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TITLE: Clinical Application of the American College of Veterinary Emergency and Critical Care (ACVECC) Consensus on the Rational use of Antithrombotics in Veterinary Critical Care (CURATIVE) Guidelines to Small Animal Cases

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**Title:** Clinical Application of the American College of Veterinary Emergency and Critical Care (ACVECC) Consensus on the Rational use of Antithrombotics in Veterinary Critical Care (CURATIVE) Guidelines to Small Animal Cases

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**Disclaimers:** None

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Running title: Application of CURATIVE Guidelines

### List of abbreviations:

ATE	arterial thromboembolism
CURATIVE	$\underline{C}$ onsens <u>u</u> s on the <u>R</u> ational use of <u>A</u> nti <u>t</u> hrombotics <u>in</u> <u>V</u> eterinary Critical Car <u>e</u>
НОСМ	Hypertrophic obstructive cardiomyopathy
GN	glomerulonephritis
LMWH	low molecular weight heparin
PICO	population or patient, intervention, control, outcome
PLN	protein losing nephropathy
UFH	unfractionated heparin
UPC	urine protein to creatinine ratio
VTE	venous thromboembolism

#### Abstract

**Objective** – To illustrate the application of the <u>Consensus</u> on the <u>Rational use of <u>Antithrombotics in</u> <u>Veterinary Critical Care</u> (CURATIVE) guidelines to the management of dogs and cats at risk of developing thrombosis using a case-based approach.</u>

**Etiology** – Dogs and cats become at risk of developing thrombosis from a wide range of conditions. These conditions often involve a specific insult followed by an inflammatory response and when combined with other contributing factors (eg, hypercoagulability, vascular endothelial injury, hemodynamic changes) create favorable conditions for thrombosis.

**Diagnosis** – Development of thrombosis in small animals remain challenging to demonstrate. Compatible clinical signs, the presence of known risk factors, and supporting diagnostic tests may be highly suggestive of the development of thrombosis

**Therapy** - Therapeutic recommendations in accordance with the CURATIVE guidelines for dogs and cats are described in specific case vignettes presented. Discussion is centered on antithrombotic drug choices and dosing protocols, as outlined in Domain 2 and 3 of the CURATIVE guidelines. Where appropriate, guidelines related to therapeutic monitoring (Domain 4) and discontinuation of antithrombotics (Domain 5) were included.

**Prognosis** – In small animals at risk of developing thrombosis, overall prognosis may be improved by following consensus-based recommendations on the use of antithrombotics as outlined in the CURATIVE guidelines. Whether such interventions have any impact on outcome requires further investigation.

Keywords: cats, dogs, thromboprophylaxis, therapeutic monitoring, antiplatelet agent, anticoagulant

#### Introduction

Following the development of the first consensus guidelines for the rational use of antithrombotics in dogs and cats at risk of thrombosis,<sup>1</sup> the Consensus working group created a series of clinical cases that could be used to demonstrate how guideline recommendations could be applied. The body of work conducted as part of the <u>Consensus</u> on the <u>Rational use of Antithrombotics in Veterinary Critical Care</u> (CURATIVE) initiative encompasses a summary of the guidelines,<sup>1</sup> as well as the individual domain manuscripts that provided the PICO (population/patient, intervention, control, outcome) questions and evidence summaries used to generate the guidelines.<sup>2-6</sup> The aim of this manuscript is to provide additional direction on the practical application of these guidelines.

The CURATIVE recommendations are intended for the "average" dog or cat at risk of thrombosis, receiving care in a "typical" veterinary emergency and critical care practice or specialty hospital. Nonetheless, the CURATIVE contributors recognize that there is considerable variation in clinical cases presenting to veterinarians and in the practice settings in which these guidelines may be applied. As such, the objective of this manuscript is to provide a discursive illustration of the application of the guidelines to the management of dogs and cats at risk for thrombosis using a case-based approach.

Cases scenarios were developed based on populations at risk of thrombosis as outlined in CURATIVE Domain 1.<sup>2</sup> Case descriptions were left deliberately vague to encompass a variety of different disease presentations and severities. Therapeutic recommendations for dogs and cats were tailored to specific case vignettes based on the CURATIVE guidelines regarding antithrombotic drug choices and dosing protocols, as outlined in Domains 2 and 3.<sup>3,4</sup> Where appropriate, guidelines describing therapeutic monitoring (Domain 4)<sup>5</sup> and discontinuation of antithrombotics (Domain 5)<sup>6</sup> were included.

