



A Practical Approach to Using the IRIS CKD Guidelines and the IDEXX SDMA® Test in Everyday Practice

Jane Robertson, DVM, DACVIM

Content presented at the 2017 Hill's Global Symposium
in Washington D.C., May 5 - 6, 2017.

Kidney disease is common in cats with at least 1 in 3 cats¹ and 1 in 10 dogs² likely to develop some form of kidney disease in their lifetime and its occurrence increases with age. The IDEXX SDMA® Test helps to identify kidney disease earlier than was previously possible. This test is also more specific for kidney function than traditional diagnostics. Symmetric dimethylarginine (SDMA) will increase with both active or acute kidney injury (AKI) as well as chronic kidney disease (CKD) and has been shown to increase when there is on average 40% loss of kidney function as compared to creatinine, which does not increase above the reference interval until up to 75% of kidney function is lost. In addition, SDMA is not impacted by lean muscle mass, making it a more reliable indicator of kidney function especially in pets with decreased muscle. For pets with CKD, identifying this disease in the early stages provides the practitioner the opportunity to provide therapeutic intervention earlier which is easier for the pet owner and could have the greatest impact on outcome. Treatments provided for CKD should be based on the International Renal Interest Society (IRIS) stage of the disease. SDMA has been added to the IRIS CKD guidelines as a useful adjunct for diagnosing, staging and treating CKD.

Clinical Presentation

Dogs and cats can be diagnosed with kidney disease when presenting to the veterinarian for a variety of reasons. Evidence of kidney disease can be identified on diagnostic testing performed during a wellness visit, on a preanesthetic screen for an elective or emergency procedure, on diagnostic testing performed when there are clinical signs consistent with kidney disease or when the pet presents for clinical signs of another illness, and during treatment for hyperthyroidism in cats.

Clinical signs of kidney disease depend on whether the disease is acute or chronic and on the severity of the disease. Animals with acute disease typically present for clinical signs associated with an acute onset of kidney injury whereas animals with CKD may present with no clinical signs, especially early in the course of their disease. However, it is always important to rule out an active or acute component anytime you diagnose kidney disease in a dog or cat since CKD implies an irreversible disease that is often progressive.

In dogs, polyuria (PU) and polydipsia (PD) may be the first indication of CKD. Cats maintain their urine concentrating ability further into the disease process than dogs; therefore, PU/PD is often not recognized in early stages of CKD in cats. As urine concentrating ability is lost later as the disease progresses, cat owners are more likely to recognize PD than PU. In addition, dogs and cats in IRIS stages 3 and 4 often present with nonspecific signs, including poor body condition, weight loss and muscle loss, decreased appetite, lethargy and dehydration. Intermittent vomiting

secondary to uremic gastric ulceration may occur.

Physical examination findings in animals with kidney disease will also depend on whether the disease is acute or chronic and vary depending on the severity and/or stage of disease. With AKI kidneys may palpate normally, be enlarged and painful or, if AKI is superimposed on CKD, then kidneys may still be small and irregular. In addition, it is not uncommon, especially in cats, to have one enlarged kidney and one small kidney. This can occur for example with an acute ureteral obstruction resulting in hydronephrosis and swelling of the obstructed kidney with the smaller kidney being indicative of underlying CKD.

With early CKD, physical examination may be within normal limits. Palpable renal abnormalities may be detected especially in cats (e.g., small, firm and irregular kidneys). As CKD progresses clinical signs will become more apparent and reflect the chronic nature of the disease. General physical examination findings include poor body condition, unkempt hair coat, dehydration and palpable kidney abnormalities. Oral examination may reveal pale mucous membranes, ulcers and/or uremic breath. Secondary systemic hypertension may cause retinal hemorrhages, arterial tortuosity or detached retinas presenting as acute blindness.

The IDEXX SDMA Test

SDMA is a revolutionary new kidney function test. IDEXX Reference Laboratories began adding the IDEXX SDMA Test to all routine chemistry panels during summer 2015. The

Catalyst® SDMA Test will become available in late 2017 in-clinic on the IDEXX Catalyst® platform.

SDMA is a methylated form of the amino acid arginine found in intracellular proteins. SDMA is released into the circulation during protein processing and is excreted by the kidneys. Stable production of SDMA is part of daily cell activity. SDMA is a proven renal biomarker that has been shown to correlate with glomerular filtration rate (GFR) in humans, dogs, and cats. SDMA is a more reliable indicator of kidney function because it is more sensitive and increases earlier than creatinine and it is more specific as it is not impacted by lean body mass like creatinine is.

