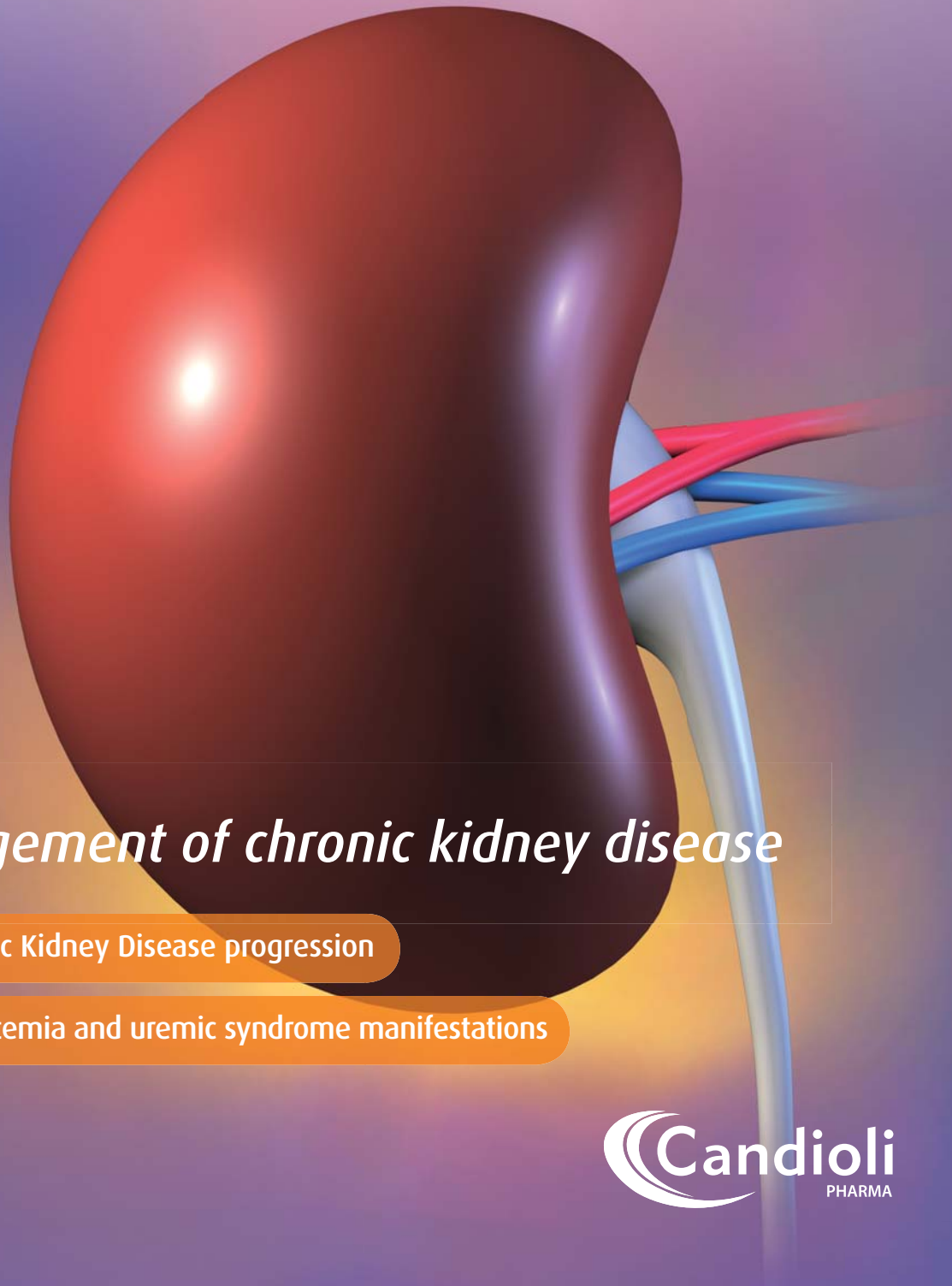


Renal Renal Advanced



The management of chronic kidney disease

Reduction of Chronic Kidney Disease progression

Control of hyperazotemia and uremic syndrome manifestations

Chronic Kidney Disease (CKD)

A common pathology?

- ➔ CKD is a clinical condition commonly found in dogs and very often in cats, particularly those adult or elderly
- ➔ In dogs chronic nephropathy is recognised as the third cause of death, whereas in cats it is recognised to be the first
- ➔ The onset of CKD is insidious, considering that kidney function generally declines over a period of months or years
- ➔ The Uremic Syndrome clinically appears when progressive functioning loss of kidney mass supersedes 75% of its original, and compensatory modifications cannot compensate the metabolic and excretion needs of the organism to maintain homeostasis

What causes CKD?

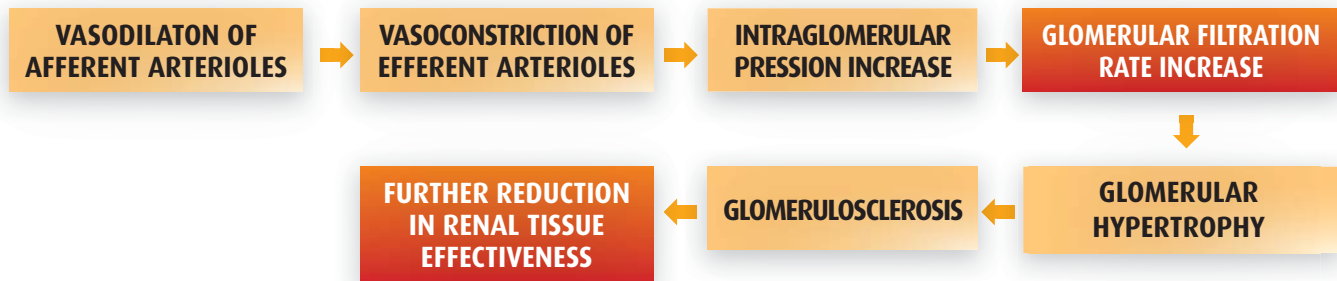
Tab.1 Principal causes of CKD in cats and dogs

	CATS	DOGS
Hereditary nephropathy	Polycystic nephropathy Amyloidosis	Amyloidosis Renal dysplasia Polycystic nephropathy
Infectious diseases	Pyelonephritis (ascending) FIP	Pyelonephritis Leptospirosis Piroplasmos
Malignancy	Lymphoma	Renal Lymphoma
Idiopathic/immunity/ inflammatory causes	Chronic interstitial nephritis Glomerulonephritis	Amyloidosis Glomerulonephritis Chronic interstitial nephritis
Toxic/iatrogenic causes	Anesthesia Pyometra Septic shock Nephrotoxic drugs (NSAIDS, ATB, antithyroid) Giglio	Anesthesia Pyometra Septic shock Nephrotoxic drugs (NSAIDS, ATB) Ethylene glycol
Vascular	Hypotension, hypertension	Congestive heart failure Renal infarction
Metabolic	Hyperthyroidism	Hypoadrenocorticism Hypercalcemia
Traumatic/obstructive	"Large kidney, small kidney" syndrome	Rupture of the bladder and/or urethra Renal trauma and/or ureters