The CURATIVE contributors from 4 different geographic areas (the US, Canada, the UK, and Australia) provided information regarding drug formulations available to them with the estimated costs for each antithrombotic drug. Specific information regarding pricing was avoided, rather a general estimate is provided to illustrate the potential financial implications of different therapies for the pet

owner. Not all of the antithrombotic drugs discussed in the CURATIVE guidelines will be available in all in-house veterinary hospital pharmacies, thus some cost estimates are based on prices from human pharmacies. Clinicians are encouraged to seek out local information when prescribing specific antithrombotic therapies.

It should also be noted that these case scenarios do not include mention of thrombolytic therapies. Some specialists in veterinary emergency and critical care, and allied specialists that treat patients with thrombosis, may consider the use of thrombolytic drugs in some of the case scenarios provided herein. Since the use of thrombolytics in dogs and cats was outside the scope of the CURATIVE guidelines, such therapies are not addressed in this manuscript.

# Case scenario 1 - A dog with immune-mediated hemolytic anemia

A 6-year-old, 8 kg, female neutered, Shih Tzu is diagnosed with immune-mediated hemolytic anemia (IMHA) based on the presence of severe anemia, spherocytosis, a positive saline agglutination test, and evidence of extravascular hemolysis (hyperbilirubinemia). No identifiable cause was found despite an extensive diagnostic evaluation and as such the dog was considered to have primary IMHA. Treatment included immunosuppressive medications, packed red blood cell transfusion, and symptomatic care.

# Application of the CURATIVE guidelines

Immune-mediated hemolytic anemia is strongly associated with the development of thrombosis in dogs and as such antithrombotic therapy is recommended in this patient (**Guideline 1.1**). Canine IMHA is most frequently associated with venous thrombosis and hence anticoagulant therapy may be considered first (**Guideline 2.1**). It should also be noted that since both arterial and venous thromboembolic complications have been reported in dogs with IMHA the concurrent use of an antiplatelet drug and anticoagulant may be indicated in dogs with IMHA where the risk of thrombosis likely outweighs the risk of bleeding (**Guidelines 2.16 and 2.18**). There is insufficient evidence to make strong recommendations regarding which anticoagulant is most appropriate in dogs at risk of venous thrombosis, such as those with IMHA. Specifically, clinicians may consider unfractionated heparin (UFH) versus low molecular weight heparin (LMWH) (**Guideline 2.9a**) or the use of direct Xa inhibitors versus UFH in dogs (**Guideline 2.11a**). Although the guidelines suggest that LMWH may be used in preference to UFH and direct oral Xa inhibitors may be used in preference to UFH, based on evidence of equivalent efficacy combined with more reliable pharmacokinetics and ease of dosing, there is evidence of benefit of individually adjusted UFH (based on anti-Xa activity) in dogs with IMHA.<sup>7</sup>

There is insufficient evidence to make strong recommendations regarding the choice of antiplatelet agent in dogs, but we suggest that clopidogrel may be more effective than aspirin in dogs at risk of arterial thromboembolism (ATE) (**Guideline 2.5**). Dual antiplatelet therapy could also be considered; however, this was not specifically addressed in the CURATIVE guidelines.

Information regarding the aforementioned antithrombotic drugs, their dosing regimen, and approximate costs of therapy for this dog are provided in Table 1. Dosing oral medications is usually straightforward in that tablets can be divided as needed, although equal distribution of active ingredient throughout the tablet is not guaranteed for non-scored tablets. For the injectable LMWHs, formulations vary from multidose vials, to syringes designed for single-dose administration to people. When only single-dose syringes of dalteparin or enoxaparin are available, administration of the appropriate dose to small patients can be challenging. For a small dog such as this, it is likely cost prohibitive to administer the required dose from an individual dose syringe, and discard the remainder. It may be more practical to aseptically decant the contents of the syringe into a sterile vial, from which subsequent doses can be removed with a needle and syringe. The authors suggest that clinicians consult with their local pharmacy on the optimal method to achieve this in their practice setting.

Therapeutic monitoring would not be recommended for this dog unless UFH or a LMWH is selected. If UFH was chosen as the anticoagulant we recommend monitoring with anti-Xa activity to target 0.350.7 U/mL (**Guideline 4.3a, b**) 2 hours post-dose. If a LMWH is selected as the anticoagulant we suggest that adjusting therapy in dogs, targeting anti-Xa activity of 0.5-1.0 U/mL 2-4 hours post-dose can be considered (**Guideline 4.4b**).