SDMA is a Biomarker for Kidney Function

GFR is the gold standard for measuring kidney function, but it is expensive and cumbersome to perform and therefore not done routinely in practice. A meta-analysis of 18 studies involving human patients showed that SDMA concentrations correlated highly with GFR by inulin clearance ($r = -0.85$).³ The first evidence for using SDMA to assess renal disease in dogs was published in 2007, which showed a strong correlation of SDMA with GFR by inulin clearance ($r = -0.851$).⁴ A more recent study performed with 24 female dogs that were carriers of sex-linked hereditary nephropathy confirmed this strong correlation of SDMA and GFR measured by iothexol clearance (R2 of 0.85, as observed by Mary Nabity, DVM, PhD, DAVCP, Texas A&M University) and even a higher correlation was found in affected male adolescent dogs ($r = -0.95$).⁵ SDMA has

been shown to strongly correlate with GFR (R2 of 0.82) in cats.⁶

SDMA Increases Earlier than Creatinine

It is generally accepted that creatinine does not increase above the reference interval until up to 75% of renal function is lost. Clearly, there has been a need for a more sensitive test of renal function. SDMA has been shown in dogs and cats to increase when there is as little as 25% kidney function loss and on average when there is 40% loss of kidney function.^{5,7,8}

SDMA has been shown in dogs and cats to increase when there is as little as 25% kidney function loss and on average when there is 40% loss of kidney function.^{5,7,8}

A study in cats with CKD found that SDMA increased on average 17 months earlier and as long as 48 months earlier than creatinine.⁷ A similar study in dogs with CKD found that SDMA increased on average 9.8 months earlier and as long as 27 months earlier than creatinine.⁸

SDMA is Specific for Kidney Function

SDMA is specific to kidney function. SDMA is not increased in animals with various diseases including liver disease, Cushing's disease and heart disease unless there is concurrent kidney disease. SDMA is also not impacted directly by diet, which can have significant impact on BUN

and even on creatinine is some circumstances. Unlike creatinine, SDMA is not impacted by lean muscle mass. Loss of total lean body mass associated with aging and chronic disease can lower creatinine concentrations, resulting in a poor estimation of renal function. A study in older cats, confirmed that as cats aged, they lost muscle mass and creatinine decreased even as the GFR decreased. SDMA increased as kidney function declined with no correlation between total lean mass and SDMA ($P>0.05$).⁹ A similar study performed in dogs revealed that lean body mass and creatinine were positively correlated ($r=0.55$; $P<0.001$) whereas there was no correlation between SDMA and total lean body mass ($P>0.05$).¹⁰

Prevalence Of Kidney Disease Increases With Age

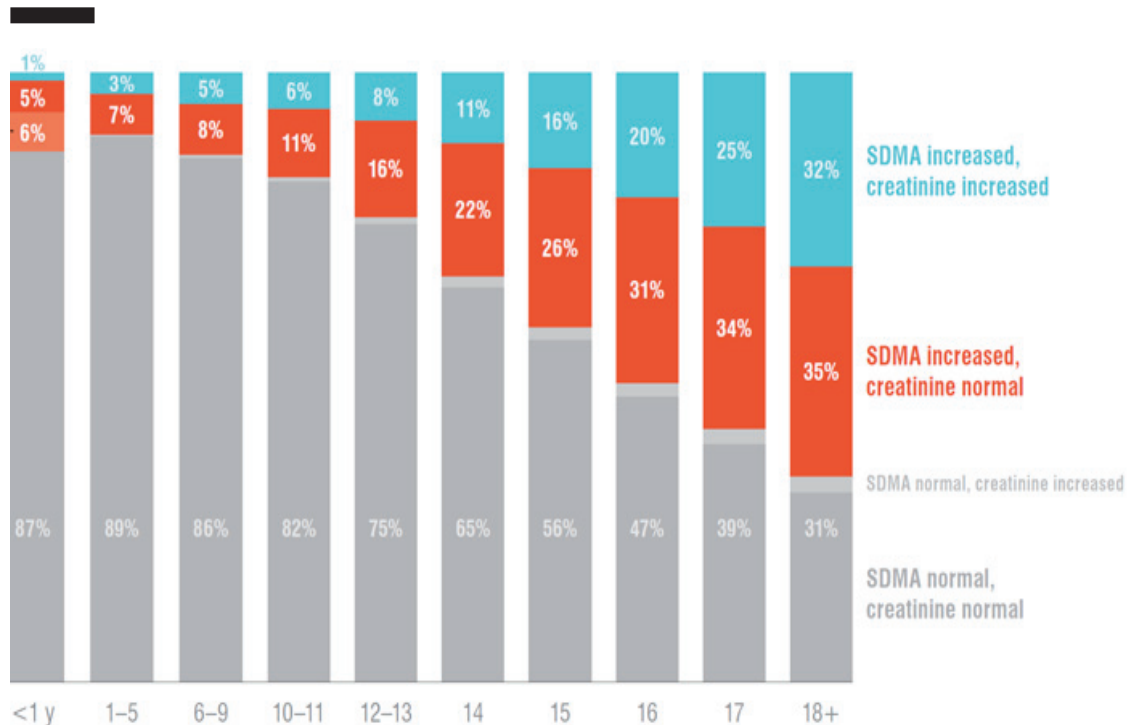
Previous studies have found that 1 in 3 cats are likely to develop kidney disease in their lifetime.¹ However, in these earlier studies, azotemia was used to make the diagnosis of kidney disease and nonazotemic cats with CKD were likely missed, particularly those with IRIS CKD Stage 1 or Stage 2 disease. In a recent study in cats, the prevalence of CKD was even higher than previously believed, with 50% of cats of all ages and as high as 80.9% of cats 15 years of age and older diagnosed with CKD.¹¹ In this study performed at North Carolina State University, cats were diagnosed with CKD based on results of complete blood count (CBC), serum chemistry, urinalysis and radiographic

determination of degenerative kidney changes and kidney size. They were then staged per the IRIS CKD Staging Guidelines. The majority of the cats (>90%) had IRIS CKD Stage 1 or Stage 2 disease, which highlights that prior to the introduction of SDMA, CKD has been underrecognized.