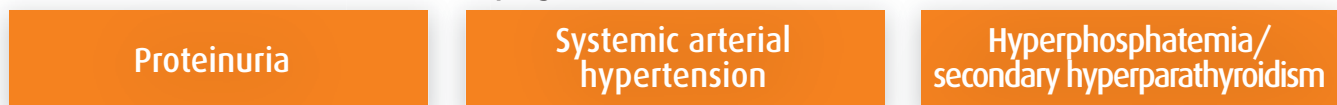


How does CKD progress?

- ➔ CKD develops and evolves in a complex auto-degenerative pattern, even after the initial cause has disappeared
- ➔ At the initial injury that affects a portion of the parenchyma, the surviving renal tissue responds with adaptive compensatory mechanisms of the glomerulus:



- ➔ Other factors that contribute to the progression of CKD:



Consequences and symptoms of CKD

Tab.2 Principal functional alterations induced by CKD, symptoms and relative treatment

APPARATUS OR FUNCTION INVOLVED	CONSEQUENCES/SYMPTOMS	RECOMMENDED TREATMENT
DIGESTIVE FUNCTION	Eating disorder, nausea, vomiting, diarrhea, uremic breath, stomatitis	Antacids, antimetetics, gastro-enteric protectors, prebiotics, probiotics, group B vitamins
URINARY TRACT	PD/PU, proteinuria	ACE-inhibitors
	Urinary tract infections	Antibiotics
	Dehydration	Fluidotherapy
SECONDARY HYPERPARATHYROIDISM	Increased phosphatemia	Reduction of food phosphorous Binding phosphorous (Ca and A1 carbonated, A1 hydroxide)
	Renal osteodystrophy	Calcitrol
METABOLIS ACIDOSIS	Muscle weakness, weight loss, lethargy, nausea, vomiting. Increased muscle catabolism, hypokalaemia, loss of urinary Ca	Potassium citrate Sodium bicarbonate
ELECTROLYTIC IMBALANCE (HYPOKALAEMIA)	Generally poor conditions, atrophy and muscular weakness	Potassium citrate Potassium gluconate
HYPERAZOTHEMIA	Urea and creatinine plasmatic levels increase	Dietary proteic restriction Intestinal entrapping of nitrogen
HYPERTENSION	Ventricular left hypertrophy, myocardial ischemia, retinal haemorrhaging	Amlodipine ACE inhibitors Beta blocker Omega 3 fatty acids

Hyperphosphatemia

DEFINITION

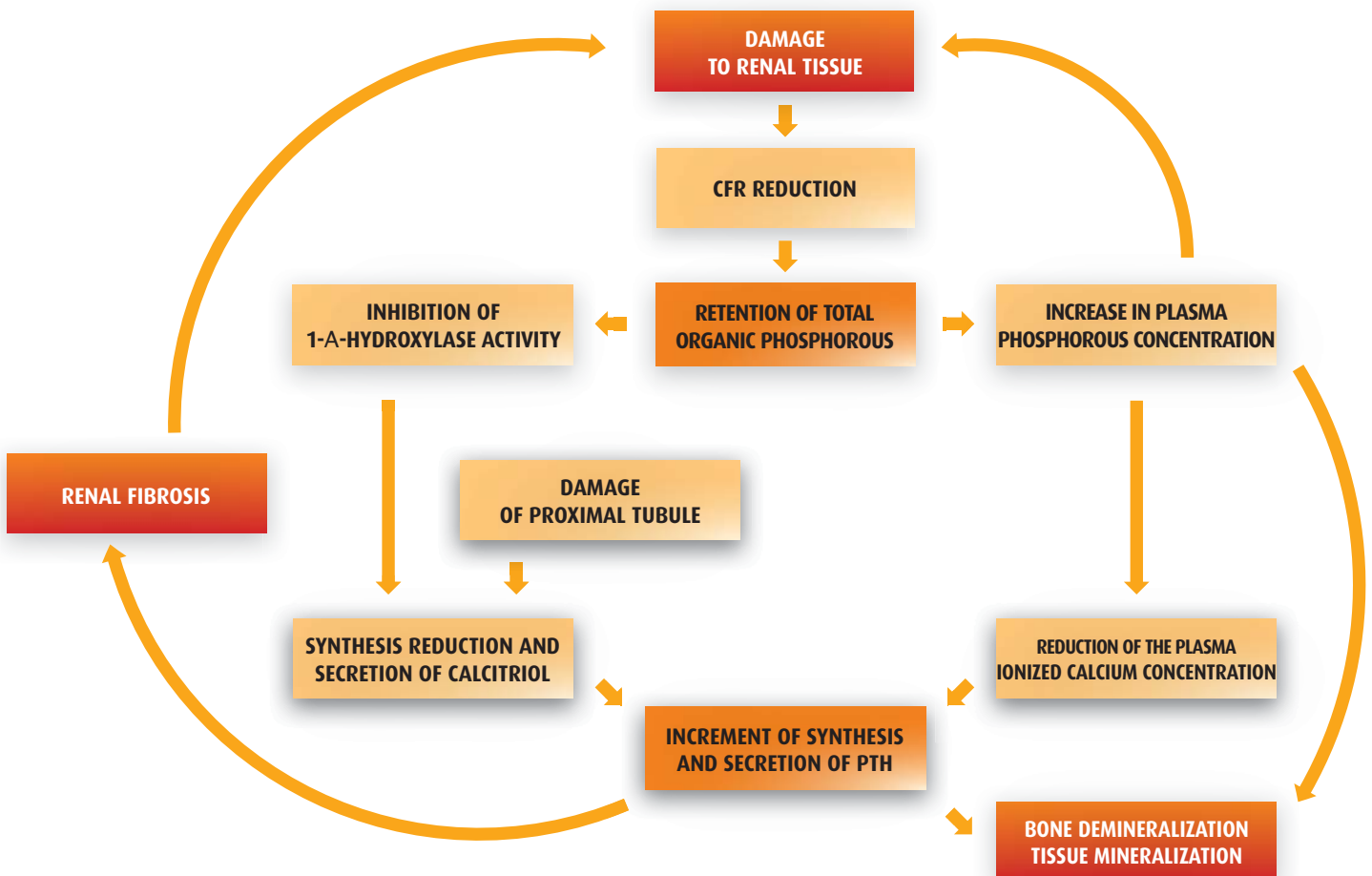
- ➔ It is an increase in phosphate plasma levels resulting from the reduction of glomerular filtration rate (GFR)
- ➔ Phosphorus is filtered and partially reabsorbed in the proximal nephron tubule
- ➔ When the glomerular filtration rate is reduced beyond 50% and absorption of intestinal food phosphorus remains constant, the phosphorus is retained by the body inasmuch as the amount introduced exceeds the renal excretion capacity