The appropriate duration of antithrombotic therapy in dogs with IMHA was not specifically addressed in the CURATIVE guidelines. In addition to the inherent risk of thrombosis due to IMHA, glucocorticoid administration promotes a hypercoagulable state and may be associated with the development of thrombosis (**Guideline 1.4**). Both factors should be taken into consideration when determining the duration of antithrombotic therapy in dogs with IMHA treated with glucocorticoids. Other immunosuppressive medications such as cyclosporine or mycophenolate mofetil have not been associated with the generation of prothrombotic state.

#### Case scenario 2a – Aortic thrombosis in a dog with protein losing nephropathy

An 8-year-old, male neutered, Labrador retriever with a history of histologically confirmed glomerulonephritis (GN) resulting in protein losing nephropathy (PLN) is presented with an acute onset of pelvic limb paresis. He weighs 30kg. The dog receives therapy with benazepril, amlodipine for systemic hypertension, and mycophenolate mofetil as an immunosuppressive agent, according to standard of care.<sup>8</sup> On physical examination the dog lacks femoral arterial pulses bilaterally. An abdominal ultrasound identifies a thrombus in the descending aorta, confirming a diagnosis of aortic thrombosis. After extensive diagnostic evaluation, no other potential causes of thrombosis were identified.

### Application of the CURATIVE guidelines

Protein losing nephropathy is reliably associated with the development of thrombosis in dogs (Guideline 1.2a). Specifically, dogs with PLN are defined as being at high risk for thrombosis (Guideline 1.11). The CURATIVE guidelines recommend antithrombic therapy for dogs with PLN (Guideline 1.2b). We suggest that antiplatelet agents may be more effective than anticoagulants for the

prevention of ATE in dogs (**Guideline 2.3a**), but nonetheless, we suggest that anticoagulants may also be effective for the prevention of ATE in dogs (**Guideline 2.3b**).

Although there is insufficient evidence to make strong recommendations regarding clopidogrel versus aspirin in dogs (**Guideline 2.5a**), the CURATIVE group suggests that clopidogrel may be more effective than aspirin in dogs at risk of ATE (**Guideline 2.5b**). New antiplatelet agents could also be considered given evidence of favorable safety and efficacy (**Guideline 2.7**). Although this dog already has a diagnosed ATE, the same recommendations seem reasonable to apply as for ATE prevention. Approach to the thrombus itself is outside the scope of the CURATIVE guidelines; the reader is directed to recent literature.<sup>9</sup>

There is insufficient evidence to make strong recommendations for or against the use of combination antiplatelet and anticoagulant therapy in dogs at risk of ATE (**Guideline 2.18a**). We suggest that combination antiplatelet and anticoagulant therapy can be considered when the risk of thrombosis is felt to outweigh the increased risk of bleeding resulting from combination therapy (**Guideline 2.17b**). We suggest that the administration of clopidogrel or aspirin with LMWH may be considered in dogs at risk for ATE (**Guideline 2.18b**). With regard to the choice of anticoagulant in dogs, we suggest that the direct Xa inhibitors or LMWH may be used in preference to UFH (**Guidelines 2.9b and 2.11b**). Warfarin is not recommended (**Guideline 3.5**). Information regarding the aforementioned antithrombotic drugs, their dosing regimen, and approximate costs of therapy for this dog are provided in Table 2.

Therapeutic monitoring would not be recommended for this dog unless a LMWH is selected as the anticoagulant. We suggest that adjusting therapy in dogs, targeting anti-Xa activity of 0.5-1.0 U/mL 2-4 hours post-dose can be considered (**Guideline 4.4b**).

Antithrombotic therapy would be a lifelong recommendation in this dog, since the underlying condition cannot be cured or resolved (**Guideline 5.10**), even after resolution of the thrombus.

#### *Case scenario 2b – A dog receiving antithrombotic drugs now requires surgery*

Twelve months later the same dog described in case scenario 2a, now recovered from ATE, returns to the emergency room for evaluation of lethargy and inappetence. He is receiving clopidogrel and enoxaparin in addition to his GN specific therapies. Screening diagnostics reveal a large cavitated mass at the tail of the spleen with a small volume of echogenic peritoneal effusion, confirmed to be hemorrhage after aspiration and fluid analysis. The owners are keen to pursue a splenectomy given the high risk of the mass being neoplastic<sup>10</sup>; nonetheless the dog is cardiovascularly stable and it is considered that splenectomy may not need to be performed immediately. Attention is given as to whether the antithrombotic therapy should be discontinued prior to surgery.

