Trazodone can reliably and safely induce sedation and anxiolysis in dogs and cats, making it a useful pharmacologic agent beyond the treatment of behavior problems.

INDICATIONS
Trazodone has been clinically used in both dogs and cats; however, its use has been more extensively researched in dogs.

- Situational anxiety related to
  - Separation
  - Noise phobia (eg, fireworks, thunderstorms)
  - Veterinary visits
  - Hospitalization
  - Travel
- Postoperative confinement
- Adjunct therapy used in combination with other psycho-pharmacological agents to treat anxiety-related behavioral problems (eg, fearful behavior toward humans or other animals)

PHARMACOLOGY & CLINICAL APPLICATIONS
Trazodone is an atypical antidepressant used to treat anxiety and depression by acting as a serotonin antagonist/reuptake inhibitor (SARI).

- Trazodone is most often prescribed as an augmenting agent to selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants (TCAs).
- It globally increases serotonin levels by blocking presynaptic reuptake in humans and presumably in dogs and cats.
  - Higher doses (see Recommended starting dose, next page) are typically required to achieve reuptake inhibition.
  - The drug also readily antagonizes postsynaptic serotonin 2A and 2C receptors (5-HT_{2A} and 5-HT_{2C}, respectively), thereby inhibiting glutamate release and stimulating dopamine and norepinephrine release in the prefrontal cortex.

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5-HT_{2A} = serotonin 2A receptor
5-HT_{2C} = serotonin 2C receptor
SARI = serotonin antagonist/reuptake inhibitor
SSRI = selective serotonin reuptake inhibitor
TCA = tricyclic antidepressant
In addition to antagonizing serotonin receptors, trazodone antagonizes histamine 1 (H\(^1\)) and \(\alpha\)-adrenergic receptors, resulting in a sedative-hypnotic effect.\(^4\)

- Sedation may be achieved at lower doses as compared with doses needed for treatment of anxiolysis (see **Recommended starting dose**).\(^4\)
- May be used to facilitatepostsurgical confinement\(^3\)
- Could also promote calm behavior in other situations (eg, travel/transport, nighttime restlessness associated with cognitive dysfunction)

**Recommended starting dose for dogs is 3-7 mg/kg PO once to twice a day.**\(^5\) If the drug is used to treat situational anxieties, the same dose can be administered as needed 1 to 2 hours before the anticipated event; that dose may be further increased to effect.\(^5\)

- When prescribing trazodone for the first time, instruct clients to administer a test dose at home in a quiet and calm environment to monitor for
  - Time to onset of sedation or behavioral calming
  - Duration of effect
  - Adverse events and side effects

- If behavioral calmness and/or anxiolysis are not achieved, the dose or administration frequency may be increased to effect.
- Studies have reported a large PO dose range of up to 14 mg/kg once a day (for as-needed administration only) and 19.5 mg/kg once a day (for both daily and as-needed administration).\(^1\)

**In dogs, latency to onset is typically <2 hours following oral administration, permitting use as a faster-acting sedative/anxiolytic for situational anxiety.**\(^1,3\)

- Anxiety-provoking situations that may benefit from trazodone treatment include veterinary visits, travel/transport, separation anxiety, and noise phobias associated with fireworks or thunderstorms.
- Oral trazodone may also be administered by veterinary staff to anxious hospitalized patients as long as there are no contraindications.
- Preemptively administer trazodone 1 to 2 hours before onset of anxiety to prevent emotional sensitization.
- Presence of food in the upper GI tract may delay absorption.\(^6\)
- For dogs, trazodone may be used on an as-needed basis for situational anxieties, as daily medication administered every 8 to 10 hours, or when a combination of daily and as-needed administration is required.\(^1\)
  - Duration of effect is variable.
    - Median duration of action when used to facilitate postsurgical calming was ≥4 hours.\(^3\)

A recent study in cats showed that trazodone was well-tolerated and caused sedation at doses of 50, 75, and 100 mg.\(^2\)

- Cats achieved peak sedation at 2 to 2.5 hours after oral administration.\(^2\)
- Trazodone may be a good alternative fast-acting anxiolytic in cats that exhibited adverse events to benzodiazepines (eg, lorazepam).
- It may be used in similar situations as for dogs.
- Recommended starting dose in adult cats\(^7\)
  - 25 mg/cat
  - Can be titrated to effect

**ADVERSE EVENTS & WITHDRAWAL EFFECTS**

Adverse events associated with oral administration of trazodone in dogs and cats are typically mild and well-tolerated.

- Potential effects include\(^1,2,6\)
  - Sedation
  - Ataxia
  - GI effects (eg, vomiting, diarrhea)
  - Increase or decrease in appetite
  - Agitation
  - Tachycardia
  - Behavioral disinhibition
- IV administration of trazodone has only been investigated in dogs and is not recommended, as doing so may trigger aggressive behavior in some dogs.\(^5\)
  - An injectable form of trazodone is not commercially available.

**Tolerance, withdrawal effects, and dependence have not been reliably demonstrated.**

- As a precaution, patients may be tapered off medication to

**Patients may be tapered off medication to reduce the likelihood of withdrawal effects.**
reduce the likelihood of withdrawal effects and to observe the patient for increased anxiety while trazodone is withdrawn.

**CAUTIONS**

Because of potential risk for serotonin syndrome, use caution when combining trazodone with other serotonergic agents and/or monoamine oxidase inhibitors (MAOIs).

- Although trazodone is most often used to augment SSRIs and TCAs, caution must be taken when it is administered with these other agents.
  - Signs of serotonin syndrome include
    - Cardiovascular changes (ie, tachycardia, bradycardia, hypertension, arrhythmias)
    - Tachypnea
    - Hyperthermia
    - Nervous system effects (ie, disorientation, weakness, hyperexcitability, agitation, hyperreflexia, hyperesthesia, tremors, seizures, coma)
    - GI changes (ie, vomiting, diarrhea, hypersalivation)
  - Signs can lead to death.
- Close patient monitoring via recheck appointments and/or client communication is recommended.

When writing prescriptions or discharge instructions for trazodone, do not mistake trazodone for tramadol.

- On the prescription label, specify FOR ANXIETY as treatment indication.
- Educate clients about the difference between trazodone and tramadol, particularly if the pet receives both medications.
- To minimize prescription errors, use exaggerated lettering, also known as Tall Man Lettering, to distinguish look-alike medications (eg, traZODone vs traMADol).

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**References**

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