Figure 1 shows the IDEXX SDMA Test helps to detect more kidney disease in cats of all ages. It also clearly shows that as cats age, kidney disease becomes more prevalent, providing strong evidence that the prevalence of kidney disease in older cats is much higher than previously reported. Therefore, in older cats, it is more likely that they have kidney disease even if they are presenting for preventive care or for routine

FIGURE 1

Prevalence of kidney disease increases with age in cats (n = 1,107,146)¹²



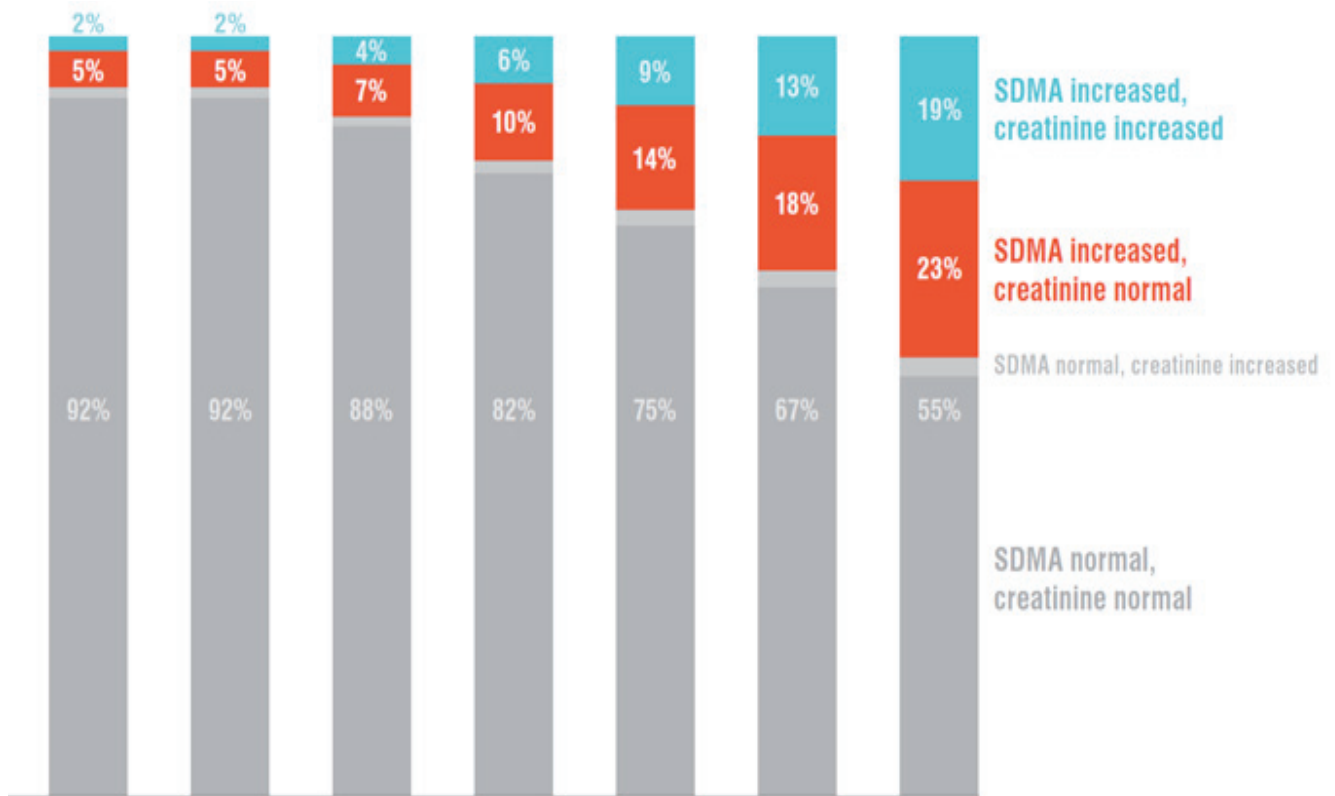
age-related procedures (e.g., dental cleaning). This finding emphasizes the importance of performing preventive care and preanesthetic diagnostics

including CBC, chemistry profile with SDMA and complete urinalysis in cats of all ages and particularly in senior cats. **Figure 2** similarly shows how

the IDEXX SDMA Test can help detect kidney disease in dogs of all ages and that prevalence of kidney disease increases as dogs age.

FIGURE 2

Prevalence of kidney disease increases with age in dogs (n = 2,524,031)¹²



Implications of Early Diagnosis of Kidney Disease

The IDEXX SDMA Test helps practitioners diagnose kidney disease earlier than previously possible. The IDEXX SDMA Test diagnostic algorithm (**Figure 3**) provides an outline of what actions should be taken when SDMA is increased to determine if kidney disease is probable and what steps should be

taken to investigate, manage and monitor kidney disease.