# Application of the CURATIVE guidelines

This dog is considered a high risk for thrombosis based on underlying history of PLN and a history of aortic thrombosis (**Guideline 1.11**). As such we recommend that antiplatelet therapy with a single antiplatelet agent (in this case, clopidogrel) be continued prior to an elective procedure (ie, not discontinued) (**Guideline 5.3a**).

Similarly, we recommend that LMWH therapy should not be discontinued prior to an elective procedure. We recommend that surgery should be planned to occur at the nadir of the anticoagulant effect (**Guideline 5.5**), which is likely to occur just prior to the next scheduled dose (ie, 12 hours after the previous enoxaparin dose when administered at q12 hour intervals). The surgery team should be prepared for an increased risk of bleeding due to treatment with clopidogrel and LMWH, and close attention should be paid to surgical hemostasis, including the use of electrocautery. Appropriate ancillary diagnostic tests (eg, blood type, or crossmatch if indicated) should be performed prior to surgery in anticipation of potential need of blood product transfusion, and non-steroidal anti-inflammatory drugs should be avoided as part of the analgesic regimen due to potential adverse effects on platelet function.

In the situation where surgery on a patient receiving both antiplatelet and antithrombotic medications is not desired, consideration may be given to partial discontinuation of therapy prior to the procedure. Because abrupt discontinuation of LWMH is not associated with a rebound prothrombotic state (**Guideline 5.14**), and because the dog primarily had an arterial thrombotic event, it can be considered to continue clopidogrel therapy through the surgical period and discontinue LMWH for the perioperative period, with a recognition that the dog may be at a higher risk for the development of perioperative thrombosis.

After surgery, we recommend that antithrombotic therapy is continued on the same schedule, or restarted as soon as possible, provided there is no evidence of ongoing bleeding, since this patient is considered to be at high risk for thrombosis due to the underlying PLN and prior history of thrombosis (**Guideline 5.9**). Thrombosis is also reported to be a complication that can occur after splenectomy in dogs.<sup>11</sup>

## Case scenario 3 - A dog with sepsis

A 12-year-old, male neutered, Cavalier King Charlies Spaniel presents for evaluation of a 24-hour history of severe vomiting after dietary indiscretion. He has no past pertinent medical history. During hospitalization for treatment of gastrointestinal upset the dog develops an increased respiratory rate and effort with an intermittent soft cough. Thoracic radiographs identify an alveolar pattern in the right cranial, right middle, and left cranial lung lobes. Based on the dog's history aspiration pneumonia is suspected. Oxygen supplementation is commenced for hypoxemia. He develops a fever, and hematology reveals a marked leukocytosis with a left shift. The dog is considered to have sepsis based on derangements in his vital signs and evidence of aspiration pneumonia. Broad spectrum IV antimicrobial therapy is commenced.

#### Application of the CURATIVE guidelines

Sepsis is associated with derangements in coagulation, including disseminated intravascular coagulation and less commonly macrothrombosis.<sup>2</sup> In veterinary medicine there is insufficient evidence

at this time to recommend the routine use of antithrombotics in dogs with sepsis (**Guideline 1.7a, b**). The clinician could consider performing viscoelastic testing as a global evaluation of coagulation. Antithrombotic therapy may be considered for dogs with sepsis where hypercoagulability is demonstrated (**Guideline 1.7c**) or where other risk factors including co-morbidities or drug therapies exist.

#### Case scenario 4 – A dog with hyperadrenocorticism and pancreatitis

An 8-year-old neutered male mixed breed dog (body weight 8kg) is hospitalized for a 3-day history of vomiting and anorexia. Moderate to marked abdominal pain is present on physical examination. He is treated symptomatically with intravenous fluids, opioid analgesia, antacids, and antiemetics. A nasogastric tube is placed manage ileus and provide enteral nutrition. Pancreatitis with regional peritonitis is diagnosed based on an abdominal ultrasound performed by a board certified radiologist; the pancreas is enlarged and hypoechoic, with hyperechoic peripancreatic fat and scant free abdominal fluid in the cranial abdomen. Bilateral adrenomegaly is also noted on abdominal ultrasound. The dog has a history of pituitary dependent hyperadrenocorticism diagnosed with a low dose dexamethasone suppression test 6 months prior. The owners elected not to pursue treatment for hyperadrenocorticism given that the dog had few clinical signs; rather the diagnosis was made during work-up of an increased alkaline phosphatase on screening bloodwork prior to a periodontal treatment.