CONSEQUENCES

- ➔ Hyperphosphatemia from reduced renal filtration of phosphorus induces secondary renal hyperparathyroidism, which can accelerate the progression of chronic kidney disease through inflammatory and fibrotic mechanisms. Moreover, secondary hyperparathyroidism causes bone demineralization and soft tissue calcification
- ➔ Decreased production of calcitriol and levels of serum ionized calcium, stimulate a further release of parathyroid (PTH)
- ➔ PTH is seen as a true uremic toxin, and is an important factor in the progression and worsening of chronic kidney pathology

Fig. 1 Mechanisms of stimulation of PTH secretion in chronic renal pathology

Prepared and mod. by: J. Elliot - Hyperphosphataemia and chronic kidney disease - Outcomes of the roundtable in 2006 in Louisville, KY (USA).
State of the art in renal disease in cats and dogs. Nice (FR) 2007



CONTROL OF HYPERPHOSPHATEMIA

- ➔ Dietetic restriction of phosphorous
- ➔ Using ligands/binders of phosphorus in the intestine (*aluminum salts, calcium salts, Chitosan, Sevelamer*)
- ➔ Calcitriol in case of renal osteodystrophy

REDUCTION OF HYPERPHOSPHATEMIA SLOWS THE AUTO-DESTRUCTIVE CYCLE OF CKD AND INCREASES LIFE EXPECTANCY

Tab. 3 Guidelines for the control of phosphatemia in relation to the stage of renal dysfunction
Tratto da: J. Elliot *Phosphate via Management, A roundtable discussion. Seville, KY (USA) 2006*

STATE	CREATININE	OBJECTIVES OF PHOSPHATEMIA	PRESCRIPTIONS
II	1.6-2.8 mg/dl	2.5-4.5 mg/dl (0.81-1.45 mmol/l)	Restricted diet or usual diet ± binders of intestinal phosphorous
III	2.9-4.9 mg/dl	2.5-5 mg/dl (0.81-1.61 mmol/l)	Restricted diet ± binders of intestinal phosphorous
IV	≥ 5 mg/dl	2.5-6 mg/dl (0.81-1.94 mmol/l)	Restricted diet ± binders of intestinal phosphorous

Renal

**EFFECTIVELY CONTROLS
HYPERPHOSPHATEMIA
AT ANY STAGE OF CKD**

Hyperazotemia

DEFINITION

- ➔ It is an accumulation of urea, creatinine, ammonia and other non-protein nitrogen molecules in plasma, derived from a proportional reduction of the glomerular filtration rate
- ➔ The uremic or uremic syndrome is a toxic polysystemic syndrome characterized by accumulation in the blood of urinary waste products as a result of a significantly reduced renal function (more than 75%) and the consequent inability to maintain metabolic homeostasis

CLINICAL SIGNS

- ➔ Metabolic acidosis
- ➔ Symptoms connected to toxicosis

MANAGEMENT

- ➔ Protein food restriction
- ➔ ACE inhibitors to increase the glomerular filtration rate and slow the progression of nephropathy
- ➔ Hypoazotemizer substances/reducers of hepatic synthesis of urea
- ➔ Trapping nitrogen or “nitrogen traps”
- ➔ Dialysis or kidney transplant



DEFINITION OF THE “NITROGEN TRAP”

Renal Advanced

**HELPS METABOLIZING NITROGEN MOLECULES
IN THE INTESTINAL LUMEN, AND REDUCING
PLASMA CONCENTRATION OF UREMIC TOXINS.**

Fig. 2 Metabolization of uremic toxins in the intestinal lumen by **Renal Advanced**

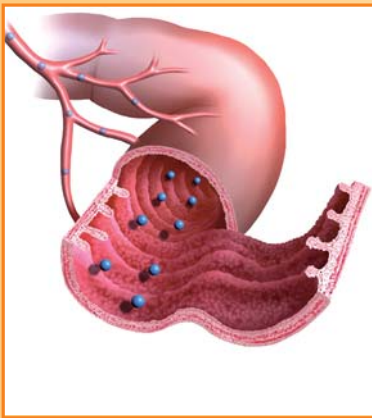


Fig. 2a
In normal conditions
a part of the nitrogen
molecules enters
the intestinal lumen
by osmotic diffusion
through intestinal
mucosa

Fig. 2b
In case of CKD,
the toxic nitrogen
molecules accumulate in
the blood and continue
to spread in the lumen
until when it maintains
an osmotic gradient
through the intestinal
epithelium

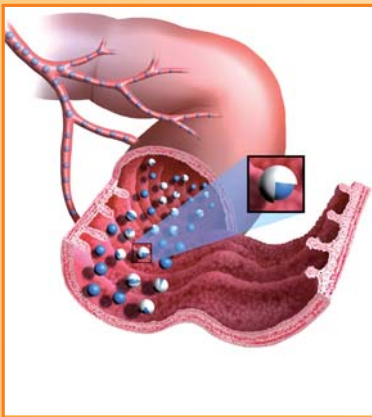
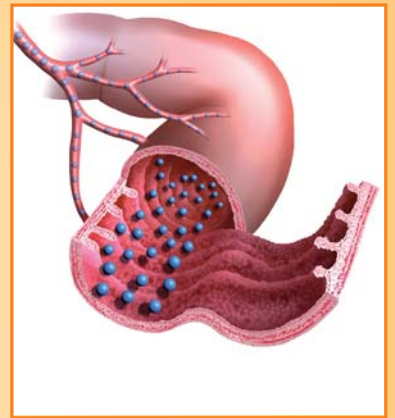


Fig. 2c
The lactobacilli
contained in
Renal Advanced
contribute toward
the metabolization
of uremic toxins,
maintaining
such gradient of
concentration

Fig. 2d
The process of
spreading the nitrogen
molecules is permitted,
contributing to
keep their plasma
concentration
at a low level



Renal Advanced

**MOREOVER, DUE TO ITS FOS CONTENT,
CAPTURES THE HYDROGEN IONS AT INTESTINAL LEVEL,
CONTROLLING METABOLIC ACIDOSIS.**

Renal

1 → REDUCES PHOSPHATEMIA

Calcium carbonate ^{2,5,17,20,23,24,30,32,33,39,53,57}

- Acting as binder, reduces intestinal absorption of phosphorous

Chitosan ^{7,34,36,57}

- Reduces phosphorous absorption at intestinal level
- Produces no increment in plasma calcium levels

2 → RESTORES ACID-BASIC AND ELECTROLYTIC EQUILIBRIUM

Potassium citrate ^{17,20,22,23,24,32,44,45,47,52}

- Action as metabolic acidosis buffer
- Anty hypokaliemic activity

Renal cats (2 measuring cups) supplies 385 mg of potassium citrate, equal to 27.6 mg (0.7 mfq) of potassium/kg p.v.

