

ORAL VETERINARY PSYCHOTROPIC DRUGS

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Updated by M. Leanne Lilly, DVM (2016-2019), Maggie O'Brian, DVM (2019), and Kyle Bohland, DVM (2020)

Class	Mechanism	Indications	Side effects	Drug	Dose (dog)	Dose (cat)	Other
Selective serotonin reuptake inhibitors (SSRIs)	Inhibits presynaptic reuptake of serotonin 5HT1A receptor: ↓arousal, anxiolysis	Anxiety disorders Compulsive disorders Aggression Urine marking * Reconcile : FDA label for separation anxiety in dogs	Anorexia (fluoxetine) Sedation (fluoxetine) V+/D+ (worse fasted) Mild anticholinergic effects (urinary/fecal retention, dry eye/ mouth) Loose stool (sertraline) *Mediated by 5HT2A/2C; resolve in weeks (5HT1A upregulates, other 5HT receptors downregulate)	Fluoxetine (Prozac, Reconcile)	0.5mg/kg q24 x 14d, then 1mg/kg q24hr; maximize up to 2mg/kg q24	0.25mg/kg q24hr x 14d, then 0.5mg/kg q24hr; only titrate up if necessary	Reconcile: manufacturer claims 20% better absorption vs. generic
				Paroxetine (Paxil)	0.5mg/kg -2mg/kg Q12		Anecdotally, similar efficacy to fluoxetine; some case studies, no controlled trials; most anticholinergic SSRI
				Sertraline (Zoloft)	1-2mg/kg PO q24hr x 14d, then 3-4 mg/kg PO		0.5 mg/kg PO q24hr x 14d, then 1 mg/kg q24hr
Tricyclic anti-depressants (TCAs)	Inhibits presynaptic reuptake of serotonin, norepinephrine, and some dopamine	Anxiety disorders Compulsive disorders Aggression Urine marking Stereotypic behaviors * Clomicalm : FDA label for separation anxiety in dogs	Sedation (antihistamine): worse than SSRIs Moderate anticholinergic effects (urinary/fecal retention, dry eye/mouth) Potentially arrhythmogenic (amitriptyline) Possible ↓seizure threshold	Clomipramine (Clomicalm)	1-2mg/kg PO q12hr x 2w, then 3mg/kg PO q12hr	0.25-1.25mg/kg q24hr	Clomicalm expensive. Some manufacture issues at times Label dose is q24hr = WRONG!
				Amitriptyline (Elavil)	2.0-4.0 mg/kg q12hr		Weaker anxiolytic than clomipramine (↑NERI, ↓SRI); more side effects Used in FIC and feline urolithiasis
				Doxepin (Sinequan)	3-5mg/kg PO q12hr		0.5-1.0 mg/kg q24hr
Serotonin Nor-epinephrine Reuptake Inhibitors	Inhibit presynaptic re-uptake of serotonin and NE	Anxiety disorders with hyperkinetic component	Sedation GI upset	Venlafaxine (Effexor)	2mg/kg q12h (up to 4mg/kg)	Not regularly used- no safety data, no efficacy data	No data on ER release, caution in houses with cats, common spontaneous drug ingestion May be helpful in treating chronic neuropathic pain
Azapirones	5HT1A serotonergic agonist; some dopaminergic	Anxiety disorders Compulsive disorders Urine marking Phobias/fear disorders	Behavioral disinhibition (friendlier, can ↑aggression) V+/D+ (rare) Bradycardia (rare)	Buspirone (Buspar)	1.0-2.0 mg/kg q12hr	0.5-1.0 mg/kg q12-24hr	NOT indicated for aggressive animals Can use for “bullied” animal (fearful), not aggressor animal
MAO-B Inhibitor	Decreases breakdown of serotonin, norepinephrine, and dopamine (also inhibits presynaptic reuptake of all three NT's) Also some MAO-A inhibiting effects.	FDA approved for use in dogs with CCD Generalized anxiety	Restlessness, agitation, vomiting, disorientation, diarrhea, salivation, and diminished hearing. Also less commonly increased aggression. Five week washout period required after stopping selegiline before starting other serotonergic medications.	Selegiline (Eldepryl, Anipryl)	0.5-1.0 mg/kg q24hr in AM	0.5-1.0 mg/kg q24hr in AM	Used to treat Parkinson's disease and depression in people Also used to treat pituitary-dependent hypoadrenocorticism in dogs

