**Dogs:** The recommended dosage of CLAVAMOX CHEWABLE Tablet is 6.25 mg/lb of body weight twice a day.

Skin and soft tissue infections such as abscesses, cellulitis, wounds, superficial/juvenile pyoderma, and periodontal infections should be treated for 5-7 days or for 48 hours after all symptoms have subsided. If no response is seen after 5 days of treatment, therapy should be discontinued and the case reevaluated. Deep pyoderma may require treatment for 21 days; the maximum duration of treatment should not exceed 30 days.

**Cats:** The recommended dosage of CLAVAMOX CHEWABLE Tablet is 62.5 mg twice a day.

Skin and soft tissue infections such as abscesses and cellulitis/dermatitis should be treated for 5-7 days or for 48 hours after all symptoms have subsided, not to exceed 30 days. If no response is seen after 3 days of treatment, therapy should be discontinued and the case reevaluated.

Urinary tract infections may require treatment for 10-14 days or longer. The maximum duration of treatment should not exceed 30 days.

**CONTRAINDICATIONS:** The use of this drug is contraindicated in animals with a history of allergic reaction to any of the penicillins or cephalosporins.

**WARNINGS:** Store CLAVAMOX CHEWABLE out of reach of dogs, cats, and other pets in a secured location in order to prevent accidental ingestion or overdose.

**HUMAN WARNINGS:** Not for human use. Keep this and all drugs out of reach of children.

Antimicrobial drugs, including penicillins and cephalosporins, can cause allergic reactions in sensitized individuals. To minimize the possibility of allergic reactions, those handling such antimicrobials, including amoxicillin and clavulanate potassium, are advised to avoid direct contact of the product with the skin and mucous membranes.

**ADVERSE REACTIONS:** CLAVAMOX CHEWABLE contains a semisynthetic penicillin (amoxicillin) and has the potential for producing allergic reactions. If an allergic reaction occurs, administer epinephrine and/or steroids.

To report suspected adverse events, for technical assistance or to obtain a copy of the SDS, contact Zoetis Inc. at 1-888-963-8471 or [www.zoetis.com](http://www.zoetis.com).

For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at <http://www.fda.gov/AnimalVeterinary/SafetyHealth>.

**HOW SUPPLIED:** CLAVAMOX CHEWABLE Tablets in the following strengths are supplied in strip packs. Each carton holds 10 strips with 10 tablets per strip (100 tablets per carton).

Each 62.5-mg tablet contains amoxicillin trihydrate equivalent to 50 mg of amoxicillin activity and 12.5 mg of clavulanic acid as the potassium salt. For use in dogs and cats.

Each 125-mg tablet contains amoxicillin trihydrate equivalent to 100 mg of amoxicillin activity and 25 mg of clavulanic acid as the potassium salt. For use in dogs only.

Each 250-mg tablet contains amoxicillin trihydrate equivalent to 200 mg of amoxicillin activity and 50 mg of clavulanic acid as the potassium salt. For use in dogs only.

Each 375-mg tablet contains amoxicillin trihydrate equivalent to 300 mg of amoxicillin activity and 75 mg of clavulanic acid as the potassium salt. For use in dogs only.

Dispense according to recommendations outlined in Dosage and Administration section.

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