



Anticonvulsants

A seizure is an uncontrolled, abnormal electrical discharge arising from the thalamus and/or cortex of the brain. *The origin, generation and propagation of generalized seizures are poorly understood at this time. Current knowledge of seizures is based upon studies of focal seizure models.* A seizure represents the clinical, or outward appearance of abnormal, excessive brain (**cerebral cortex**) discharge. The nerve cells (neurons) of the cerebral cortex of the brain operate under the strict control and regulation of the surrounding population of neurons. When the intrinsic control measures of the cerebral cortex fail, uncontrolled and excessive discharge of one, or a group of neurons (**seizure focus**), may occur. This excessive and continuous discharge of a group of nerve cells or neurons can pull other neurons into the electrical discharge resulting in excessive and inappropriate stimulation to the muscles or the body, internal organs, and regions of the brain (**generalized seizure**). If the seizure focus remains localized to one area of the brain, a portion of the body will be involved in the abnormal cortical discharge (**partial seizure**).

Anticonvulsants are natural or synthetic pharmaceutical or salt agents that when administered act to prevent or abolish seizures by suppressing the origin and/or spread of abnormal electrical discharge from one neuron to another. Few anticonvulsants are approved for use in companion animals. To date, Phenobarbital and Diazepam remain FDA approved for use in the dog. This necessitates the need for off label use of most anticonvulsants in the treatment of companion animal seizures. In addition, **most anticonvulsants are controlled substances requiring strict monitoring and annual physical examination for renewed prescriptions.** Significant advances in the understanding of the pharmacodynamic properties of these agents in companion animals has resulted in improved use and greater control of seizures in the dog and cat.

The use of anticonvulsants should be based upon the type of seizure as well as cause of seizures in your pet. Side effects, potential toxicity, and frequency of administration and cost are all factors, which are considered when choosing an anticonvulsant agent. Strict adherence to dosage, dosing frequency, and serum testing is vital for the long-term success and management of your pet's seizures. Despite current treatment options, adequate control is accomplished in 66-75 % of the cases. This leaves 25-33% of all cases of recurrent seizures without adequate control.

Phenobarbital is one of the most common anticonvulsants employed in the treatment of seizures in dogs and cats. Phenobarbital is a controlled drug, which is inexpensive with a twice-a-day administration frequency. Phenobarbital induces behavioral side effects of increased appetite, increased thirst, and increased urinary habits. Long-term use has been associated with bone marrow suppression of white blood cells, red blood cells, and platelets and liver disease (chronic active hepatitis and cirrhosis). The frequency of idiosyncratic and/or toxic reactions due to Phenobarbital is felt to be infrequent and is more common when used at high dosages over long period of time and in combination with multiple anticonvulsants.

Potassium and Sodium Bromide are natural, salts with anticonvulsant properties when taken in a chronic fashion. Bromide is the active component of these salts. Hyperpolarization of neuronal membranes and inhibition of generation and spread of the seizure is felt to be the mechanism of action of the Bromide ion. The efficacy of either form of the salt is the same, with the bioavailability of the sodium form greater than the potassium form. The reduced amount required to produce similar serum bromide concentrations is offset by the higher cost of the sodium form of the bromide salt. Bromide therapy is felt to be to the safest anticonvulsant management therapy in the dog at this time. The long **half-life** (duration of action of the drug) allows for once or twice a day therapy. Steady-state (**where serum concentrations are the same throughout the day and night**) serum concentrations are not attained until 4 months in the dog. Potassium and/or sodium Bromide is often used in combination at this time in canine and recurrent seizures. Potassium and sodium Bromide is also used with success in feline seizures, although the long-term use of Bromide in cats has been associated with asthma-like respiratory disease. Because of this, utilization of either form of the Bromide salt on a long-term basis is discouraged in the feline species.

Newer anticonvulsants are being utilized with greater knowledge of efficacy and side effects. These **tertiary** anticonvulsants include **Zonisamide, Felbamate, and Chlorazepate dipotassium, Clonazepam, Gabapentin and Levetiracetam.** Greater expense and more frequent administration is a reality of with these newer agents. The need for the use of for a tertiary agent will be left up to the managing doctor and owners' wishes. Implementation of **combination** anticonvulsant therapy allows for greater seizure control due to **synergism** (one agent increasing the effectiveness of another, only when both agents are used together) between anticonvulsants with lessened toxicity and potential for idiosyncratic reaction due to the allowance for lower dosing. Adequate serum level testing coupled with laboratory testing to ensure safety of the bone marrow and internal organs is vital when utilizing combination anticonvulsant therapy.