If the SDMA result is ≥ 20 $\mu\text{g/dL}$, then kidney disease is probable and it is recommended to act immediately by following the investigate, manage and monitor (IMM) protocol. (See box.) If the SDMA result is 15-19 $\mu\text{g/dL}$, determine if there is other evidence of kidney disease including:

clinical signs or physical findings; increasing creatinine within the reference interval or azotemia; urine changes such as inappropriate urine specific gravity, active urine sediment or proteinuria; or abnormal kidney imaging. These findings suggest that kidney disease is probable and immediate action should be taken using the IMM protocol. If there is no other evidence of kidney disease,

then it is recommended to recheck the SDMA in 2 to 4 weeks. At recheck if the SDMA is persistently increased, then kidney disease is probable and the IMM protocol should be followed. A complete urinalysis should always be performed when assessing kidney function.

The benefits of diagnosing kidney disease earlier and more reliably

In summary, there are many benefits of diagnosing kidney disease earlier and more reliably, which include the ability to:

- ▶ Find active and potentially reversible disease, including pyelonephritis, ureterolithiasis.
- ▶ Treat confounding conditions, including hypertension, proteinuria.
- ▶ Better detect and co-manage concurrent diseases, including hyperthyroidism.
- ▶ Prevent acute on chronic kidney injuries, including taking precautions with anesthesia and drugs.
- ▶ Delay progression of CKD and increase survival time by using the IRIS CKD staging and treatment guidelines, including feeding a renal therapeutic diet.
- ▶ Implement easier treatment so that owner compliance is better and pets live longer, happier lives.
- ▶ Monitor closely and intervene earlier with appropriate treatment as soon as indicated.

IMM Protocol

- ▶ **Investigate** for an underlying cause of kidney disease, especially more treatable conditions such as infection, obstruction or exposure to toxins or potentially nephrotoxic drugs, and to look for confounding conditions by assessing hydration status, blood pressure and thyroid status. Urine cultures should be strongly considered if any evidence of a urinary tract infection or the urine is not well concentrated, since these conditions may mask evidence of infection. Diagnostic imaging including radiographs and/or ultrasonography should be considered. Blood pressure should be measured and proteinuria should be quantified if present.
- ▶ **Manage** any identified underlying causes or confounding conditions appropriately. In addition, take precautions when prescribing any potentially nephrotoxic drugs and take appropriate precautions if the pet is undergoing anesthesia to protect the kidneys and prevent acute on chronic kidney injury.
- ▶ **Monitor** the patient as indicated based on treatments initiated for any identified underlying diseases or confounding conditions. If no underlying diseases or confounding conditions are identified, then an initial recheck 2 weeks after kidney disease is first suspected or identified would be reasonable to determine if disease is stable or progressing. If the SDMA and creatinine are stable at this time, then CKD is likely and IRIS CKD staging can be done with appropriate treatment initiated based on IRIS stage.

Staging Of Chronic Kidney Disease

Historically, CKD has been classified as mild, moderate, or severe, based on laboratory findings and clinical signs. A less arbitrary classification system has been developed by the International Renal Interest Society (IRIS), a multinational board of 15 independent veterinarians with particular interest in veterinary nephrology.¹³ CKD has to be first diagnosed, and then IRIS staging can be applied. IRIS staging is based initially on fasting plasma creatinine, assessed on at least two occasions in the stable patient, and then the patient is substaged based on proteinuria and blood pressure (**Figure 4**).