Phenothiazine neuroleptics	↑dopamine in brainstem → ↓motor activity (tranquilization)	Restraint Sedation for travel Situational adjunct to anxiolytics (boarding, storms)	Hypotension (α-blockade) Sedation Antiemetic Paradoxical excitation (cats) Possible ↓seizure threshold	Acepromazine	0.5-1.0 mg/kg PRN up to q6hr	0.5-1.0 mg/kg PRN up to q6hr	NO anxiolytic properties Possible increase in noise sensitivity	
Benzo-diazepines	GABA agonist → anxiolysis, sedation, muscle relaxation, appetite stimulation	Anxiety disorders Phobias/fear disorders Sedation for travel Urine marking Aggression Idiosyncratic hepatic necrosis (oral diazepam in cats, within 2-3d of starting) *Do “test dose” to assess sedation/paradoxical excitation Avoid in narrow angle glaucoma	Sedation Appetite stimulation Muscle relaxation Paradoxical excitation Idiosyncratic hepatic necrosis (oral diazepam in cats, within 2-3d of starting) *Do “test dose” to assess sedation/paradoxical excitation Avoid in narrow angle glaucoma	Alprazolam (Xanax)	0.02-0.1mg/kg PRN or q6-12hr	0.125-0.25 mg/cat PRN or q12hr	Onset 30-60 mins, lasts 2-4 hrs Least sedating benzodiazepine	
				Diazepam (Valium)	0.5-2.0mg/kg PRN or q6-12hr	AVOID	Onset 30-60 mins, lasts 4-6 hrs	
				Clorazepate (Tranxene)	0.55-2.2mg/kg PRN or q8-24hr	AVOID	Onset 30-60 mins, lasts 8 hrs (“long-acting diazepam” including metabolites)	
				Lorazepam (Ativan)	0.1-0.5mg/kg PRN or q8-12hr	0.125-0.25 mg/cat PRN or q12hr	Onset 30-60 mins, lasts 8 hrs No active liver metabolites = best for cats	
				Clonazepam (Klonopin)	0.1-0.5mg/kg q8-12h (dosages up to 2mg/kg have been reported)	0.02-0.25mg/kg Q12 to 24 or PRN (mostly avoided in cats)	Onset 30-60 mins longest lasting (8-12+ hours) Similar metabolism to diazepam, orally dispersible tablets (ODT) contain xylitol (unknown quantity)	
Serotonin antagonist and reuptake inhibitor (SARI)	Inhibit presynaptic serotonin reuptake; block 5HT1B receptors → ↑5HT1A effect	Adjunct to SSRI/TCA: Anxiety disorders Compulsive disorders Phobias/fear disorders	Sedation Diarrhea/loose stool Others (rare): vomiting, behavior change, excitement, increased appetite	Trazodone (Desyrel)	Weight	Initiation dosage range	Target dosage range	Generally target 5mg/kg to start, up to 18mg/kg q8 hours with a “Maximum” k9 dose of 300mg/dose
GABA Analogs	Variety of mechanisms, do not activate benzo site Voltage gated Ca ²⁺ α2-δ blocker	Anxiolytic, sedative, abnormal sensations, neuropathic pain, adjunct seizure control	Sedation, Ataxia GI upset Disinhibition of vocalization (w or w/o aggression)	Gabapentin (Neurontin)	5-50mg/kg Q8-12	5-50mg/kg Q8-24; 50-100mg/cat 2 hours prior to stressful events.	Cleared by kidneys May increase levels secondary to use of morphine Oral availability may decrease 20% with antacids	
α-2 agonists	Blocks NE release in locus ceruleus by activating pre-synaptic α-2 receptors → ↓α/β stimulation	Anxiety disorders Compulsive disorders Phobia/fear disorders	Sedation (dose-dependent; not seen at doses used) Possible bradycardia/hypotension (dose-dependent) Increased noise sensitivity with clonidine? (1/8 dogs tested with noise/storm sensitivity had increased sensitivity after 0.03mg/kg of clonidine in Ogata/Dodman, 2011)	Clonidine (Catapres)	0.01-0.05mg/kg PRN up to q8hr	(not routinely used)	Contraindicated with acepromazine (counteract α-effects)	
				Dexmedetomidine gel (0.25ml per dot, 0.1mg/ml) (Sileo)	Weight (lb) Number of dots k9 only 4.4-12.1 ● 12.2-26.5 ●● 26.6-44.0 3 ●●● 44.1-63.9 ●●●● 64.0-86.0 ●●●●● 86.1-110.2 ●●●●●● 110.3-137.8 ●●●●●●● 137.9-166.4 ●●●●●●●● 166.5-196.2 ●●●●●●●●● 196.3-220.5 ●●●●●●●●●●	Contraindicated with cardiac compromise Vomiting most common side effect Will cause pale spot on gums!		