Renal dogs (2 measuring cups) supplies 192.5 mg of potassium citrate, equal to 13.8 mg (0.35mfq) of potassium/kg p.v.

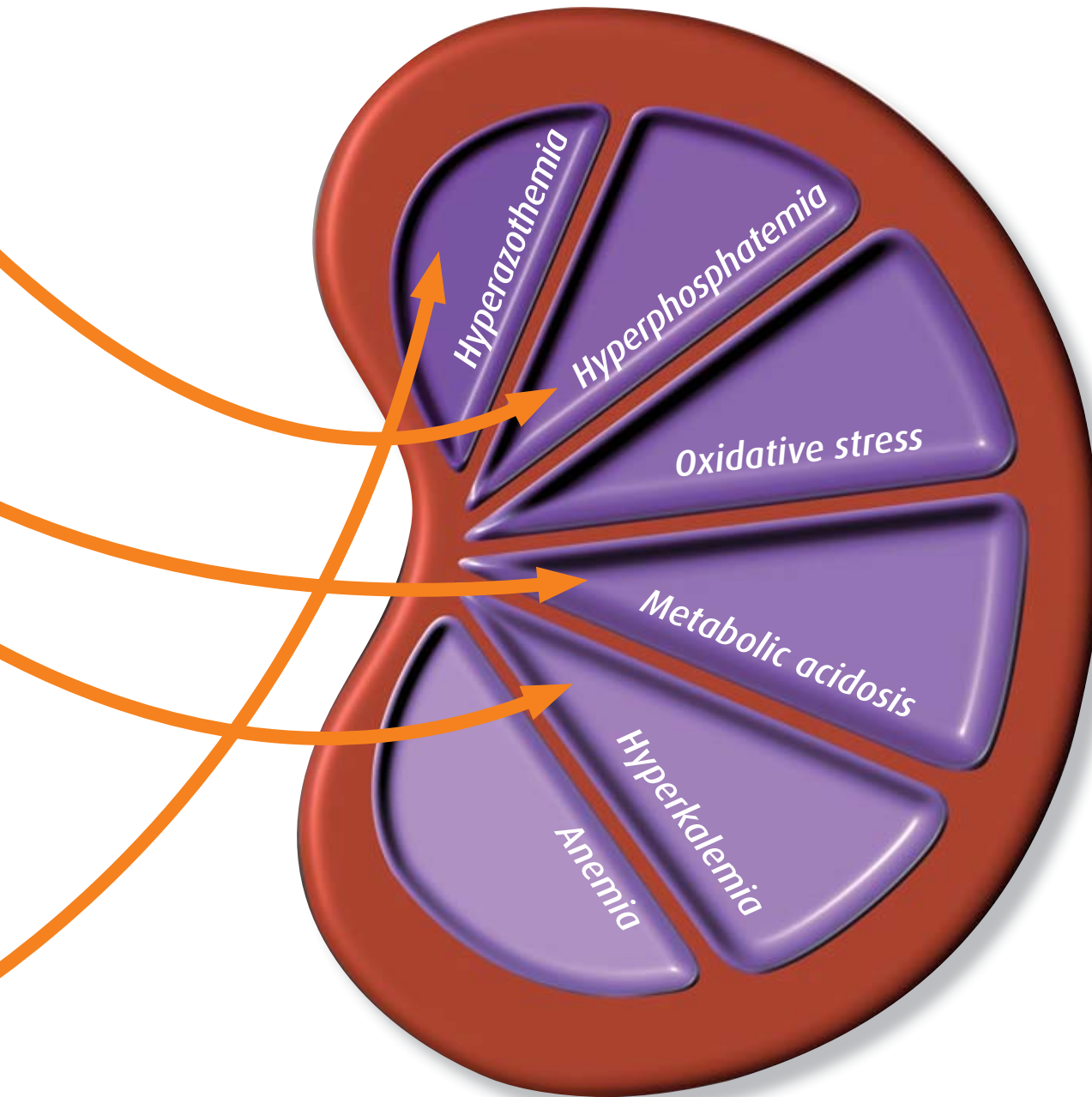
3 → CONTROLS HYPERAZOTHEMIA

Chitosan ^{7,34,36,57}

- Reduces plasma levels of urea and creatinine

CHRONIC KIDNEY DISEASE

6 major metabolic dysfunctions

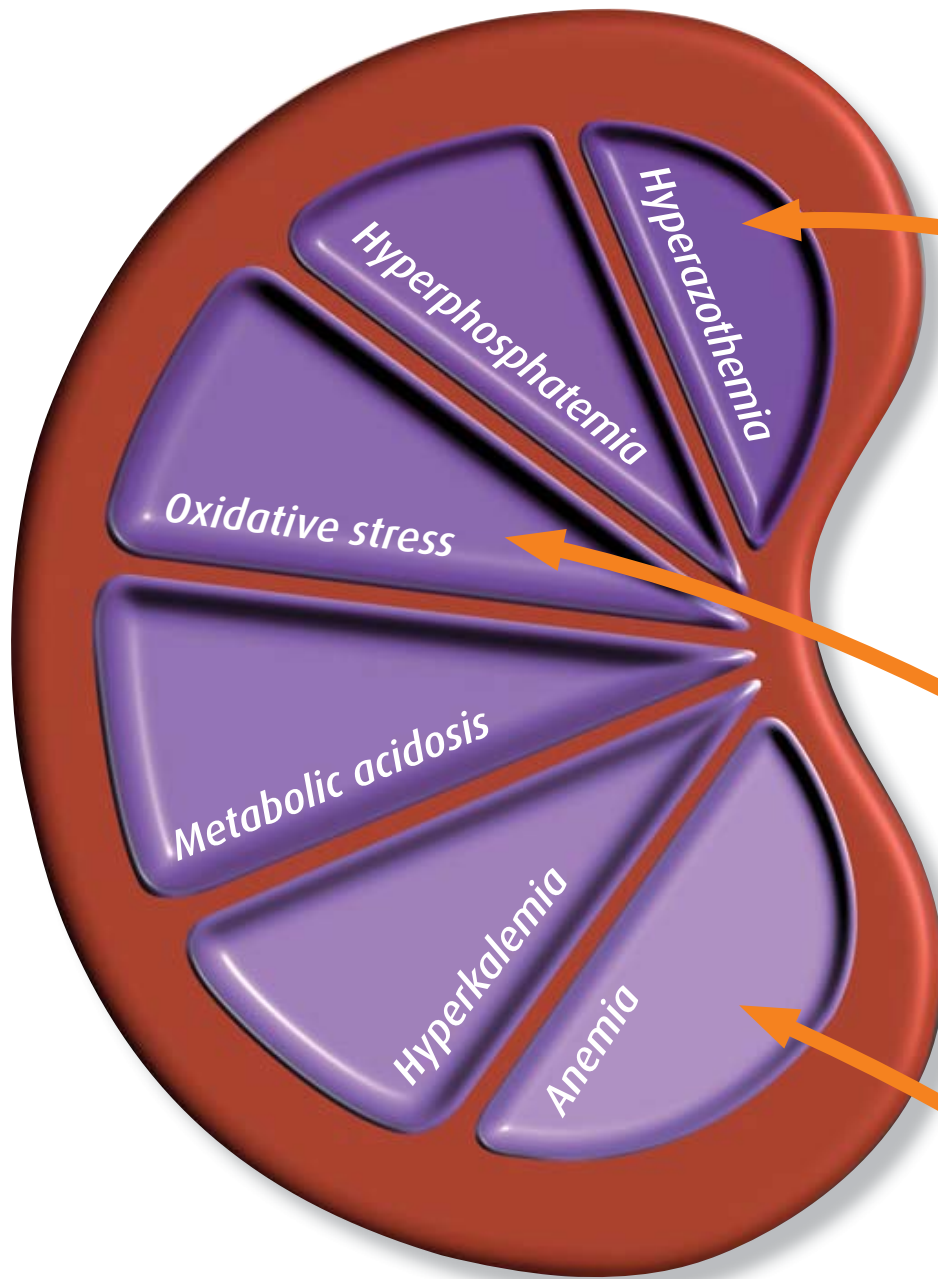


Renal

➔ FOR ALL STAGES OF KIDNEY DYSFUNCTION

CHRONIC KIDNEY DISEASE

6 major metabolic dysfunctions



Renal Advanced

➡ FOR KIDNEYS IMPAIRMENT WITH HYPERAZOTHEMIA

Renal Advanced

4 → CONTROL OF HYPERAZOTHEMIA

FOS + *Lactobacillus acidophilus* + *Enterococcus faecium* ^{18,22,23,24,31,45,49}

- They act as a “nitrogen trap” at the intestinal level. The two bacterial strains are selected for their affinity and ability to metabolize the uremic toxins that spread in intestinal lumen
- They improve the digestive function by stimulating the appetite and increasing the endogenous synthesis of group B vitamins
- The fermentable fibers trap hydrogen ions in the bowel, controlling metabolic acidosis

Lespedeza capitata ^{16,21,27,48,55,56} standardized dry extract and titrated to 4% in rutin

- Antinephrotoxic properties
- Increases the GFR (glomerular filtration rate) for vasodilatory activity, with an hypoazothemic effect

Bioflavonoids ^{3,10,22,23,24,35,42,45,54,59} standardized dry extract and titrated to 40% in hesperidine

- Reduce hepatic synthesis of urea

5 → REDUCTION OF OXIDATIVE STRESS

Bioflavonoids ^{3,10,22,23,24,35,42,45,54,59} standardized dry extract and titrated to 40% in hesperidine

- Protect renal cellular integrity through their potent antioxidant activity
- Inhibit lipoperoxidation of the cell membranes
- Activate other important anti-oxidant endogenous systems: catalase, SOD, glutathione
- Neutralize free radical activity
