Drugs Used for Appetite Stimulation in Dogs & Cats

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Appetite stimulants can be administered either temporarily while diagnostic tests are completed and long-term treatment is implemented or chronically to maintain body condition and muscle mass in patients with conditions such as chronic kidney disease or neoplasia. These drugs can also be useful in diabetic patients with inconsistent appetites. In dogs and cats, commonly used oral appetite stimulants (eg, mirtazapine, capromorelin, cyproheptadine) act centrally on receptors that control feeding behavior.

Use of injectable benzodiazepines and propofol for short-term induction of food intake in anorexic hospitalized patients has been described in the literature.[1,2] Anabolic steroids, megestrol acetate, and glucocorticoids also increase appetite, but their clinical use is limited.

The following are not listed in order of preference.

Mirtazapine

Mirtazapine is a 5-HT_{2A}-, 5-HT_{2C}-, 5-HT_3-, and H_1-receptor antagonist and a presynaptic alpha-2−autoreceptor antagonist that causes enhanced noradrenergic and serotonergic transmission. Effects on appetite may be related to antagonism of 5-HT_{2C} and H_1 receptors involved in appetite regulation; alpha-1 receptor affinity is much lower than alpha-2 receptor affinity. An antiemetic effect may also be mediated by antagonism of the 5-HT_3 receptor.[3-5]

Dosage (Cats, Dogs)

- Cats

- 0.5 mg/kg PO every 24 hours (practically, ≈1.88-3.75 mg/cat PO every 24 hours, with the larger dosage being for larger cats)[6]
    - Frequency should be decreased to every 48 hours in geriatric cats or those with kidney disease (International Renal Interest Society stage II-IV).[4]
    - Frequency should be decreased to every 48 to 72 hours in cats with liver disease (less frequently in patients with more severe disease).[7]
- 1.5-inch strip (2 mg/cat) of the FDA-approved transdermal product on pinna every 24 hours[8]
    - Onset of activity may be slower than with oral administration.[9]
- Compounded transdermal products are also available, but composition, absorption, and stability vary. These products may therefore produce substantially lower drug concentrations than intended.
    - Two commercially available compounded products had 44% to 87% and 55% to 75% of the label concentration of mirtazapine, respectively.[10]

- Dogs: 0.6 mg/kg PO every 12 hours[11]
    - Half-life is shorter in dogs than in cats.

Key Points (Cats)

- In young, healthy cats, a median dose of 0.5 mg/kg PO significantly increased food consumption; increased effect was not seen when the dose was increased to 0.9 mg/kg.[6]
- In cats with chronic kidney disease, 1.88 mg/cat PO every 48 hours increased appetite, body weight (median weight gain, 0.4 lb [0.18 kg] over 3 weeks), and activity level and reduced vomiting compared with placebo.[12]
- In cats with clinically significant weight loss and a variety of conditions (not including severe kidney disease or neoplasia) treated with the transdermal product at 2 mg/cat every 24 hours, average weight gain was 3.9% after 2 weeks.[8]
- Dual antiemetic and appetite stimulant effects may be useful in patients undergoing chemotherapy.

    - Evaluation is currently limited to an uncontrolled study in cats with lymphoma.[13]

- Adverse effects of oral administration can include vocalization, hyperactivity/agitation, vomiting, ataxia, tremors, hypersalivation, mydriasis, tachypnea/tachycardia, and lethargy.[14]

    - Adverse effects are more likely in cats given >2.5 mg/kg every 24 hours and are uncommon in cats given <0.75 mg/kg every 24 hours.

    - Subclinical ALT elevation that resolved after discontinuation of the drug was reported in one cat.[12]

- Transdermal formulations may cause erythema, flaking, crusting, or pruritus at the application site, but these effects typically resolve with discontinuation of the drug.[8,13]

- Serotonin syndrome can occur in elderly humans administered high doses and when mirtazapine is administered in conjunction with other serotonergic drugs, including selective serotonin reuptake inhibitors (eg, fluoxetine), monoamine oxidase inhibitors (eg, selegiline), and tricyclic antidepressants (eg, amitriptyline).[15] Use with tramadol in veterinary patients is also theoretically contraindicated because tramadol inhibits serotonin reuptake.[16] Although there is no documentation of serotonin syndrome in companion animals given clinically relevant dosages, these combinations should be avoided if possible, and close monitoring for adverse effects is recommended.