LITERATURE REGARDING USE OF ORAL VETERINARY PSYCHOTROPIC DRUGS

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Reference	Drug/dose	Subjects	Study design	Efficacy	Side effects	Other notes/critiques																															
<p>Herron et al. 2008. Retrospective evaluation of the effects of diazepam in dogs with anxiety-related behavior problems. JAVMA 233: 1420-1424.</p>	<p>Diazepam</p> <p>Mean low dose: -prescribed: 0.7mg/kg -administered: 0.5mg/kg</p> <p>Mean high dose: -prescribed: 1.4 mg/kg -administered: 1.0 mg/kg</p> <p>Total dose range: 0.15-2.3 mg/kg ** Owners gave lower dose than prescribed!!</p> <p>3 dosing schedules: Given 1-3 times only (41%) Given as needed (41%) Given daily (19%)</p>	<p>N = 37 dogs (73% participation)</p> <p>Inclusion criteria: Dogs prescribed diazepam by UPenn behavior service (2005-2007), excluding dogs euthanized</p> <p>Behavioral diagnoses: Separation anxiety (59%) Thunderstorm phobia (27%) Noise phobia (8%) Other anxiety disorders (19%) Many w/ multiple ddx</p> <p>Drug co-administration: Fluoxetine (51%) Clomipramine (24%) Sertraline (5%) Diazepam only (19%)</p>	<p>Retrospective cross-sectional study; owners interviewed via telephone</p>	<p>Efficacy (client-reported): Very effective: 24% Somewhat effective: 43% Not effective: 32%</p> <p>**More likely effective in thunderstorm phobia vs. separation anxiety</p> <p>Discontinuation: Total discontinued drug: 51% -For side effects: 58% -For lack of efficacy: 53%</p>	<p>Overall adverse effects: Ataxia (62%) Sedation (59%) Increased appetite (43%) Agitation (32%) Increased activity (27%) Aggression (13%) Vomiting/diarrhea (6%)</p> <p>Leading to discontinuation: Agitation (32%) Increased activity (26%) Ataxia (26%) Increased appetite (11%) Diarrhea/vomiting (10%)</p> <p>**High doses (>0.8mg/kg) more likely to have increased activity vs. low doses **As-needed dosing more likely to continue vs. daily/seldom</p>	<p>No control for severity of behavior problems</p> <p>No control for coadministration of other anxiolytics</p> <p>Only 1 owner stopped diazepam b/c behavior problem resolved</p> <p>Paradoxical excitation (agitation, increased activity) was #1 reason for discontinuing; aggression NOT common reason for discontinuing</p> <p>Take-home: Diazepam relatively effective but often discontinued d/t side effects (esp. paradoxical excitation); educate owners and start at low dose</p>																															
<p>Gruen and Sherman 2008. Use of trazodone as an adjunctive agent in the treatment of canine anxiety disorders: 56 cases (1995-2007). JAVMA 233: 1902-1907.</p>	<p>Trazodone</p> <p>See chart for dosing used</p> <p>Begun at half of target dose for 3d</p> <p>3 dosing schedules: Given daily (25%) Given PRN (36%) Given daily and PRN (39%)</p> <p>Time from behavioral diagnosis to start of trazodone: 0-228w (mean 21w)</p>	<p>N = 56 dogs</p> <p>Inclusion criteria: Dogs prescribed trazodone by NCSU behavior service (1995-2007) for 1° or 2° diagnosis of anxiety or phobic disorder with ≥1mo follow-up</p> <p>Behavioral diagnoses: Separation anxiety (48%) Thunderstorm phobia (48%) Generalized anxiety (23%) Other phobias (20%) Compulsive disorder (5%) 23% of dogs also had aggression</p> <p>Drug co-administration: **NO MAOIs or amitraz TCAs (55%) SSRIs (38%) Benzodiazepines (32%) Buspirone (21%) Reserpine (4%)</p>	<p>Retrospective case series; medical record review</p>	<p>Efficacy (client-reported): Very improved (72.5%) Somewhat improved (12.5%) No effect (7.5%) Adverse effects (7.5%) Continued >3mo (82.1%)</p> <p>Long-term follow-up: Continued >3mo: 82.1% Range 3-95mo, mean 24.8mo No changes in annual bloodwork</p> <p>Dogs showing no effect: all resistant to multiple other drugs and behavioral modification</p>	<p>Overall adverse effects: Vomiting/gagging (4%) Increased excitement (4%) Sedation (4%) Increased appetite (4%) Diarrhea (2%) Behavioral