Top 5 Uses for Gabapentin in Dogs & Cats

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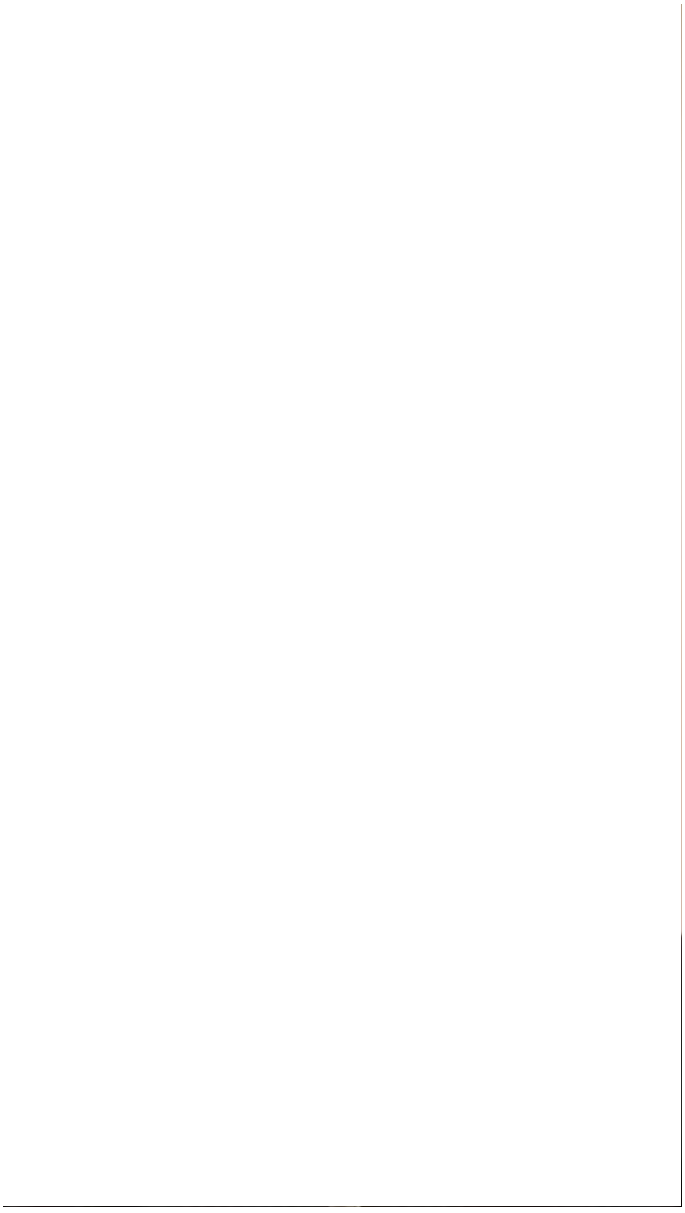

Gabapentin is a widely used antiepileptic and analgesic designed to function as a centrally acting gamma-aminobutyric acid (GABA)-receptor agonist.[1] Although gabapentin is structurally related to the GABA molecule, it does not bind to or alter the GABA receptor and is believed to bind instead to the alpha2delta subunit of voltage-gated calcium channels on

presynaptic neurons in the CNS, blocking influx of calcium into the nerve terminal and decreasing release of excitatory neurotransmitters.[2,3]

Gabapentin is FDA-approved in humans for use as an anticonvulsant, treatment of pain associated with postherpetic neuralgia and fibromyalgia, and treatment of neuropathic pain associated with diabetes and spinal cord injuries.[3] Gabapentin is the seventh most frequently prescribed drug in the United States; use has increased significantly in human medicine and is often (>80%) extra-label.[4,5]

A survey of clinicians found that gabapentin use in veterinary medicine is similar to use in human medicine; 69% of respondents indicated they prescribe gabapentin on a daily or weekly basis, most commonly for acute and chronic pain (extra-label).[1]

Following are the author's top 5 recommended uses for gabapentin based on mechanism of action and physiology of pain.

1. Gabapentin for Preclinic Sedation

At-home administration of oral sedatives/anxiolytics before visiting the clinic can reduce patient anxiety and fearful behaviors by allowing drugs to take effect before the patient encounters stressors. Gabapentin is used extra-label as an antianxiety medication in humans[6-8]; administration in cats (50-100 mg/cat PO) can decrease stress scores.[9,10]

The Chill Protocol (ie, combination drug protocol that includes gabapentin, melatonin, and oral transmucosal acepromazine) is an option for preclinic sedation developed at the Cummings School of Veterinary Medicine at Tufts University to manage fearful and aggressive dogs and cats.[11] Dose-dependent sedation is a common adverse effect of gabapentin administration in veterinary patients[12,13]; high doses of gabapentin (ie, 20-25 mg/kg PO the evening before the appointment and 20-25 mg/kg PO at least 1-2 hours before the appointment) are incorporated in the Chill Protocol to induce preclinic sedation.[11]

2. Gabapentin for Neuropathic Pain

Neuropathic pain (eg, intervertebral disk herniation, plexus avulsions, nerve root impingement) is caused or initiated by a primary lesion in the CNS or peripheral nervous system, including damage or injury to nerves that transfer information from the skin,

muscles, and/or other parts of the body to the brain and spinal cord.[14,15] Imbalances between excitatory and inhibitory pain signaling, as well as modulation of pain messages in the CNS, contribute to development of neuropathic pain.[15]

Gabapentin inhibits presynaptic calcium channels, thus decreasing release of excitatory neurotransmitters (eg, substance P, glutamate, glycine) that amplify pain signals by binding to postsynaptic neurokinin-1 (ie, NK-1), *N*-methyl-D-aspartate (ie, NMDA), and alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (ie, AMPA) receptors.

