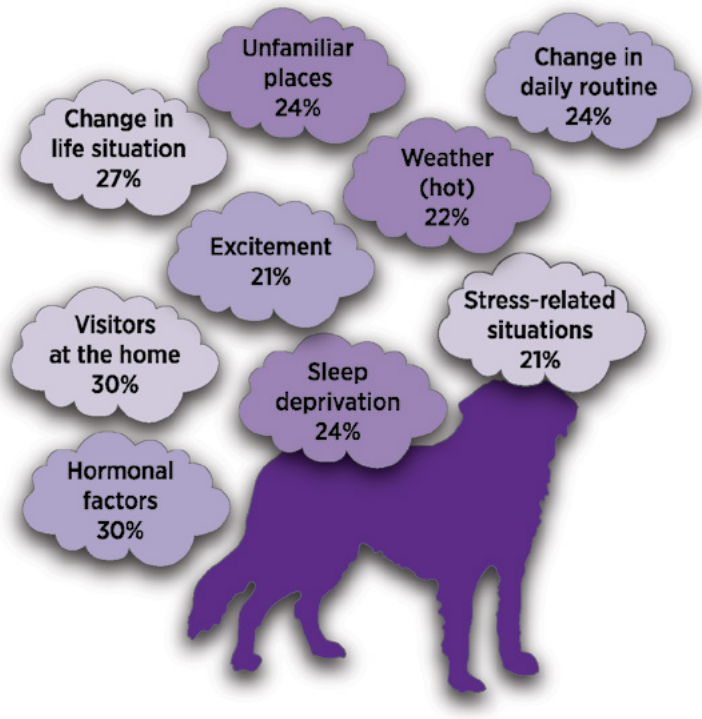

It's always there...
...looming, unpredictable, yet certain.
But idiopathic epilepsy in dogs can be safely and reliably controlled.

Witnessing your dog experiencing a seizure can be a traumatic experience that leaves you overwhelmed by a sense of helplessness and fear—like a dark cloud always hanging around, waiting for the next seizure to strike.

What is Idiopathic Epilepsy?

Idiopathic epilepsy (IE), recurrent seizures with no identifiable cause, is the **most common chronic neurologic disorder in dogs**. Epileptic seizures are temporary signs of abnormal activity in the brain. The frequency, type, and severity of seizures can vary, ranging from several a day to less than one a year. Dogs are more likely to suffer from a seizure when exposed to certain situations, such as those shown below.



Your veterinarian will diagnose IE based on age of onset, behavior between seizures, and ruling out other diseases that result in seizures.

What Does this Mean for My Dog's Quality of Life?

An IE diagnosis may impact your household through emotional stress, psychological and social challenges, and economic burden, all of which may factor into your decision to treat. Understanding the impact on your daily life and better aligning your expectations with regard to treatment and expected outcomes may result in more effective control of the disease.

The goal of medication therapy is to decrease the number of seizures a dog is experiencing.

While IE can be controlled, it is important to recognize your level of commitment and discuss the following important facts with your veterinarian.