- Reduce the activity of certain inflammatory chemical mediators (chemokine, xanthine oxidase)

Vitamin C ^{20,22,23,24,45,54}

- Reduces oxidative stress induced by free radicals

6 → COUNTERACTS ANEMIA

Vitamin B12, Folic Acid, Pyridoxine ^{22,23,45}

- Stimulate erythropoiesis
- Compensate increased urinary losses

Vitamin C ^{20,22,23,24,45,54}

- Strengthen iron intestinal absorption

IRIS Classification and therapeutic recommendations

IRIS: International Renal Interest Society

Tab. 4 IRIS classification of feline and canine CKD (2006)

IRIS CLASSIFICATION OF FELINE AND CANINE CKD	CREATININE (mg/dl) (μmol/L)	LABORATORY AND CLINICAL POSSIBLE SUBSTANTIATIONS	PROPOSED TREATMENTS	
I NO AZOTAEMIA	CATS DOGS < 1.6 <1.4 <140 <125	Dehydration Hypertension Proteinuria*** UTI*	Renal therapeutic diet Calcium antagonists ACE inhibitors Antibiotics**	
II MILD AZOTAEMIA	CATS DOGS 1.6-2.8 1.4-2.0 140-249 125-179	Dehydration Hypertension Proteinuria Hyperphosphatemia Metabolic acidosis Anemia* Digestive symptoms*	AT STAGE I + NEPHROPROTECTIVE THERAPY Chelating phosphorous Hypoazothemia action ** Metabolic alkalizer	Renal
			ANTI-ANEMIA THERAPY ** Nutritional agents Erythropoietin (non reg. for vet. use) Anabolic (non demonstrated)	Renal Advanced
			SYMPTOMATIC THERAPY ** Improved digestive function	Renal Advanced
III MODERATE TO SEVERE AZOTAEMIA	CATS DOGS 2.9-5.0 2.1-5.0 250-439 180-439	AT STAGE II + Hypokaliemia Hyperazotaemia Disorexia	AT STAGE II + SYMPTOMATIC THERAPY Improved digestive function Antiemetics, antiacids, gastroprotective Supplementation of potassium	Renal + Renal Advanced
			NEPHROPROTECTIVE THERAPY Hypoazothemia action	Renal Advanced
IV END STAGE RENAL FAILURE	> 5.0 G and C > 440 G and C	AT STAGE III + Anorexia Critical dehydration	AT STAGE III (if possible) + INTENSIVE THERAPY Parenteral introduction of fluids, forced-feeding probes, dialysis	Renal + Renal Advanced