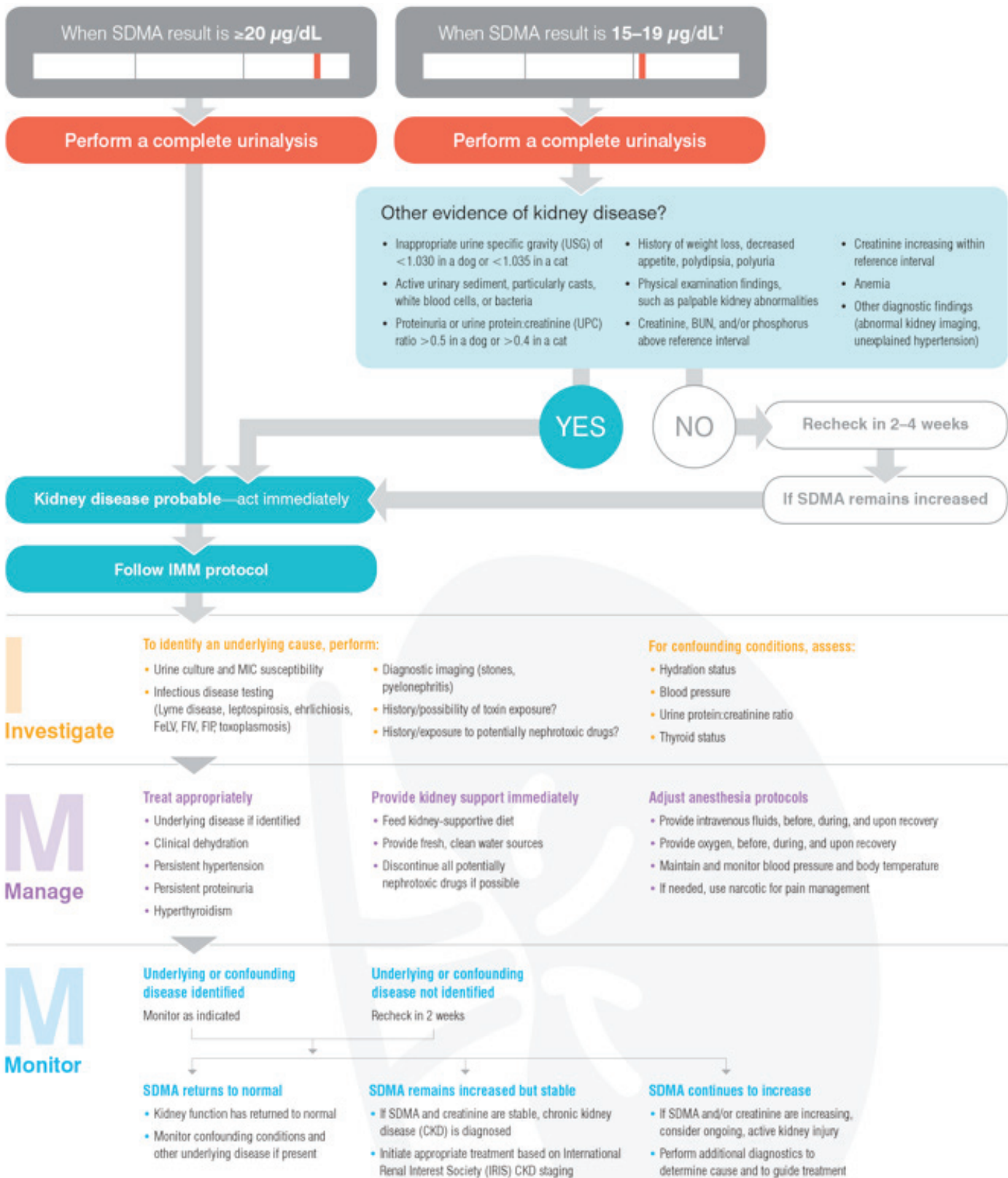
One challenge with the IRIS staging system has been the ability to detect dogs and cats in IRIS Stage 1 and

cats in early IRIS Stage 2 because, by definition, these animals are not yet azotemic. Some other evidence of a renal abnormality (i.e., inadequate urine concentrating ability without identifiable non-renal cause, abnormal renal palpation and/or abnormal renal imaging findings, proteinuria of renal origin, abnormal renal biopsy) needs to be detected.

SDMA has recently been recognized by IRIS as a valuable tool to help detect dogs and cats with IRIS CKD Stage 1 disease and to help correctly stage CKD in underweight patients. The following interpretive comments for the diagnostic and therapeutic utilization of SDMA were incorporated into the 2015 IRIS CKD Staging Guidelines, which are available in their entirety at www.iris-kidney.com.

FIGURE 3

The IDEXX SDMA™ Test diagnostic algorithm



“SDMA concentrations in blood (plasma or serum) may be a more sensitive biomarker of renal function than blood creatinine concentrations. A persistent increase in SDMA above 14 µg/dl suggests reduced renal function and may be a reason to consider a dog or cat with creatinine values <1.4 or <1.6 mg/dl, respectively, as IRIS CKD Stage 1.

In IRIS CKD Stage 2 patients with low body condition scores, SDMA ≥25 µg/

dl may indicate the degree of renal dysfunction has been underestimated. Consider treatment recommendations listed under IRIS CKD Stage 3 for this patient.

In IRIS CKD Stage 3 patients with low body condition scores, SDMA ≥45 µg/dl may indicate the degree of renal dysfunction has been underestimated. Consider treatment recommendations listed under IRIS CKD Stage 4 for this patient.”

These additions to the guidelines are preliminary, based on early data derived from the use of SDMA in veterinary patients. The IRIS board fully expects them to be updated as the veterinary profession gains further experience using SDMA alongside the long-established marker, creatinine, in the diagnosis and therapeutic monitoring of canine and feline CKD.

FIGURE 4

International Renal Interest Society CKD staging guidelines

		Stage 1 No azotemia	Stage 2 Mild	Stage 3 Moderate	Stage 4 Severe
Creatinine in mg/dL	Canine	<1.4	1.4–2.0	2.1–5.0	>5.0
	Feline	<1.6	1.6–2.8	2.9–5.0	>5.0
SDMA in µg/dL		>14	>14	Moderately increased	Markedly increased
			≥25	→	
				≥45	→
UPC ratio					
Substage based on proteinuria	Canine	Nonproteinuric <0.2	Borderline proteinuric 0.2–0.5	Proteinuric >0.5	
	Feline	Nonproteinuric <0.2	Borderline proteinuric 0.2–0.4	Proteinuric >0.4	
Systolic blood pressure in mm Hg					
Substage based on blood pressure		Normotensive <150	Borderline hypertensive 150–159	Hypertensive 160–179 Severely hypertensive ≥180	

SDMA = IDEXX SDMA™ Test
See iris-kidney.com for more detailed staging, therapeutic, and management guidelines.