Key Points (Dogs)

- Efficacy data in dogs are primarily anecdotal, except for a noncontrolled case series.[17]

- May be used anecdotally in combination with capromorelin or as an alternative, particularly in dogs that do not tolerate liquids or have excessive salivation when given capromorelin

- Adverse effects are possible.

- In research beagles, no adverse effects were seen with chronic administration of 2.5 or 15 mg/kg every 24 hours for 1 year.[18] Mild ALT and ALP elevation, mild anemia, and

weight loss were seen within 6 months with administration of 80 mg/kg every 24 hours.

Capromorelin

Capromorelin is a ghrelin-receptor agonist that causes the sensation of hunger and stimulates feeding behavior. This drug also triggers pituitary release of growth hormone (via the same receptor) and subsequent hepatic release of insulin-like growth factor 1 (IGF-1), which reduces growth hormone secretion in humans and dogs.[21]

Dosage (Cats, Dogs)

- Cats: 2 mg/kg PO every 24 hours (available as 20 mg/mL oral solution)
- Dogs: 3 mg/kg PO every 24 hours (available as 30 mg/mL oral solution)
    - 4.5 mg/kg PO every 24 hours or 3 mg/kg PO every 12 hours did not increase effect[21]

Key Points

- Dogs and cats receiving this drug have increased food consumption and significant weight gain compared with those given placebo.
    - Dogs given 3 mg/kg PO every 24 hours for 4 days gained a mean 1.8% of body weight compared with 0.1% in dogs given placebo. In the dogs receiving capromorelin, 76% gained weight and 68.6% had increased appetite (as assessed by owners) compared with 44.6% both gaining weight and having increased appetite in dogs given placebo.[22]
    - Cats with chronic kidney disease and ≥5% unintended weight loss given the recommended dose regained 3.5% of their body weight after 2 weeks and 5.2% of their body weight after 8 weeks. Cats receiving placebo had no weight change after 2 weeks and a loss of 1.6% of body weight after 8 weeks.[23]
- Adverse effects in dogs can include hypersalivation, GI upset, and abdominal discomfort.[22,24]

- Adverse effects in cats can include hypersalivation, GI upset, behavior changes (eg, lethargy, hiding), and transient decreases in heart rate and blood pressure, which may be clinically significant in older or debilitated cats. Capromorelin may need to be avoided in critically ill cats or cats with potential cardiovascular compromise.[23,25]

- This drug may be contraindicated in patients with acromegaly and should be used with caution in patients with current or prior diabetes mellitus.

    - In cats and dogs, increased growth hormone secretion subsequent to capromorelin administration persists with repeated administration but is attenuated by suppression of the growth hormone by IGF-1 after 7 days in dogs. IGF-1 levels, however, remain elevated throughout treatment.[21,26]

    - In dogs, postprandial glucose was elevated after capromorelin administration.[26] In healthy cats, daily administration resulted in early decrease in insulin secretion and glycemic control and increase in glycemic variability[27]; effects were attenuated toward the end of a 30-day course.

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Other Agents

- Propofol (2 mg/kg IV once) administered to anorexic dogs following ovariohysterectomy resulted in voluntary food consumption within 15 minutes in 87% of dogs compared with 5% in dogs given placebo.[1]

    - Although propofol may be used for acute appetite stimulation, chronic administration is not practical because of the need for intravenous

administration.

- Benzodiazepines (eg, diazepam, oxazepam) increase appetite temporarily, presumably by binding to gamma-aminobutyric acid type A receptors in the parabrachial nucleus in the caudal brainstem and enhancing sensory characteristics of food.[2]

    - Repeated oral administration of diazepam in cats has been associated with potentially fatal hepatic necrosis.[28]

- Glucocorticoids and megestrol acetate can result in polyphagia; however, chronic use of these drugs as appetite stimulants may be appropriate only in the context of palliative care because of other possible adverse effects (eg, insulin resistance, polydipsia, behavior changes).[29,30]

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