* not constant ** treatment necessary only in presence of symptomatology

*** referring to PU/CU rapport (urinary protein/ urinary creatinine)

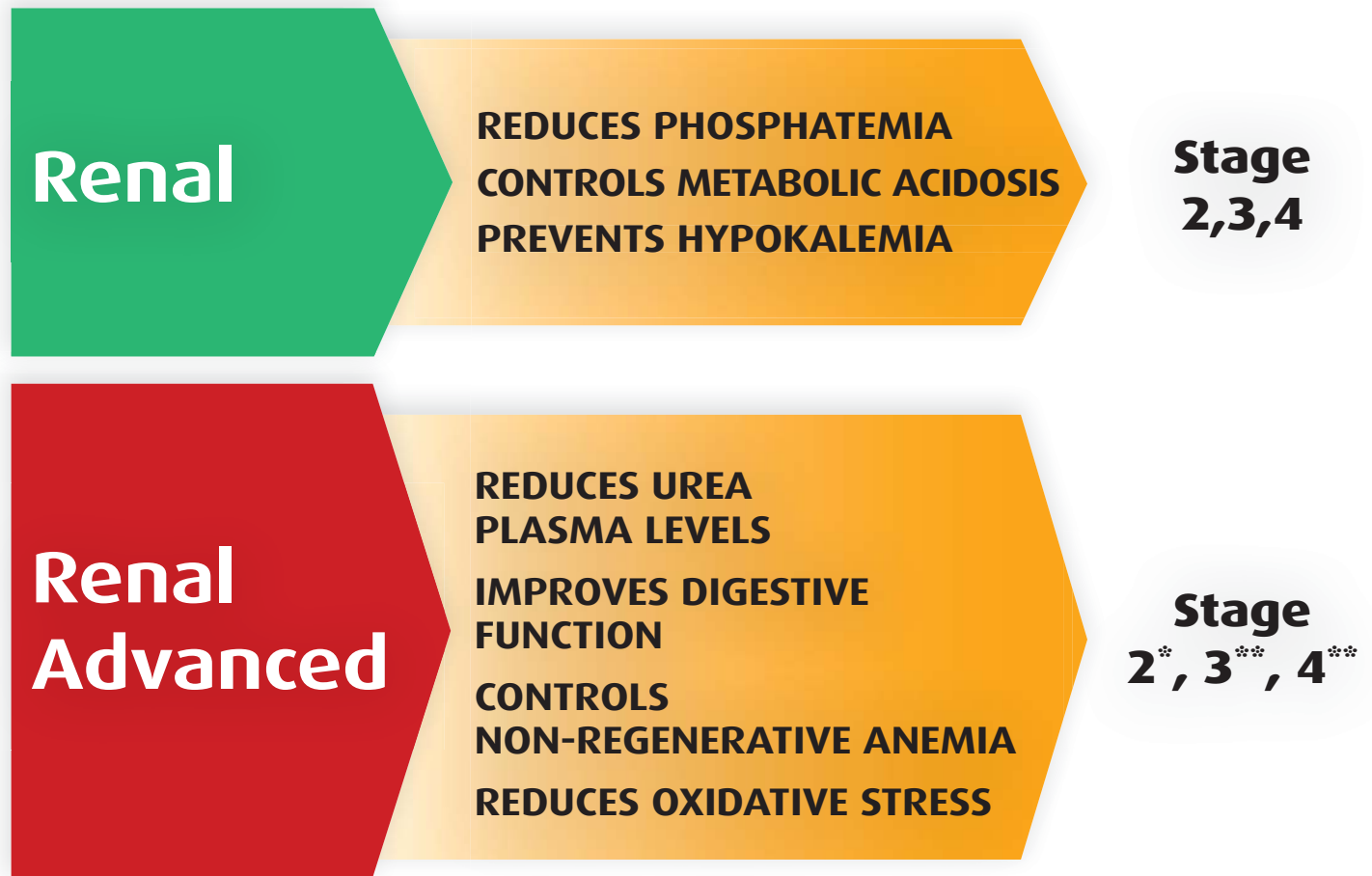
stage 1 can be sub-divided into 2 substages:

1a PU/CU cat 0.2-0.4 dog 0.2-0.5

1b PU/CU cat >0.4 dog > 0.5



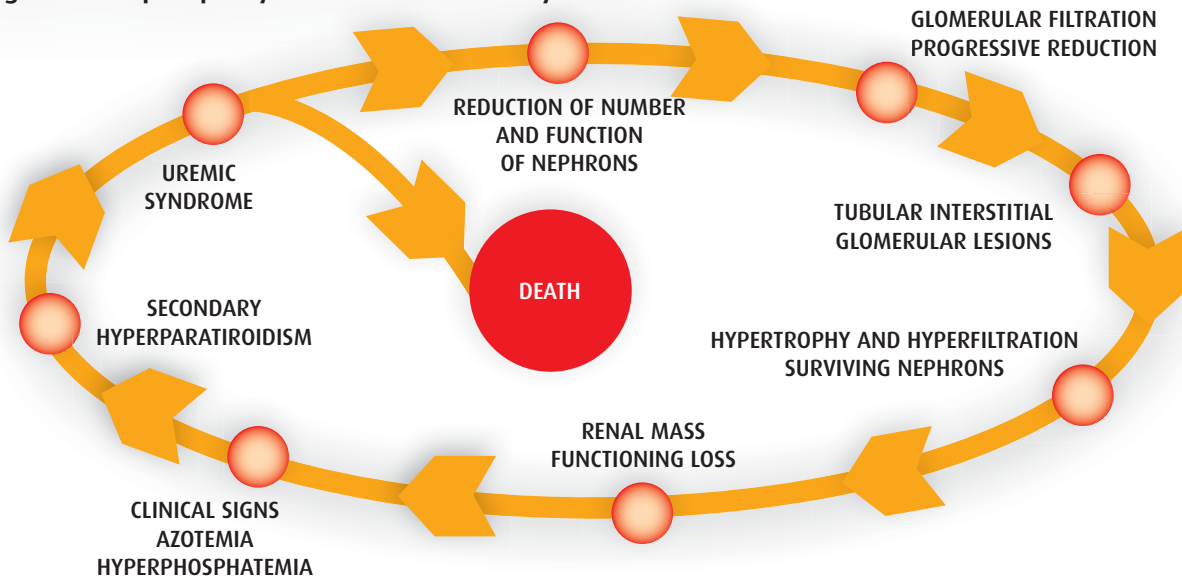
Management of CKD



* to be used in stage 2 if necessary ** to be used always

CAN BE USED ALONE OR IN COMBINATION

Fig. 3 Progress of nephropathy and of Chronic Kidney Disease



RENAL CATS

SPC

1. Composition

Maltodextrin, Potassium citrate (K 36%), Kitosan, Calcium carbonate (Ca 38%)

2. Product description

Specifically recommended to support renal function, both in the early and late stages of chronic renal failure in cats, **Renal cats** can control metabolic imbalances resulting from chronic renal dysfunction.