Treatment Recommendations

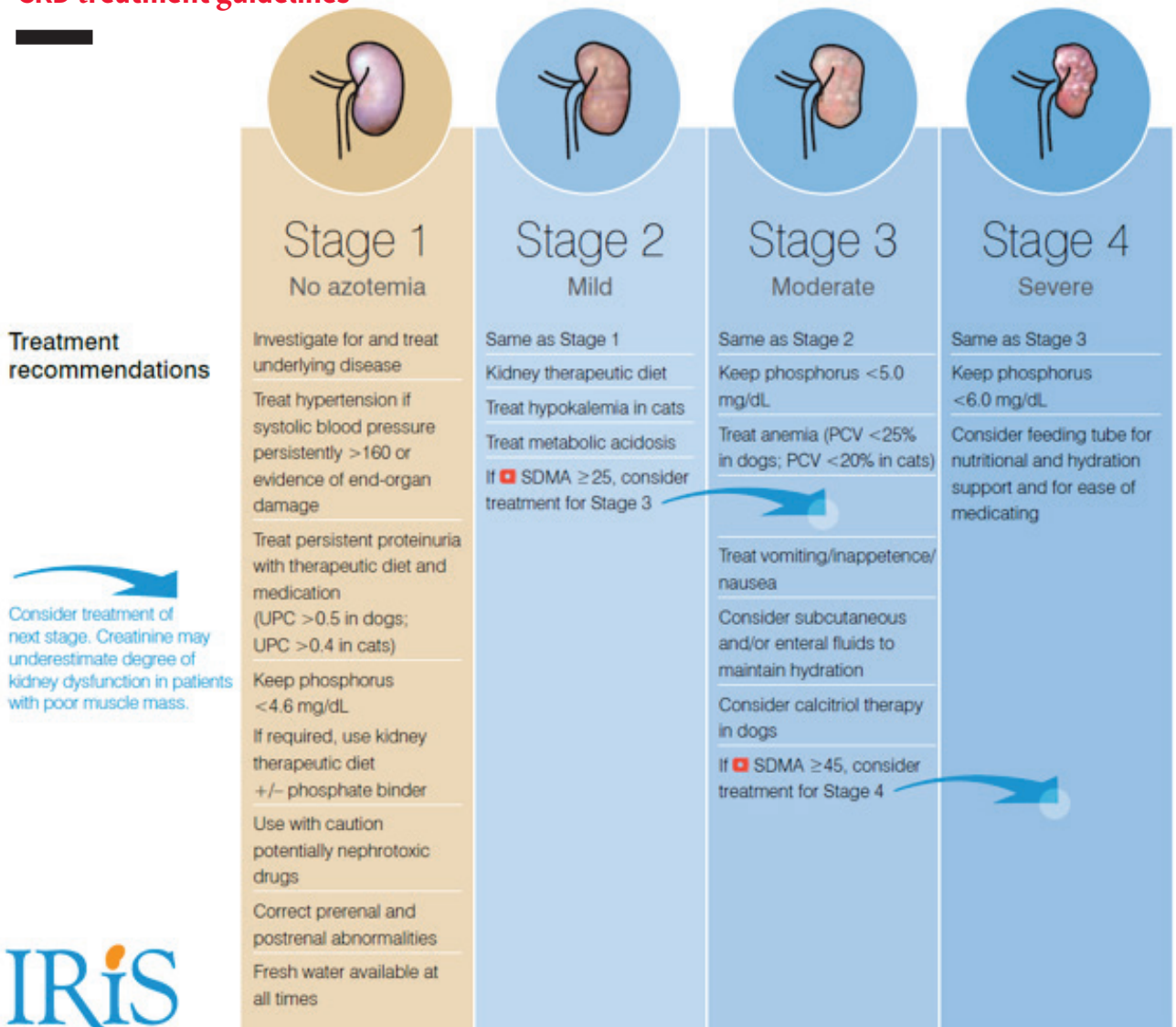
Once any underlying active disease has been ruled out or diagnosed and treated, and CKD is diagnosed and staged, then an individualized therapeutic approach should be designed based on the IRIS stage of disease and the individual pet's needs. Early management of CKD may slow progression of the disease.

Closer monitoring will help identify progression and when additional therapies should be initiated. **Figure 5** outlines the IRIS CKD treatment guidelines by stage of the disease. Key therapies for dogs and cats with CKD are listed in the table in the appendix.

It should be noted that several treatments are recommended in stage 1 and 2 CKD. This emphasizes the point that there is something that can be done to treat pets with early CKD and that treatment should not be delayed until later in the disease process, which is when these patients typically present with clinical signs.

FIGURE 5

International Renal Interest Society CKD treatment guidelines



Consider treatment of next stage. Creatinine may underestimate degree of kidney dysfunction in patients with poor muscle mass.



International Renal Interest Society

\square SDMA = IDEXX SDMA™ Test

See iris-kidney.com for more detailed staging, therapeutic, and management guidelines.