disinhibition (2%)</p> <p>Leading to discontinuation: Gagging Behavioral disinhibition (getting on counters) Diarrhea</p> <p>No evidence of serotonin syndrome despite co-administration of other serotonergic drugs at published doses</p> <p>No increase in aggression despite many dogs having aggression disorders</p>	<p>No control for coadministration of other anxiolytics</p> <p>Bias toward dogs who were nonresponsive to other treatments</p> <p>Starting at ½ target dose effectively prevented diarrhea/loose stool in all but 1 dog</p> <p>Low risk of serotonin syndrome even when used with other serotonergic drugs</p> <p>Take-home: Trazodone useful and well-tolerated as adjunct to other anxiolytics, even in refractory patients</p> <table border="1" style="width: 100%; font-size: small;"> <thead> <tr> <th>Weight</th> <th>Initiation dosage range</th> <th>Target dosage range</th> </tr> </thead> <tbody> <tr> <td>< 10 kg</td> <td>≤ 25 mg, q 8-24 h</td> <td>≤ 50 mg, q 8 h-24 h</td> </tr> <tr> <td>10-20 kg</td> <td>50 mg, q 12-24 h</td> <td>100 mg, q 8-24 h</td> </tr> <tr> <td>20-40 kg</td> <td>100 mg, q 12-24 h</td> <td>200 mg, q 8-24 h</td> </tr> <tr> <td>> 40 kg</td> <td>100 mg, q 12-24 h</td> <td>200-300 mg, q 8-24 h</td> </tr> </tbody> </table> <table border="1" style="width: 100%; font-size: x-small;"> <thead> <tr> <th>Administration schedule</th> <th>Minimum</th> <th>Maximum</th> <th>Mean</th> </tr> </thead> <tbody> <tr> <td>Daily medication only</td> <td>1.9 mg/kg/d</td> <td>16.2 mg/kg/d</td> <td>7.3 mg/kg/d</td> </tr> <tr> <td>As needed only</td> <td>2.2 mg/kg/d</td> <td>14 mg/kg/d</td> <td>7.6 mg/kg/d</td> </tr> <tr> <td>Daily medication and as needed</td> <td>1.7 mg/kg/d</td> <td>19.5 mg/kg/d</td> <td>7.25 mg/kg/d</td> </tr> </tbody> </table>	Weight	Initiation dosage range	Target dosage range	< 10 kg	≤ 25 mg, q 8-24 h	≤ 50 mg, q 8 h-24 h	10-20 kg	50 mg, q 12-24 h	100 mg, q 8-24 h	20-40 kg	100 mg, q 12-24 h	200 mg, q 8-24 h	> 40 kg	100 mg, q 12-24 h	200-300 mg, q 8-24 h	Administration schedule	Minimum	Maximum	Mean	Daily medication only	1.9 mg/kg/d	16.2 mg/kg/d	7.3 mg/kg/d	As needed only	2.2 mg/kg/d	14 mg/kg/d	7.6 mg/kg/d	Daily medication and as needed	1.7 mg/kg/d	19.5 mg/kg/d	7.25 mg/kg/d
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<p>Stevens et al., 2016 "Efficacy of a Single Dose of Trazodone Hydrochloride given to Cats prior to Veterinary Visits to Reduce Signs of Transport- and Examination-Related Anxiety."</p>	<p>Trazodone in cats: 50mg per cat or placebo</p>	<p>N= 10 laboratory cats</p> <p>Drug co-administration: No concomitant anxiolytics</p>	<p>Placebo controlled cross over trial with 3 week wash out period</p>	<p>Efficacy: Owners scored before, during, and after transport and examination. Veterinarian assessed signs of anxiety during examination.</p>	<p>No change heart rate, aural temperature, and Doppler ultrasonographic measurement of arterial blood pressure.</p> <p>Respiratory rate was lower.</p>	<p>1 cat got sick, 4 didn't complete trial No drive-colony enclosure to exam room-extendibility to real life?</p>
<p>Orlando et al., 2015 "Use of Oral Trazodone for Sedation in Cats: A Pilot Study."</p>	<p>Trazodone in cats: 50, 75, or 100mg per cat</p>	<p>N= 6 colony cats</p> <p>Drug co-administration: No concomitant anxiolytics</p>	<p>Placebo controlled</p>	<p>Efficacy: trazodone 50, 75 and 100 mg caused sedation as measured by activity reduction (83%, 46% and 66%, respectively)</p> <p>Response to examination, at 90 min post-tx not significantly different between cats receiving trazodone 100 mg and placebo., decreased signs of stress at 50mg</p>	<p>No adverse effects such as anorexia, vomiting, diarrhea, ataxia, tremor, paradoxical excitation or disinhibition in any cat throughout the course of the study</p>	<p>1 cat couldn't be medicated</p>