In advanced stages **Renal cats** can be administered in combination with **Renal Advanced cats**.

3. Instruction for use

Mix **Renal cats** with feed according to the following daily dosages:

- up to 2.5 kg : 1 measuring cup per day
- between 2.5 and 5 kg : 2 measuring cups per day
- over 5 kg : 3 measuring cups per day

It is possible to split the daily dosage in 2-3 administrations, according to the number of meals.

Administer **Renal Cats** for 30 days, or for longer periods depending on your veterinarian's instructions.

It is preferable to mix the product with moist food. In case of a diet based only on dry food: slightly moisten the food to ensure good adhesion of the powder and its complete intake.

Renal cats can be used either alone or in combination with the usual therapies for chronic renal failure and with specific diets for renal dysfunction, on the basis of your veterinarian's instructions.

4. Packaging

50 g powder jar with measuring cup



RENAL DOGS

SPC

1. Composition

Maltodextrin, Calcium carbonate (Ca 38%), Potassium citrate (K 36%), Kitosan

2. Product description

Specifically recommended to support renal function, both in the early and late stages of chronic renal failure in dogs, **Renal dogs** can control metabolic imbalances resulting from chronic renal dysfunction.

In advanced stages **Renal dogs** can be administered in combination with **Renal Advanced dogs**.

3. Instruction for use

Mix **Renal dogs** with feed according to the following daily dosages:

Weight in kg	Small measuring cups	Weight in kg	Large measuring cups
up to 2.5	1	from 10 to 15	2
from 2.5 to 5	2	from 15 to 25	3
from 5 to 7.5	3	from 25 to 35	4
from 7.5 to 10	4	from 35 to 50	5
		over 50	6

It is possible to split the daily dosage in 2-3 administrations, according to the number of meals.

Administer **Renal dogs** for 30 days, or for longer periods depending on your veterinarian's instructions.

It is preferable to mix the product with moist food. In case of a diet based only on dry food: slightly moisten the food to ensure good adhesion of the powder and its complete intake.

Renal dogs can be used either alone or in combination with the usual therapies for chronic renal failure and with specific diets for renal dysfunction, on the basis of your veterinarian's instructions.

4. Packaging

100 g powder jar with small and large measuring cup

RENAL ADVANCED CATS

SPC

1. Composition

Maltodextrin, Fructooligosaccharides, Lespedeza capitata dry extract (titration 4% in Rutin), Orange bioflavonoids (titration 40% in Hesperidine), Vitamin C, Enterococcus faecium SF68 (10 bln/g), Vitamin B6, Lactobacillus acidophilus DSM13241 (50 bln/g), Folic acid, Vitamin B12

2. Product description

Recommended in case of chronic renal failure in cats, **Renal Advanced cats** can control metabolic imbalances resulting from chronic renal dysfunction, specially in most advanced stages. **Renal Advanced cats** can be administered in combination with **Renal cats**, depending on the evolution stage of renal dysfunction and on the consequent metabolic conditions.

3. Instructions for use

Mix **Renal Advanced cats** with feed according to the following daily dosages:

- up to 2.5 kg : 1 measuring cup per day
- between 2.5 and 5 kg : 2 measuring cups per day
- over 5 kg : 3 measuring cups per day

It is possible to split the daily dosage in 2-3 administrations, according to the number of meals.

Administer **Renal Advanced cats** for 30 days, or for longer periods depending on your veterinarian's instructions.

It is preferable to mix the product with moist food. In case of a diet based only on dry food: slightly moisten the food to ensure good adhesion of the powder and its complete intake.

Renal Advanced cats can be used either alone or in combination with the usual therapies for chronic renal failure and with specific diets for renal dysfunction, on the basis of your veterinarian's instructions.

4. Packaging

40 g powder jar with measuring cup



RENAL ADVANCED DOGS

SPC

1. Composition

Maltodextrin, Fructooligosaccharides, Lespedeza capitata dry extract (titration 4% in Rutin), Orange bioflavonoids (titration 40% in Hesperidine), Vitamin C, Enterococcus faecium SF68 (10 bln/g), Vitamin B6, Lactobacillus acidophilus DSM13241 (50 bln/g), Folic acid, Vitamin B12

2. Product description

Recommended in case of chronic renal failure of the dog, **Renal Advanced dogs** can control metabolic unbalances resulting from chronic renal dysfunction, specially in most advanced stages. **Renal Advanced dogs** can be administered in combination with **Renal dogs**, depending on the evolution stage of renal dysfunction and on the consequent metabolic conditions.

3. Instructions for use

Mix **Renal Advanced dogs** with feed according to the following daily dosages:

Weight in kg	Small measuring cups	Weight in kg	Large measuring cups
up to 2.5	1	from 10 to 15	2
from 2.5 to 5	2	from 15 to 25	3
from 5 to 7.5	3	from 25 to 35	4
from 7.5 to 10	4	from 35 to 50	5
		over 50	6

It is possible to split the daily dosage in 2-3 administrations, according to the number of meals.

Administer **Renal Advanced dogs** for 30 days, or for longer periods following your veterinarian's instructions.

It is preferable to mix the product with moist food. In case of a diet based only on dry food: slightly moisten the food to ensure good adhesion of the powder and its complete intake.

Renal Advanced dogs can be used either alone or in combination with the usual therapies for chronic renal failure and with specific diets for renal dysfunction, on the basis of your veterinarian's instructions.