#### Application of the CURATIVE guidelines

Both pancreatitis and hyperadrenocorticism are considered low risk diseases for the development of thrombosis. The ACVECC CURATIVE guidelines state that antithrombotic drugs can be considered for dogs with pancreatitis (**Guideline 1.3**), and are not recommended for dogs with hyperadrenocorticism alone given weak evidence of an increased risk of thrombosis (**Guideline 1.5**). However, given that this dog has both pancreatitis and hyperadrenocorticism, the risk of thrombosis may be increased, and this dog is considered to be at higher risk of thrombosis than if either disease were present alone (**Guideline 1.11**). As such, antithrombotic therapy should be strongly considered.

Confirmatory testing, such as viscoelastic and plasmatic coagulation testing may help to clarify the individual patient risk.<sup>12,13</sup>

When pancreatitis and hyperadrenocorticism have been associated with thrombosis, venous thromboembolism is most common. As such, anticoagulant drugs would be the antithrombotic class of choice (Guideline 2.1). Options for this dog include UFH, LMWH, and oral direct Xa inhibitors (eg, rivaroxaban). Although there is insufficient evidence to make strong recommendations regarding the use of UFH versus LMWH in dogs, the ACVECC CURATIVE guidelines suggest that LMWH may be used in preference to UFH because of the positive safety profile of LMWH and more reliable bioavailability of the LMWH products compared to UFH (Guideline 2.9). Similarly, there is insufficient evidence to make strong recommendations regarding the use of the direct Xa inhibitors versus UFH in dogs; the ACVECC CURATIVE guidelines suggest that direct Xa inhibitors may be used in preference to UFH based on evidence of equivalent efficacy, combined with reliable pharmacokinetics and the ease of oral dosing (Guideline 2.11). As such, the two obvious choices for VTE prevention in this dog are a LMWH or direct-Xa inhibitor. Some of the CURATIVE panel members suggested that in a case scenario such as this, where only a short-course of antithrombotic therapy is indicated, LMWH may be preferable as there is no concern for rebound hypercoagulability with discontinuation (Guideline 5.14) as there may be with rivaroxaban (Guideline 5.15). In this case, the administration of aspirin or clopidogrel in addition to LMWH or a direct Xa inhibitor is not recommended, as the risk of clot formation is unlikely to outweigh the increased risk of bleeding resulting from combination therapy (Guideline 2.16).

Information regarding a two-week course of LMWH or a direct Xa inhibitor is provided in Table 3. Therapeutic monitoring could be considered for this dog if LMWH was chosen as the antithrombotic drug of choice. We suggest that adjusting therapy in dogs, targeting anti-Xa activity of 0.5-1.0 U/mL 2-4 hours post-dose can be considered (**Guideline 4.4b**).

Antithrombotic therapy would only be a short-term recommendation in this dog, since one of the underlying conditions (pancreatitis) can completely resolve with treatment (**Guideline 5.11**). Although there is insufficient evidence to make specific recommendations regarding the duration of antithrombotic treatment, a two-week course of antithrombotics is likely to be adequate. Alternatively, the clinician could consider discontinuation based on ultrasonographic evidence of resolution of disease. Since clinical signs often resolve prior to resolution of pancreatic inflammation, it is possible that the risk period for thrombosis continues beyond resolution of clinical signs, and thus so should antithrombotic therapy. Using blood-based biomarkers of systemic inflammation such as C-reactive protein, may also be useful.<sup>14</sup>

If LMWH was chosen as the antithrombotic, weaning prior to discontinuation is not recommended (**Guideline 5.14**). If rivaroxaban was chosen as the antithrombotic, weaning can be considered (**Guideline 5.15**). For this particular patient, a rivaroxaban dosing schedule of one 10 mg tablet once a day for two weeks, followed by one half tablet once a day for two days, followed by one half tablet every other day for two doses, then discontinuation, would be a reasonable approach.