<p>Crowell-Davis et al. 2003. Use of clomipramine, alprazolam, and behavior modification for treatment of storm phobia in dogs. JAVMA 222:744-748.</p>	<p>Clomipramine: 2mg/kg PO q12hr x 3mo, then 1mg/kg PO q12hr x 2w, then 0.5mg/kg PO q12hr x 2 weeks</p> <p>*If no effect at 30-60d: increase to 3mg/kg *If adverse effects: decrease to 1mg/kg</p> <p>Alprazolam: 0.02mg/kg PO as needed 1 hour before storms and q4hr as needed</p>	<p>N = 40 dogs; 32 dogs completed entire 120d study</p> <p>Inclusion criteria: Dogs recruited/referred to UGA behavioral clinic Diagnosis of storm phobia based on behavioral hx (fear response to >3 recent storms) and response to recordings Healthy (PE/CBC/Chem/UA) Normal cognitive function Excluded if history of aggression</p> <p>Behavioral diagnoses: Storm phobia</p> <p>Drug co-administration: Not reported</p> <p>Behavioral modification: DSCC w/ audio storm sounds (practice 1x/day); IGNORE dog during actual storms</p>	<p>Prospective non-controlled open clinical trial</p> <p>Assessment @ day 0 and 120: PE, labwork, dogs videotaped during sound simulations</p> <p>Caregivers complete Storm Phobia Assessment (Likert scale) and global improvement scores at day 0, 30, 60, 90, 120</p>	<p>Efficacy (client-reported) at 120d: Resolved: 6.3% Substantially better: 37.5% Somewhat better: 50% Unchanged: 6.3% Worse: 0%</p> <p>Efficacy (SPA scores): Scores for total SPA and all individual behaviors decreased from day 0 to 120 (panting, pacing, trembling, hiding, salivation, destructiveness, vocalization, self-trauma, elimination) When follow-up available, scores remained decreased at 4mo</p> <p>Global improvement scores for each 30d period ↑w/ each period</p>	<p>Adverse effects (first 30d only): Vomiting: 13% Lethargy: 21% Diarrhea: 11% Constipation: 5% Increased appetite: 8% Increased thirst: 18% Decreased thirst: 3% Changes in sleep: 13% None consistent</p> <p>Unclear whether any owners decreased dose or discontinued d/t side effects</p> <p>No significant changes in laboratory values over time</p>	<p>Drug co-administration NOT reported</p> <p>Severity of side effects (leading to dose change, discontinuation, etc) not reported</p> <p>No improvement in videotaped behavior over time; owners say recordings less intense than home behaviors</p> <p>Most dogs will always require back-up "rescue" doses of alprazolam (storm phobia behaviors won't be completely resolved)</p> <p>Take-home: combination of clomipramine, alprazolam, and DSCC can be effective in decreasing storm phobias; videotaping response to sound recording NOT a good way to assess improvement</p>

Reference	Drug/dose	Subjects	Study design	Efficacy	Side effects	Other notes/critiques
<p>Hart et al. 1993. Effectiveness of buspirone on urine spraying and inappropriate urination in cats. JAVMA 203: 254-258.</p>	<p>Buspirone 2.5mg/cat PO q12hr x 2w initially -If favorable reduction in spraying (19%): continue dose x 8w -If no favorable reduction: increase dose to 5mg PO q12hr x 2w (73%) and repeat assessment; up to 7.5mg PO q12hr (8%)</p> <p>If effective during 8w: gradual taper over next 2w; if relapse, return to effective dose for 6-12mo</p> <p>If ineffective during 8w: attempt diazepam or progestins</p>	<p>N = 62 cats -76% MC, 24% FS -89% multi-cat, 11% 1-cat</p> <p>Inclusion criteria: Cats recruited/referred to UC Davis behavioral clinic Excluded if severe medical disease or history if FIC</p> <p>Behavioral diagnoses: Urine spraying (79%) Urine marking (21%) Inappropriate urination (9 cats)</p> <p>Previous drug administration: Progestin (48%; 75% did not respond) Diazepam (27%; 47% did not respond, 53% side effects)</p>	<p>Prospective non-controlled open clinical trial</p> <p>Multiple phone interviews with owners to assess improvement and adverse effects</p>	<p>Efficacy (client-reported): Favorable response (52%) - Cessation (34%) -75% reduction (18%) Unfavorable response: -50%, 25%, 0% reduction</p> <p>Household effect: More favorable response in multi-cat houses (58%) vs. single-cat (0%)</p> <p>Sex effect: no sex effect</p> <p>Drug withdrawal: of favorable resp, 50% didn't relapse; 2 did not respond to buspirone when resumed for 6-12mo</p> <p>Inappropriate urination: Favorable response (56%); 60% did not relapse with drug withdrawal</p>	<p>Adverse effects: Increased friendliness toward humans (19%) Increased aggression (15% = more assertive behavior in previously timid cats) Agitation after pilling (8%) Sedation (6%) NO ataxia</p> <p>Long-term treatment up to 18mp: no adverse effects</p>	<p>Buspirone more effective than progestins (30% respond, more males) and as effective as diazepam (55-75% respond, equal sex), but saw MUCH less relapse with buspirone when treatment stopped (91% of diazepam cats relapsed)</p> <p>Unclear if inappropriate urination cats were separate cats or among urine marking group</p> <p>Specific data for "unfavorable responses" not given</p> <p>Knew w/in 1 week if buspirone work = recommend 1w trial at 5mg PO q12hr; if successful, continue for 8w then reduce; if relapse, go 6-12mo</p> <p>Take-home: use buspirone as first-line drug for urine marking in cats d/t low side effect profile and lack of dependence</p>
<p>Ogato and Dodman 2011. The use of clonidine in the treatment of fear-based behavior problems in dogs: an open trial. Journal of Veterinary Behavior 6: 130-137.</p>	<p>Clonidine PRN 1.5-2hrs before fear-inducing event</p> <p>Initial dose: 0.01mg/kg PO PRN (up to q12-24), increased up to 0.05mg/kg</p> <p>Optimal dose: A: 0.026 mg/kg B: 0.017 mg/kg</p> <p>Time between initial behavior diagnosis and initiation of clonidine: A: 0-12mo (med 4mo) B: 6-48mo (med 12mo)</p>	<p>N = 22 dogs</p> <p>Inclusion criteria: Dogs treated by Tufts behavioral clinic for fear-based behavior problems; previous tx ineffective</p> <p>Behavioral diagnoses: Group A (N=10): separation anxiety, noise/storm phobia Group B (N=12): fear or territorial aggression</p> <p>Drug co-administration: A: clomipramine, fluoxetine, or sertraline (all); buspirone (4); previous PRN alprazolam or propranolol (7) B: fluoxetine, sertraline, buspirone, or F+B (11)</p>	<p>Prospective non-controlled open clinical trial</p> <p>Multiple telephone interviews with owners: assess response after 3 optimal doses at least 24hrs apart</p>	<p>Efficacy (client-reported): Improved: 70% A, 92% B (total 82%) Greatly (>70%) improved: 30% A, 25% B Moderately (30-70%) improved: 30% A, 50% B Slightly (<30%) improved: 10% A, 18% B Unchanged: 30% A, 8 %B Worsened: None</p> <p>No difference in improvement or optimized dose between groups A/B</p>	<p>Adverse effects: One noise phobic dog showed increased noise sensitivity</p> <p>Sedation, hypotension, bradycardia NOT seen (due to extremely low doses used?)</p> <p>Owners reported effect 1.5-2hrs after administration, lasting 4-6hrs</p>	<p>Owners in this study found clonidine more effective than prior PRN meds (alprazolam or propranolol)</p> <p>Take-home: clonidine can be useful adjunct PRN medication for dogs with fear-based disorders</p>

Reference	Drug/dose	Subjects	Study design	Efficacy	Side effects	Other notes/critiques
<p>King et al. 2000. Treatment of separation anxiety in dogs with clomipramine: results from a prospective, randomized, double-blind, placebo-controlled, parallel-group, multicenter clinical trial. Applied Animal Behavior Science 67: 255-275.