Evidence Supporting Treatments for Chronic Kidney Disease

While many treatment options exist for feline patients with CKD, nutritional management with a therapeutic renal food is supported by the highest level of evidence for IRIS Stages 2-4 and is recommended as the standard of care.^{11,14-17} In one study, a renal therapeutic diet for cats was associated with a significantly longer median survival time (633 days) compared with regular food (264 days).¹⁴ In a randomized, double-

In a randomized, double-blinded clinical study comparing effects of feeding a therapeutic renal food (Hill's® Prescription Diet® k/d® Feline) with a control food, significantly more cats (26%) fed the control food had uremic episodes compared with the renal food (0%).¹⁶

blinded clinical study comparing effects of feeding a therapeutic renal food (Hill's® Prescription Diet® k/d® Feline) with a control food, significantly more cats (26%) fed the control food had uremic episodes compared with the renal food (0%).¹⁶ There was also a significant reduction in renal-related mortality in cats fed the renal food; none of the cats in the renal food group died from renal causes, whereas, 22% of cats in the control food group died.

Features of Therapeutic Renal Foods

Compared with typical maintenance foods, therapeutic renal foods contain a “package” of nutrients that are believed to be helpful for patients with CKD. These include controlled amounts of high quality/ highly digestible protein, phosphorus and sodium; increased buffering capacity to help combat metabolic acidosis; added potassium to manage hypokalemia; and increased amounts of omega-3 fatty acids. Antioxidants such as vitamins E and C and β -carotene are added to minimize oxidative stress, which has been documented in cats with CKD and may contribute to disease progression.^{18,19} When communicating with pet parents, it's helpful to explain that foods designed for CKD include several features that distinguish them from typical cat foods versus referring to them only as low-protein foods. While renal foods contain less protein compared with adult maintenance pet foods, these proteins are of high quality (providing essential amino acids only) and are highly digestible. Lower-quality protein sources typically contain non-essential amino acids, which are not required by the patient but may be catabolized to urea and other nitrogen-containing wastes that normally are eliminated by the kidneys and may contribute to clinical signs in later stages of CKD.

Summary

The IDEXX SDMA Test is a new kidney function test that enables veterinarians to

detect kidney disease earlier and more reliably in pets presenting to the veterinarian for a variety of reasons. Early diagnosis has many benefits including providing the opportunity to identify an underlying cause of kidney disease, which could result in treatment that has the potential to reverse or stop the progression of the disease. Recognition and treatment of confounding conditions such as hypertension and proteinuria are also beneficial in delaying progression of kidney disease. For CKD, earlier diagnosis allows for earlier and easier transition to renal therapeutic foods. As the kidney disease

Based on published evidence, feeding a therapeutic renal food is the single most effective treatment for improving survival and quality of life in dogs and cats with CKD.

progresses, additional therapies can be implemented at the earliest appropriate time to improve quality of life and slow disease progression. Based on published evidence, feeding a therapeutic renal food is the single most effective treatment for improving survival and quality of life in dogs and cats with CKD.

References

- Lulich JP, Osborne CA, O'Brien TD, et al. Feline renal failure: Questions, answers, questions. *Compend Contin Educ Pract Vet.* 1992; 14:127-152.
- Brown SA. Renal dysfunction in small animals. The Merck Veterinary Manual website. www.merckmanuals.com/vet/urinary_system/noninfectious_diseases_of_the_urinary_system_in_small_animals/renal_dysfunction_in_small_animals.html. Updated October 2013. Accessed October 13, 2015.
- Kielstein JT, Salpeter SR, Bode-Boeger SM, et al. Symmetric dimethylarginine (SDMA) as endogenous marker of renal function – a meta-analysis. *Nephrol Dial Transplant.* 2006; 21:2446-2451.
- Tatematsu S, Wakino S, Kanda T, et al. Role of nitric oxide-producing and -degrading pathways in coronary endothelial dysfunction in chronic kidney disease. *J Am Soc Nephrol.* 2007; 18:741-749.
- Nabity MB, Lees GE, Boggess M, et al. SDMA assay validation, stability, and evaluation as a marker for early detection of chronic kidney disease in dogs. *J Vet Intern Med.* 2015; 29(4):1036-1044.
- Braff J, Obare E, Yerramilli M, et al. Relationship between serum symmetric dimethylarginine concentration and glomerular filtration rate in cats. *J Vet Intern Med.* 2014; 28:1699-1701.
- Hall JA, Yerramilli M, Obare E, et al. Comparison of serum concentrations of symmetric dimethylarginine and creatinine as kidney function biomarkers in cats with chronic kidney disease. *J Vet Intern Med.* 2014; 28:1676-1683.
- Hall JA et al. Serum concentrations of symmetric dimethylarginine and creatinine in dogs with naturally occurring chronic kidney disease. *J Vet Intern Med.* 2016; 30(3):794-802.
- Hall JA, Yerramilli M, Obare E, et al. Comparison of serum concentrations of symmetric dimethylarginine and creatinine as kidney function biomarkers in healthy geriatric cats fed reduced protein foods enriched with fish oil, L-carnitine, and medium-chain triglycerides. *Vet J.* 2014; 202:588-596.
- Hall JA, Yerramilli M, Obare M, et al. Relationship between lean body mass and serum renal biomarkers in healthy dogs. *J Vet Intern Med.* 2015; 29(3):808-814.
- Marino CL, Lascelles BD, Vaden SL, Gruen ME, Marks SL. The prevalence and classification of chronic kidney disease in cats randomly selected from four age groups and in cats recruited for degenerative joint disease studies. *J Feline Med Surg.* 2014; 16(6):465-472.
- U.S. results of all canine and chemistry panels submitted between July 2015 and July 2016. Data on file at IDEXX Laboratories, Inc. Westbrook, Maine, USA.
- IRIS. www.iris-kidney.com: International Renal Interest Society, 2013 (accessed January 2016)
- Elliott J, Rawlings JM, Markwell PJ, et al. Survival of cats with naturally occurring chronic renal failure: effect of dietary management. *J Small Anim Pract.* 2000; 41:235-242.
- Harte JG, Markwell PJ, Moraillon RM, et al. Dietary management of naturally occurring chronic renal failure in cats. *J Nutr.* 1994; 124:2660S-2662S.
- Ross S, Osborne C, Kirk C, et al. Clinical evaluation of dietary modification for treatment of spontaneous chronic kidney disease in cats. *J Am Vet Med Assoc.* 2006; 229:949-957.
- Polzin DJ. Evidence-based step-wise approach to managing chronic kidney disease in dogs and cats. *J Vet Emerg Crit Care.* 2013; 23:205-215.
- Brown SA. Oxidative stress & chronic kidney disease. *Vet Clin North Am Small Anim Pract.* 2008; 38:157-166.
- Yu S, Paetau-Robinson I. Dietary supplements of vitamins E and C and beta-carotene reduce oxidative stress in cats with renal insufficiency. *Vet Res Commun.* 2006; 30:403-413.

