Drug	Phenobarbital	Potassium Bromide	Zonisamide	Levetiracetam
MOA	Increase neuronal responsivity to GABA Anti-glutamate effects Inhibition of voltage-gated Ca^{2+} channels	Br^- ion acts like Cl^- Passes through the Cl^- channel and hyperpolarizes the neuronal membrane *Chem/electrolyte panel will show elevated Cl^-	Sulfonamide derivative Blocks T-type Ca^{2+} and voltage-gated Na^+ channels Binds to Cl^- channels associated with $GABA_A$ receptor Modulates dopamine, serotonin, acetylcholine +/- Free radical scavenger	Binds synaptic vesicular protein (SV2A) ~Reduces neuronal calcium flow inhibiting neurotransmitter release May directly inhibit voltage-gated calcium channels
PK/PD	Hepatic metabolism Potent inducer of cytochrome P450 *may need to adjust/increase dose over time $T_{1/2}$ (oral) Dogs 40-90h Cats 40-50h Steady State: 10-15 days	Renally excreted -Watch diet, changes in Cl^-/Na^+/ and water can alter KBr excretion Safe in patients with liver disease Can be given as KBr or NaBr NaBr: when K^+ needs to be limited (hypoadrenocorticism) KBr: when Na^+ needs to be limited (congestive heart failure) $T_{1/2}$ (oral) Dogs ~ 24 days Steady state: 3-4 months	Hepatic metabolism $T_{1/2}$ (oral) Dogs: 15 hours *shorter when simultaneously given with other drugs that stimulate hepatic enzymes Steady state: 5-7 days	Minimal hepatic metabolism 70-90% of drug excreted in urine Nearly 100% bioavailability $T_{1/2}$ (oral) Dogs: 4 hours Cats: 3 hours Steady state: ~24 hours

Common Adverse Effects	PU/PD/PP Sedation and Ataxia Elevation of ALP, GGT *may see pseudohypoparathyroidism Decreased T4 and fT4 with increased TSH, usually not accompanied with clinical signs	PU/PD/PP Sedation and Ataxia (worse in large-breed dogs) Weight Gain GI upset Hyperactivity	Sedation and ataxia (usually self-limiting within the first two weeks and worse in large-breed dogs) GI Upset <u>Sulfonamide</u> Immune mediated KCS, polyanthropy Renal tubular acidosis Decreased T4	Mild and transient Dogs: Sedation and ataxia Cats: Sedation, ataxia, and anorexia Poor efficacy as a monotherapy for epilepsy *Feline audiogenic reflex seizures: 28/28 cats had a >50% reduction in seizure frequency
Uncommon Adverse Effects	<u>Dogs</u> Clinical hepatic failure Blood dyscrasias Superficial necrolytic dermatitis <u>Cats</u> Facial pruritus, Generalized pruritus with distal limb edema, thrombocytopenia, leukopenia Single case of severe cutaneous eruptions and lymphadenopathy	<u>Cats</u> Pneumonitis (~40%) may be FATAL <u>Dogs</u> Bromism -Clinically heterogeneous neurotoxicosis -Altered consciousness, ataxia, paresis, weakness -Treat via diuresis (watch for breakthrough seizures) Pancreatitis Behavioral abnormalities	Acute hepatic necrosis	Major adverse events are uncommon
Dosing the Patient	Dogs: 3-5 mg/kg po q 12h Cats: 1-2 mg/kg po q 12h	Dogs: 20-35 mg/kg po q 24 hours *can divide dose in 2 and give q12h to reduce adverse effects	Dog 5 mg/kg po q 12 hours OR	20 mg/kg po q 8 hours Transdermal application *may* be an option for cats

		Decrease dose by 15% for NaBr	10 mg/kg po q 12 hours if concurrently receiving phenobarbital	
Contraindications	Liver disease Concurrent use of drugs inhibiting cytochrome P450 -Ketoconazole, cimetidine, chloramphenicol	Renal disease History of pancreatitis Rapid control of seizures needed	Pre-existing KCS	

Emergency Drugs!

Diazepam: IV (0.5 mg/kg) or per rectum (1-2 mg/kg)

Midazolam: IV or intranasal (0.2-0.5 mg/kg)

Quick Math: 20lb dog = 0.5mL midazolam IV/IN or 1mL diazepam IV