</p>	<p>Clomipramine 3 treatments (random): -Standard-dose clomipramine (SDC): 1-2mg/kg PO q12hr -Low-dose clomipramine (LDC): 0.5-1 mg/kg PO q12hr -Placebo (P): PO q12hr</p> <p>Clomipramine and placebo supplied by Novartis (Clomicalm and vehicle)</p>	<p>N = 95 dogs (France, UK, US) SDC (28), LDC (35), P (32)</p> <p>Inclusion criteria: Dogs recruited from rDVM/newspaper; separation anxiety >1mo; excluded if systemic dz (CBC/chem) or other behavioral disorder (aggression, urine marking)</p> <p>Behavioral diagnoses: Separation anxiety: 3 signs of hyper-attachment to owner AND at least 1 behavior in absence of owner (destruction, defecation, urination, vocalization)</p> <p>Drug co-administration: all drugs with CNS activity stopped 2w prior to trial</p> <p>Behavioral modification: used for all dogs; standardized instructions for owners (at home, before leaving, when returning)</p>	<p>Prospective, randomized, double-blind, placebo-controlled, parallel-group, multicenter clinical trial</p> <p>Visits at d0, 28, 56, and 84; dogs examined and owners questioned</p>	<p>Efficacy (client-reported): <i>Assessment</i> (cured, much/moderate/little/no improvement): greater much/mod improvement for SDC vs. P at all 3 time points; significant for 1-2 time points</p> <p><i>Individual scores</i> for each sign (disappeared, improved, no change, or worse vs. day 0): more improvement for 3 signs (destruction, defecation, and urination) for SDC vs. LDC/P at all 3 time points; significant for 1-2 time points per sign; NO difference for vocalization</p> <p>SDC: improved 3x faster for destruction, defecation, and urination vs placebo, 1.5-3x faster for vocalize</p> <p>LDC: no difference compared to placebo</p>	<p>Adverse effects (higher in SDC/LDC vs. P): Vomiting/gastritis Lethargy</p> <p>All mild/transient; no dogs withdrawn due to adverse effects; most owners did not think caused by drug</p> <p>No changes in CBC/Chem</p> <p>One serious medical event: greyhound in SDC group → collapse, hyperthermia, DIC; clomipramine discontinued and dog recovered; idiosyncratic reaction vs. unrelated event?</p>	<p>Efficacy of SDC equivocal for: -vocalization (owners can't assess?) -total disappearance of signs (difficult goal to achieve in 3mo)</p> <p>SDC/P difference was greater at d56 than d84 for all 4 behavior scores = possible that behavior modification alone "caught up" to clomipramine? BUT global score still better for SDC; authors suspect problems with statistical power at d84.</p> <p>Some dogs appeared to "deteriorate" during trial (worse scores in subsequent time periods), but happened in all treatment groups</p> <p>Take-home: addition of standard-dose clomipramine to behavioral modification can decrease severity and/or frequency of signs of separation anxiety in dogs, and may cause faster resolution of signs, compared to behavior modification alone.</p>
<p>Sherman et al. 2007. Effects of Reconcile (Fluoxetine) chewable tablets plus behavior management for canine separation anxiety. Veterinary Therapeutics 8: 18-31.</p>	<p>Fluoxetine 2 treatments (random): -Reconcile (R): 1-2mg/kg PO q24hr -Placebo (P): PO q24hr</p> <p>Fluoxetine tablets and placebo supplied by Lilly (Reconcile beef-flavored chewable tablets)</p>	<p>N = 242 recruited, 197 used R (101), P (96)</p> <p>Inclusion criteria: from rDVMs; SA >1mo with 4+ events/week; excluded systemic disease, seizures, if aggression causing risk of human injury</p> <p>Behavioral diagnoses: SA with at least 1: destruction, urination, defecation, salivation, licking/grooming, vocalization, shaking, restlessness, depression; confirmed by veterinary behaviorist after 14d pretreatment</p> <p>Drug co-administration: Psychoactive drugs stopped 30d prior</p> <p>Behavioral modification: used for all dogs; standardized instructions for owners (at home, before leaving, when returning)</p>	<p>Prospective, randomized, double-blind, placebo-controlled, parallel-group, multi-center clinical trial</p> <p>Visits: 0, 4w, 8w Phone calls: 2w, 6w</p>	<p>Efficacy (client-reported): Overall severity score (OSS) & individual SA behaviors (0-4); binary scale for improvement in OSS (calculated weekly)</p> <p>Improved global OSS: At 1w: 42% R, 17% P At 8w: 72% R, 50% P Higher R>P each week, significant all except w3</p> <p>Improved: - Destruction, vocalize, restlessness: R>P, significant most