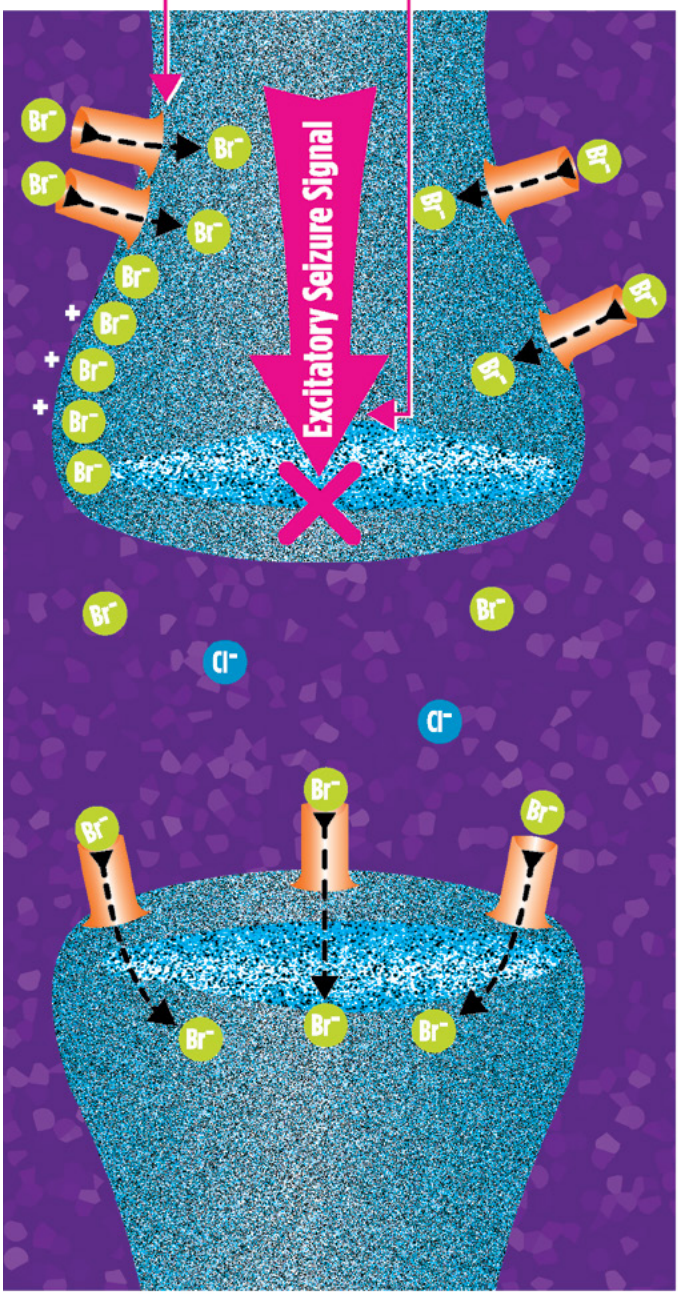
- A pet experiencing seizures is NOT in pain – your dog does not realize they have had a seizure; it is not a quality-of-life issue for them.
- Epilepsy is a chronic, lifelong condition; we cannot cure the disease, but it can be controlled.
- Appropriate control will require some trial and error to regulate the levels of medication, including office visits and diagnostic tests.
- The goal of medication therapy is to decrease the number of seizures a dog is experiencing.

What is Potassium Bromide?

Potassium bromide (KBr) is considered a well-known choice for long-term control of seizures associated with idiopathic epilepsy in dogs.

How Does KBr Work to Decrease Seizures?

- Bromide passes through channels along a nerve, creating a negative charge.
- This negative charge decreases the chance of a seizure signal being sent to the next nerve, thereby decreasing the possibility that a dog experiences a seizure.



How KBroVet®-CA1 Can Help Steady the Storm

KBroVet-CA1 is conditionally approved by the FDA for the control of idiopathic epilepsy in dogs. It was developed to provide a consistent and reliable source of KBr for veterinary patients. To learn more about KBroVet-CA1, talk to your veterinarian or visit SteadyTheStorm.com.

IMPORTANT SAFETY INFORMATION: KBroVet®-CA1 is conditionally approved by FDA pending a full demonstration of effectiveness under application number 141-544. See prescribing information for complete details regarding adverse events, warnings, and precautions. It is a violation of Federal Law to use this product other than as directed in the labeling. Contraindicated in dogs with a history of hypersensitivity to bromide. Not for use in cats. Not for human use. Keep out of reach of children. Contact a physician in case of accidental ingestion by humans. The most commonly reported side effects were increased appetite and thirst, increased urination, weight gain, sedation, and ataxia. Reversible neurologic signs (sedation, ataxia, weakness) were generally associated with adjunctive potassium bromide treatment or high serum bromide concentrations. Animals with kidney disease may be predisposed to bromide toxicities. The safe use of KBroVet-CA1 has not been evaluated in dogs that are intended for breeding, are pregnant or lactating, or less than 6 months of age. Use caution when changing diets, administering chloride-containing IV fluids, and administering concurrent medications. Careful monitoring is important in dogs that have a condition that may cause difficulty maintaining electrolyte balance.