APPENDIX TABLE

COMMON DRUGS USED DURING TREATMENT OF CKD IN DOGS AND CATS

Therapy	Dose	Frequency	Route	Indications
Renal therapeutic diet	Achieve and maintain ideal body weight	Ad libitum or meal feed 2 to 3 times per day	PO	IRIS CKD Stage 1 if persistently proteiunuc; All IRIS CKD Stages 2-4
SQ fluid therapy (balanced electrolyte solution)	Cat: 75-125 mL Dog: 30-- 60 mL/kg	Every 1 to 3 days	SQ	Maintain hydration
Cyproheptadine	Cat: 1-2 mg	BID	PO	Stimulate appetite
Mirtazapine (15 mg tablet)	Cat: 1.88 mg (1/8 of 15 mg tablet)	Every other day	PO	Stimulate appetite Antiemetic
Maropitant citrate (Cerenia® 16 mg tablet)	Cat: 4 mg (1/4 of 16 mg tablet) Dog: 1-2 mg/kg	Once daily	PO	Antiemetic

Therapy	Dose	Frequency	Route	Indications
Famotidine (Pepsid® 10 mg tablet)	Dog: 0.5 mg/kg	Once daily	PO	Antacid
Omeprazole (Prilosec® 20 mg capsule)	Dog: 20 mg or 0.7 mg/kg	Once daily	PO	Antacid
Aluminum hydroxide (Alternagel®; 600 mg/5 mL; also available in powder)	30-90 mg/kg/day	Dose divided and given with meals	PO	Maintain phosphorus below target for stage
Lanthanum carbonate (Fosrenol®; 500 mg/chewable tablet)	12.5-25 mg/kg/day	Dose divided and given with meals	PO	Maintain phosphorus below target for stage
Lanthanum carbonate octahydrate (Renalzin®; 200 mg/ml)	2 mL in food 1-2 times/day	Dose divided and given with meals	PO	Maintain phosphorus below target for stage
Sevelamer hydrochloride (Renalgel®; 400 mg/tab)	33-54 mg/kg	Dose divided and given with meals	PO	Maintain phosphorus below target for stage
Chitosan and calcium carbonate (Epakitin®)	4.4 gm/10 kg	Dose divided and given with meals	PO	Maintain phosphorus below target for stage
Potassium gluconate	Cat: 2-6 mEq/day Dog: 0.5 mEq/kg	BID with food	PO	Maintain phosphorus below target for stage
Potassium citrate	40-60 mg/kg	BID or TID with food	PO	Maintain phosphorus below target for stage
Sodium bicarbonate	8-12 mg/kg	BID to TID	PO	Maintain phosphorus below target for stage
Amlodipine	Cat: 0.625 mg <5 kg; 1.25 mg ≥5 kg Dog: 0.1-0.3 mg/kg	Once daily		Maintain phosphorus below target for stage
Benazepril and enalapril	0.5-1 mg/kg	Once daily	SQ	Maintain phosphorus below target for stage
Telmisartan (Semintra®)	1 mg/kg	Once daily		Maintain phosphorus below target for stage
Darbopoetin (Aranesp®)	1.0 µg/kg	Weekly*	IM	Maintain phosphorus below target for stage
Iron dextran	Cat: 50 mg Dog: 50-300 mg	Every 3-4 weeks		Maintain phosphorus below target for stage
Calcitriol	Dog: 2-3 ng/kg	Once daily	PO	Maintain phosphorus below target for stage

*Once target PCV is reached, reduce dose by 20%-25% or decrease to every 2 weeks. Then adjust monthly.