weeks -Defecation, urination, licking/grooming, shaking, depression: but not significant</p> <p>Weekly rate of improvement for OSS depression/vocalize: significantly more rapid R>P</p>	<p>Adverse effects: Lethargy: 45% R, 17% P Anorexia: 29% R, 11% P Shaking /tremor: 16% R, 4% P Vomiting: 15% R, 9% P Restlessness: 14% R, 6% P Vocalization: 11% R, 6% P Seizures: 3 R, 1 P (2 after fluoxetine discontinued); none definitively associated with drug</p> <p>Most resolved within 1-2w; some (shaking, restlessness, vocalization) may be manifestations of separation anxiety that improved w/ tx</p> <p>Dose reduction effectively reduced severity of adverse effects</p> <p>Palatability: (voluntarily ingesting within 3mins) R: 70.5% P: 85.4%</p> <p>No changes in CBC/Chem</p>	<p>Take-home: Reconcile is palatable and effective for treatment of SA when administered in conjunction with behavior management plan (increased overall success and rate of success)</p>

Reference	Drug/dose	Subjects	Study design	Efficacy	Side effects	Other notes/critiques																		
Sileo FDA product application 2015	Sileo (dexmedetomidine 0.25ml/dot 0.1mg/ml)	N= 71 sileo dogs and 73 control dogs	Owner reported behavior changes on NYE in Finland and Germany Measured mean behavior scores of anxiety/fear	125 mcg/m2 lowest effective dose. confirmed safety and efficacy at 125 mcg/m2 SILEO had excellent or good treatment effect in 75% of dogs Placebo had excellent or good treatment effect in 33% of dogs SILEO dogs displayed less panting, trembling, trying to hide than control	<table border="1"> <thead> <tr> <th>Adverse Reactions</th> <th>Control N=92</th> <th>Dexmedetomidine 125 mcg/m² N=89</th> </tr> </thead> <tbody> <tr> <td>Emesis</td> <td>1 (1.1)</td> <td>4 (4.5)</td> </tr> <tr> <td>Gastroenteritis</td> <td>0</td> <td>1 (1.1)</td> </tr> <tr> <td>Periorbital Edema</td> <td>0</td> <td>1 (1.1)</td> </tr> <tr> <td>Drowsiness</td> <td>0</td> <td>1 (1.1)</td> </tr> <tr> <td>Sedation</td> <td>0</td> <td>1 (1.1)</td> </tr> </tbody> </table> <p>Additionally, transient pale mucous membranes were noted in SILEO-treated dogs. Gel application did not result in mucosal irritation</p>	Adverse Reactions	Control N=92	Dexmedetomidine 125 mcg/m ² N=89	Emesis	1 (1.1)	4 (4.5)	Gastroenteritis	0	1 (1.1)	Periorbital Edema	0	1 (1.1)	Drowsiness	0	1 (1.1)	Sedation	0	1 (1.1)	Intensity of Effect: 28 percent OTM bioavailability, peak plasma concentration is approximately ¼ of the same dosage with IV or IM administration. About ¼ of the dose of dexmedetomidine administered is absorbed. There is a dose-dependent effect on behavioral and physiological responses. Duration of Effect: The half-life of SILEO is 0.5–3h; therefore, SILEO has a duration of effect of 2–3 hours.
Adverse Reactions	Control N=92	Dexmedetomidine 125 mcg/m ² N=89																						
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Pankratz et al (2017) Use of single-dose oral gabapentin to attenuate fear in cage-trap confined community cats...	Gabapentin 50mg, 100mg per cat	N= 53 cats (21 intact males, 30 intact females, 2 spayed females) Placebo n=19 50mg n=17 (M=16.3mg/kg) 100mg n=17 (M= 35.3mg/kg) Range 9.2-47.6 mg/kg	Double-blind placebo-controlled filed trial	@ 2 and 3 hour after admin Low and high doses had lower stress scores No change in global sedation score	No adverse effects specific to gabapentin detected	Standard sedation scales not used due to disturbing near by cats earlier admin may decrease self-trauma																		
Delucci et al. (2010) Use of Venlafaxine in cataplexy.BSAVA	Venlafaxine 2.5mg/kg/day		Lit review, BSAVA letter	Decreased cataplexy attacks																				
Tonokura et al (2007) Review of pathophysiology and clinical management of narcolepsy in dogs	Venlafaxine 6-12 mg/kg/day	None listed	None listed	?	No anti-cholinergic sides noted	Max use 12mg/kg/day for cataplexy																		