KBroVet-CA1 Product Facts

- **KBroVet-CA1 is the only FDA conditionally approved drug for seizure control in dogs,** providing you better assurance of a reliable and trusted product.
- **KBroVet-CA1 is a once a day, liver-flavored, chewable tablet specifically formulated for dogs,** making it easier for you to administer and more palatable for your dog.
- **KBroVet-CA1 remains in the bloodstream for at least 21 days,** minimizing the occurrence of a seizure if a dose is missed.

KBroVet-CA1 Chewable Tablets have been conditionally approved by FDA pending a full demonstration of effectiveness under application number NADA 141-544.

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian. Use only as directed. It is a violation of Federal Law to use this product other than as directed in the labeling.

KBroVet®-CA1
(potassium bromide chewable tablets)

Anti-epileptic for use in dogs only.
Conditionally approved by FDA pending a full demonstration of effectiveness under application number 141-544.

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian. Use only as directed. **It is a violation of Federal Law to use this product other than as directed in the labeling.**

CONTRAINDICATIONS:
KBroVet-CA1 should not be used in animals with a history of hypersensitivity to bromide.

DESCRIPTION:
KBroVet-CA1 are liver-flavored chewable tablets that contain potassium bromide (KBr). KBr is an odorless, colorless crystal or white crystalline powder or white granular solid with a pungent bitter saline taste. The molar mass of KBr is 119.002 g/mol, with high solubility in water, glycerol and ethanol.

INDICATION:
KBroVet-CA1 (potassium bromide chewable tablets) are indicated for the control of seizures associated with idiopathic epilepsy in dogs.

DOSAGE AND ADMINISTRATION:
The total recommended daily dosage range for oral administration is 25–68 mg/kg (11–31 mg/lb) of body weight. The dosage of KBroVet-CA1 should be adjusted based on monitoring of clinical response of the individual patient. KBroVet-CA1 may be dosed with or without food. Use of an initial loading dosage regimen may be considered on an individual patient basis, balancing the time required to achieve a therapeutic response while minimizing side effects.

WARNINGS:
User Safety Warnings

Not for human use. Keep out of reach of children. Contact a physician in case of accidental ingestion by humans.

Animal Safety Warnings
Not for use in cats.

Keep KBroVet-CA1 in a secured location out of reach of dogs, cats, and other animals to prevent accidental ingestion or overdose.

PRECAUTIONS:
Dogs receiving KBr should be carefully monitored when changing diets, administering chloride-containing IV fluids, and administering concurrent medications. Careful monitoring is important in dogs that have a condition that may cause difficulty maintaining electrolyte balance.

Animals with decreased renal function may be predisposed to bromide toxicosis.

Some dogs may experience epileptic episodes that are unresponsive or refractory to KBr monotherapy and KBr alone may not be adequate treatment for every dog with idiopathic epilepsy.

The safe use of KBroVet-CA1 has not been evaluated in dogs that are intended for breeding, or that are pregnant or lactating. The safe use of KBr in neonates and young animals has not been established. Reproductive effects of KBr have been reported in other species. In dogs, ataxia, diarrhea, hematochezia, excessive salivation, shivering, skin lesions, stupor progressing to coma and death have been reported with a dose of 200 to 500 mg/kg a day for 4 to 26 weeks.

ADVERSE REACTIONS:
In a retrospective field study of 51 dogs diagnosed with idiopathic epilepsy and receiving only KBr to control seizures associated with idiopathic epilepsy, adverse reactions were documented for the initial 60 days of treatment. Increased appetite, weight gain, vomiting/regurgitation and sedation were the most common clinical abnormalities documented in the 60 day period after start of KBr therapy (Table 1).