#### Case scenario 5a – Initial presentation of a cat with cardiac disease

A 6-year-old, male neutered DSH (body weight 4.8kg) undergoes an echocardiogram after detection of a new gallop rhythm at a routine vaccination appointment. On physical examination the cat had a heart rate of 200/min, and a doppler blood pressure of 130 mm Hg. The cat is clinically well, with no past pertinent medical history. Echocardiography performed by a board-certified cardiologist diagnoses hypertrophic obstructive cardiomyopathy (HOCM) based on thickening of the left ventricular free wall, and systolic anterior motion of the mitral valve. The left atrium is enlarged (left atrial: aortic ratio 1.8 [normal <1.6]).<sup>15</sup> A thyroid panel is performed to rule out thyrotoxic heart disease, and is normal.

#### Application of the CURATIVE guidelines – Initial presentation

There is a strong association between feline cardiomyopathy, including HOCM, and thrombosis (**Guideline 1.9a**). This cat is thought to be at high risk for thrombosis given the left atrial dilation

(Guidelines 1.9, 1.11). As such, antithrombotic therapy is recommended (Guideline 1.9c). The ACVECC CURATIVE guidelines recommend that antiplatelet agents be used for the prevention of ATE in cats (Guideline 2.4a). Since cats with cardiomyopathy are at greater risk for ATE, rather than VTE, an antiplatelet drug is recommended for this cat. Specifically, it is recommended that clopidogrel be used instead of aspirin in cats at risk of ATE (Guideline 2.6).

Clopidogrel at a dose of 18.75mg PO once a day (one quarter of a 75mg tablet) is prescribed for the cat, with the intention of this being a life-long therapy since the underlying heart disease is not curable (**Guideline 5.11**). The clinician chose not to give a loading dose. The owner is counselled regarding the clinical signs associated with the development of ATE and congestive heart failure.<sup>16</sup> Additionally, daily monitoring of sleeping and resting respiratory rates is instituted as a tool to assess for the development of heart failure.<sup>17</sup> An annual echocardiogram is planned to monitor the progression of heart disease.

## Case scenario 5b – Subsequent presentation of a cat with cardiac disease and ATE

Eighteen months later the cat presents on an emergency basis with an acute onset of vocalizing and nonambulatory paraplegia. Distal aortic thromboembolism was diagnosed based on the physical examination findings of pulseless, cold pelvic limbs.<sup>18</sup> The owner had been giving the clopidogrel daily since initial diagnosis. Analgesia is provided, and the cat is hospitalized for management of concurrent congestive heart failure. Oral clopidogrel is continued at 18.75mg once daily.

# Application of the CURATIVE guidelines – Initial presentation

Although no evidence-based recommendations can be made regarding the addition of anticoagulants to antiplatelet agents for the prevention of ATE in cats, the ACVECC CURATIVE guidelines suggest the administration of clopidogrel in combination with LMWH can be considered in cats at risk of ATE (**Guideline 2.19**). As such, the clinician considered the addition of dalteparin or enoxaparin to the cat's treatment regimen.

The guidelines suggest that LMWHs (specifically, dalteparin and enoxaparin) should be given to cats by subcutaneous injection every 6 hours (**Guidelines 3.10, 3.12**). The clinician should counsel the owners that bleeding complications can occur when using dalteparin in cats, although they are usually minor and self-limiting (**Guideline 3.10c**). Although there are fewer publications regarding the use of enoxaparin in cats, a dose of 0.75-1.0 mg/kg SC q 6h (**Guideline 2.12a**) is recommended to reduce inter-individual variation in peak anti-Xa activity. Examples of dosing considerations and cost comparisons for a one-month course of dalteparin versus enoxaparin for a cat is provided in Table 4.

The LMWH doses for cats result in a very low volume to be administered. Most clinicians aliquot the contents of individual dosing syringes of dalteparin or enoxaparin into a sterile empty glass vial. The dose required for the cat can then be drawn up with a tuberculin syringe from the vial to ensure accurate dosing. Although not specifically covered in the CURATIVE guidelines, the addition of rivaroxaban to clopidogrel therapy could also be considered in this cat if LMWH dosing was not practical or the frequent injections were not feasible for the clients to undertake.

## Conclusions

The CURATIVE guidelines provide the first consensus-based recommendations regarding the use of antithrombotic therapies in our dog and cat patients at risk of thrombosis. These guidelines are designed to aid the clinician in decision making, however they do not negate the need for individualized patient care. These case scenarios highlight options for best practice in the field of antithrombotic therapy, with the hope of facilitating improved outcomes for dogs and cats at risk of thrombosis.

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