Neuropathic pain is a complex pain state, and several drug classes are often required to reduce inciting nociceptive afferent impulses.[14] Gabapentin can be included in a multimodal treatment plan in conjunction with other analgesic drugs (eg, NSAIDs, opioids, *N*-methyl-D-aspartate–receptor antagonists).[14]

3. Gabapentin for Breakthrough Pain

Pain transmission involves conversion of a noxious stimulus to an electrical signal transmitted by peripheral sensory fibers to the dorsal horn of the spinal cord.[14] Pain signals are either amplified or suppressed by endogenous neurotransmitters or analgesic drugs in the dorsal horn and progress to the brain, where the signal is consciously perceived. Untreated amplification of pain signals in the dorsal horn can lead to maladaptive or chronic pain states.[14]

Gabapentin can be added to an analgesic regimen to manage heightened pain states if first-line analgesics are insufficient. Inhibition of presynaptic calcium channels can help reduce excitatory pain signaling, thus improving analgesia. Gabapentin may also act synergistically in combination with other analgesics, reducing required doses and minimizing adverse effects (eg, dysphoria, sedation). Heightened pain states that may require adjunct analgesics (eg, gabapentin) include polytrauma, pathologic fractures, thrombosis, and extensive inflammation (eg, peritonitis, fasciitis).[14]

4. Gabapentin for Osteoarthritis (OA)

Osteoarthritis is a chronic inflammatory condition involving joint pain that results in decreased mobility and muscle weakness[14]; however, there may also be a neuropathic component.[16] Inflammation of the affected joint activates peripheral nociceptors innervating

the synovial capsule, periarticular ligaments, periosteum, and subchondral bone. Repetitive activation results in peripheral sensitization and abnormally excitable pain pathways in the peripheral nervous system and CNS.[16]

Osteoarthritis treatment can be complex, and recommendations include baseline analgesics (eg, NSAIDs) and nonpharmacologic treatments (eg, exercise, weight management).[14] Gabapentin is an adjunct analgesic that can be incorporated if first-line treatments are insufficient.

5. Gabapentin for Cancer Pain

Cancer pain can range in severity, depending on the location and type of cancer. Patients may experience inflammatory pain due to tumor necrosis or pain caused by direct pressure of the tumor on nerves or muscles. Metastatic involvement of bone is also a frequent cause of cancer pain and can be associated with clinical signs related to neuropathic pain.[14]

A multimodal approach using several classes of drugs is most effective. Therapies that decrease tumor activity, reduce inflammation, or target neuropathic pain can help treat cancer pain. First-line agents often include NSAIDs with the addition of opioids and adjunctive drugs (eg, gabapentin) as indicated.[14]

GABAPENTIN DOSAGE INFORMATION FOR DOGS & CATS

- Use in veterinary patients is extra-label.
- Conditions associated with neuropathic pain
    - Dogs: 10 mg/kg PO every 8 hours[17]
    - Cats: 8 mg/kg PO every 6 hours[18]
    - Frequent administration maintains minimum target plasma concentrations in dogs and cats because gabapentin is rapidly absorbed and eliminated.[17]

- Preclinic sedation
    - Dogs/cats: 20 to 25 mg/kg PO the evening before the appointment and 20 to 25 mg/kg PO at least 1 to 2 hours before the appointment[11]
    - Sedation is likely in both dogs and cats at 20 mg/kg PO.
- The human oral liquid product contains xylitol, which is toxic to dogs.

Conclusion

Gabapentin has a narrow indication for use in veterinary patients, but administration is common. Caution should be used when prescribing gabapentin, particularly for use as a sole analgesic for conditions with little evidence for efficacy (eg, acute postoperative pain).[1]

Gabapentin can be abused in humans, and prescriptions for veterinary patients can be diverted for human recreational use (see **Drug of Abuse**). Gabapentin should thus not be prescribed when it is unlikely to be effective (see **Inappropriate Uses for Gabapentin**), the quantity should be limited, and restrictions should be placed on refill authorizations.

INAPPROPRIATE USES FOR GABAPENTIN

- Single agent for acute postoperative pain
    - Inflammation is the most common component of acute postoperative pain. Gabapentin modulates pain signals from the periphery but does not treat inflammation and can reduce (but will not stop) pain signaling in the CNS.
- Renal compromise
    - Gabapentin is removed from the body via the kidneys and should be used with caution in patients with renal insufficiency, as increased adverse effects (eg, sedation, hypotension) are possible.[24-26]

- As-needed administration
    - Frequent administration of gabapentin is required to maintain adequate plasma concentrations in dogs and cats.[17,18] Administration on an as-needed basis or at intervals less frequent than indicated by pharmacokinetic studies can result in insufficient plasma concentrations and lack of efficacy.
- Long-term postoperative sedation
    - Sedation is a common adverse effect of gabapentin, particularly with administration of high doses[12,13]; however, this effect diminishes over time, and gabapentin is unlikely to provide sedation over several days or weeks.
- Pelvic-end weakness
    - Ataxia is a common adverse effect of gabapentin.[12] Administration in patients with pelvic-end weakness may exacerbate signs and decrease the ability to ambulate without assistance.

DRUG OF ABUSE

Human recreational drug users may ingest supraclinical amounts of gabapentin for intoxication or use gabapentin to augment the effects of illicit opioids.[3-5,19-23] Patients who overdose and are taken to an emergency room are more likely to die or require a ventilator if an illicit opioid was combined with gabapentin.[4,5,22] Deaths due to overdose in which gabapentin was also detected doubled between 2019 and 2020.[4]

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