Table 1. Adverse Reactions Reported During Initial Dosing Phase (60 Day Period After Start of KBr Therapy)

Adverse reactions were also documented during the 30 days prior to KBr sample submission. Weight gain, weakness, ataxia, and increased appetite were the most common adverse reactions documented during this time period (Table 2).

Adverse Reaction	Number of Dogs with the Adverse Reaction
Increased Appetite	11
Weight Gain	8
Vomiting	5
Regurgitation	4
Sedation	3
Polydipsia	2
Ataxia	2
Polyuria	2
Weakness	2
Decreased Activity	1
Diarrhea	1
Disorientation	1
Lethargy	1
Partial Lack of Efficacy	1
Petit Mal Epilepsy	1
Seizure NOS	1
Tiredness	1
Tremors	1

Table 2. Adverse Reactions Reported During Dosing Phase (30 Day Period Before KBr Sample Submission)

Adverse Reaction	Number of Dogs with the Adverse Reaction
Weight Gain	7
Weakness	5
Ataxia	4
Increased Appetite	4
Polydipsia	3
Sedation	3
Diarrhea	2
Polyuria	2
Regurgitation	2
Vomiting	2
Decreased Appetite	1
Disorientation	1
Loose Stool	1
Panting	1
Tremors	1

Adverse events associated with concurrent use of KBr with other antiepileptic drugs such as phenobarbital have been reported. Neurologic signs were the most common adverse event and included sedation, irritability, restlessness, depression, behavioral changes, ataxia, hind limb paresis, mydriasis, stupor, and coma. The neurologic signs were reported to be reversible.

CONTACT INFORMATION:

For a copy of the Safety Data Sheet (SDS) or to report suspected adverse drug events, contact Pegasus Laboratories at 1-800-874-9764. For additional information reporting adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or http://www.fda.gov/reportanimalae

CLINICAL PHARMACOLOGY:

Mechanism of action: KBr is a halide salt that is thought to exert its antiepileptic activity by passing through neuronal chloride ion channels, thereby hyperpolarizing neuronal membranes, raising the seizure threshold, and stabilizing neurons against excitatory input from epileptic foci.

Pharmacokinetics: The pharmacokinetics of a multi-dose regimen of administration in normal dogs have been evaluated as described in a comprehensive literature review. In one study, KBr was administered at 30 mg/kg orally every 12 hrs for a period of 115 days. Serum, urine, and cerebro-spinal fluid (CSF) bromide concentrations were measured at the onset of dosing, during the accumulation phase, at steady-state, and after a subsequent dose adjustment. Median elimination half-life and steady-state serum concentration were 15.2 days and 245 mg/dL, respectively. Apparent total body clearance was 16.4 mL/day/kg and volume of distribution was 0.40 L/kg. The CSF:serum bromide ratio at steady-state was 0.77.

Distribution, Metabolism, and Elimination: Bromide distributes into the CSF and interstitial tissues of the brain and is actively transported out of the CNS via the choroid plexus. At pharmacological doses, the active transport mechanism is overwhelmed and bromide accumulates in the brain and CSF. Bromide is not metabolized by the liver and is eliminated unchanged, primarily by renal clearance. Increased dietary consumption of chloride can promote loss of bromide in the urine, leading to a lowering of serum bromide concentrations. Decreased chloride consumption will promote increased renal reabsorption of bromide, causing an increase in bromide elimination half-life in dogs.

REASONABLE EXPECTATION OF EFFECTIVENESS:

KBroVet-CA1 is conditionally approved pending a full demonstration of effectiveness.

Additional information for Conditional Approvals can be found by searching www.fda.gov for "animal conditional approval."

Two retrospective studies were used to determine the dose and demonstrate a reasonable expectation of effectiveness for KBroVet-CA1 for the control of seizures associated with idiopathic epilepsy in dogs.

In a dose determination retrospective study, the total daily oral dose of KBr given for ≥45 days (approaching steady-state conditions) was described. To be included in this study, cases were required to meet the following eligibility requirements: samples submitted for serum bromide concentration evaluation within the required date range (January 1, 2003 to August 31, 2010), and dogs were between ≥0.5 and ≤5.0 years of age, receiving only KBr to control seizures associated with idiopathic epilepsy, administered KBr once or twice daily for ≥45 days at the dose noted on the submission form, and the serum bromide concentration was ≥0.8 and ≤3.5 mg/mL.

A total of 284 case records (58.5% male and 41.6% female), with a mean age of 3.6 years (0.7–5.0 years) and a mean body weight of 20.5 kg (1.3–88.2 kg), were evaluated between January 1, 2003 to August 31, 2010. The mean total daily oral dose was 46.6 (±21.9) mg/kg with a range of 24.5–68.3 mg/kg. These results describe the total daily oral dose range to achieve serum bromide concentrations within 10% of the published therapeutic range (≥0.8 and ≤3.5 mg/mL)[1,2] for dogs with idiopathic epilepsy.

A pilot retrospective study involving review of case records of 51 client-owned dogs was conducted to evaluate the effectiveness of KBr in dogs. This retrospective study evaluated case records of dogs previously receiving only KBr to control seizures associated with idiopathic epilepsy and for which blood samples had been analyzed to quantify serum bromide concentrations for the purpose of therapeutic drug monitoring.

Seizure counts, seizure count changes, seizure event days per month and seizure severity scores were tabulated for eligible cases, comparing the 30 day period before initial treatment with KBr and the 30 day period of steady state KBr dosing. Seizure count within an individual case was required to decrease by 50% or greater in order for the case to be classified as a seizure count success. Similarly, reduction in the number of seizure event days per month by 50% was required for the case to be classified as a seizure event day count success. No increase in severity score denoted an individual case treatment success for this variable. Of the 51 evaluable cases, 27 were determined as valid for safety and effectiveness data and 24 were determined to be valid for only safety data.

Of the 27 cases, 19 (70%) were defined as "success" and 8 (30%) were defined as "failures" based on seizure count results. Eighteen (67%) were defined as "success" and 9 (33%) were defined as "failures" based on seizure event day results. Seizure severity

score decreased or did not change in 25 of the 27 cases evaluated for effectiveness. Overall, of the 27 dogs included in the effectiveness analysis, 18 (67%) were considered treatment successes and 9 (33%) were considered treatment failures.

ANIMAL SAFETY:

Safety was assessed in a systematic review of literature and a retrospective field study. Reversible neurologic signs were the most consistently reported adverse effect and were generally associated with adjunctive KBr treatment or high serum bromide concentrations. Adverse effects were also seen in some dogs with low serum bromide concentration. Dermatologic and respiratory abnormalities were rare in dogs. Evidence suggested that administration of KBr with food may alleviate gastrointestinal irritation and that monitoring for polyphagia, thyroid hormone abnormalities, and high serum bromide concentrations may be beneficial.

HOW SUPPLIED:

KBroVet-CA1 are liver-flavored, non-scored tablets containing 250 mg or 500 mg of potassium bromide per tablet. KBroVet-CA1 is packaged in bottles containing 60 or 180 tablets.

500mg Tablet (60 ct) bottle NDC 49427-398-48
250mg Tablet (60 ct) bottle NDC 49427-397-48
500mg Tablet (180 ct) bottle NDC 49427-398-50
250mg Tablet (180 ct) bottle NDC 49427-397-50

STORAGE CONDITIONS: Store at controlled room temperature 20–25°C (68–77°F).

Keep out of reach of children and animals.

[1] Boothe DM. Anticonvulsant and other neurologic therapies. In: Boothe DM, Ed. Small Animal Clinical Pharmacology and Therapeutics. Philadelphia: WB Saunders Co., 2001; 431-456

[2] Dewey CW. Anticonvulsant therapy in dogs and cats. Vet Clin North Am Small Anim Pract 2006; 36:1107-1127.

02-2022

KBroVet®-CA1
(potassium bromide
chewable tablets)

PRN®
PHARMACAL

For more information, please visit us at SteadyTheStorm.com.