4. Packaging

80 g powder jar with small and large measuring cup

Bibliography

- Adams LG, Polzin DJ. *Mixed acid-base disorders*. *Vet Clin North Am Small Anim Pract*. 1989 Mar;19(2):307-26
- Andreoli SP, Dunson JW, Bergstein JM. *Calcium carbonate is an effective phosphorus binder in children with chronic renal failure*. *Am J Kidney Dis*. 1987 Mar;9(3):206-10
- Anjaneyulu M, Chopra K. *Quercetin, an anti-oxidant bioflavonoid, attenuates diabetic nephropathy in rats*. *Clin Exp Pharmacol Physiol*. 2004 Apr;31(4):244-8
- Barber PJ, Elliot J. *Feline chronic renal failure. Calcium homeostasis in 80 cases diagnosed between 1992 and 1995*. *J Small Anim Pract*. 1998 Mar;39(3):108-16
- Barsotti G, Cupisti a, Morelli E, Meola M, Cozza V, Barsotti M, Giovanetti S. *Secondary hyperparathyroidism in severe chronic renal failure is corrected by very-low dietary phosphate intake and calcium carbonate supplementation*. *Nephron*. 1998;79(2):137-41
- Bartges JW, Willis AM, Polzin DJ. *Hypertension and renal disease*. *Vet Clin North Am Small Anim Pract*. 1996 Nov;26(6):1331-45
- Baxter J, Shimizu F, Takiguchi Y, Wada M, Yamaguchi T. *Effect of iron (III) chitosan intake on the reduction of serum phosphorus in rats*. *J Pharm Pharmacol*. 2000 Jul;52(7):863-74
- Brovida C. *Insufficienza renale cronica (IRC) nel gatto*. Atti 50° Congresso Nazionale SCIVAC 2005 Rimini.
- Brown SA. *Cos'è di nuovo nel trattamento della CKD felina?* Waltham Focus 2005;15(1):2-5
- Brown SA. *Oxidative stress and chronic kidney disease*. *Vet Clin North Am Small Anim Pract*. 2008 Jan;38(1):157-66
- Brown SA, Brown CA, Crowell WA, Barsanti JA, Finco DR. *Does modifying dietary lipids influence the progression of renal failure?* *Vet Clin North Am Small Anim Pract*. 1996 Nov;26(6):1277-85
- Brown SA, Brown CA, Crowell WA, Barsanti JA, Finco DR. *Pathophysiology and management of progressive renal disease*. *Vet J*. 1997 Sep;154(2):93-109
- Brown SA, Brown CA, Surdyk K. *Medical management of chronic kidney disease*. Proceedings of the 2006 World Congress WSAVA/FECAVA/CSAVA
- Brown SA, Finco DR, Bartges JW, Brown CA, Barsanti JA. *Interventional nutrition for renal disease*. *Clin Tech Small Anim Pract*. 1998 Nov;13(4):217-23
- Budisavljevic MN, Hodge L, Barber K, Fulmer JR, Durazo-Arvizu RA, Self SE, Kuhlmann M, Raymond JR, Greene EL. *Oxidative stress in the pathogenesis of experimental mesangial proliferative glomerulonephritis*. *Am J Physiol Renal Physiol*. 2003;285:F1138-F1148
- Campanacci L, Romagnoli GF, Borsatti A, Mendola R, Maschio G, Poli D, Todesco S. *Effetti della frazione depurata di Lespedeza capitata sulla funzione del rene nel soggetto normale e nel nefropatico*. *Minerva Medica* 1965;4288-4298
- Chew DJ. *Stato dell'arte sull'insufficienza renale cronica nel cane e nel gatto*. Atti 48° Congresso Nazionale SCIVAC. 2004 Rimini
- Chow J. *Probiotics and prebiotics: a brief overview*. *J Ren Nutr*. 2002 Apr;12(2):76-86
- Cowgill LD. *Pathophysiology and management of anemia in chronic progressive renal failure*. *Semin Vet Med Surg (Small Anim)*. 1992 Aug;7(3):175-82
- Debraekeleer J. *Nefropatia cronica: come possiamo migliorare la qualità della vita?* Atti 50° Congresso Nazionale SCIVAC 2005 Rimini.
- Desruelles J, Delmon A. *Clinical trial of treatment of azotemic conditions with an injectable extract of Lespedeza capitata*. *Lille Med*. 1969 Feb;14(2):83-7
- Elliot DA. *Gestione nutrizionale della patologia renale cronica*. Waltham Focus 2005;12(1):14-19
- Elliot D, Lefebvre H. *Nefropatia cronica: l'importanza delle nutrizione*. In *Enciclopedia delle nutrizione clinica del cane*. Royal Canin 2007;268-298
- Elliot J, Elliot D. *Gestione nutrizionale della nefropatia cronica felina*. *Veterinary Focus* 2008;18(2):39-44
- Elliot J, Rawlings JM, Markwell PJ, Barber PJ. *Survival of cats with naturally occurring chronic renal failure: effect of dietary management*. *J Small Anim Pract*. 2000 Jun;41(6):235-42
- Francey T. *Come trattare la patologia renale cronica nel gatto*. Waltham Focus 2005;12(1):28-30
- Fries D, Pozet N. *New conservative treatment for hyperazotemia: utilization of flavonic extracts of injectable Lespedeza capitata*. *Lyon Med*. 1969 Jan;221(4):167-70
- Grevel V, Opitz M, Steeb C, Skrodzki M. *Myopathy due to potassium deficiency in eight cats and a dog*. *Berl Munch Tierarztl Wochenschr*. 1993 Jan;106(1):20-6
- Harte JG, Markwell PJ, Mraillon RM, Gettinby GG, Smith BHE, Wills JM. *Dietary management of naturally occurring chronic renal failure in cats*. *J Nutr*. 1994;124:26605-26625
- Hercz G, Kraut JA, Andress DA, Howard N, Roberts C, Shinaberger JH, Sherrard DJ, Coburn JW. *Use of calcium carbonate as a phosphate binder in dialysis patients*. *Miner Electrolyte Meta*. 1986;12(5-6):314-9
- Hesta M, Hoornaert E, Verlinden A, Janssens GP. *The effect of oligofructose on urea metabolism and fecal odour components in cats*. *J Anim Physiol Anim Nutr*. 2005 Apr;89(3-6):208-14
- IRIS – International Renal Interest Society. *Trattare la nefropatia cronica nei cani e nei gatti*. 2006
- Janssen MJ, van der Kuy A, ter Wee PM, van Boven WP. *Aluminium hydroxide, calcium carbonate and calcium acetate in chronic intermittent hemodialysis patients*. *Clin Nephrol*. 1996 Feb;45(2):111-9
- Jing SB, Li L, Ji D, Takiguchi Y, Yamaguchi T. *Effect of chitosan on renal function in patients with chronic renal failure*. *J Pharm Pharmacol*. 1997 Jul;49(7):721-3
- Kahraman A, Erkasap N, Serteser M, Koken T. *Protective effect of quercetin on renal ischemia/reperfusion in rats*. *J Nephrol*. 2003 Mar-Apr;16(2):219-24
- Koguchi T, Koguchi H, Nakajima H, Takano S, Yamamoto Y, Innami S, Mae-kawa A, Tadokoro T. *Dietary fiber suppresses elevation of uric acid and urea nitrogen concentrations in serum of rats with renal dysfunction induced by dietary adenine*. *Int J Vitam Nutr Res*. 2004 Jul;74(4):253-63
- Lees GE. *Early diagnosis of renal disease and renal failure*. *Vet Clin North Am Small Anim Pract*. 2004 Jul;34(4):867-85
- Lefebvre HP, Braun JP, Watson AD. *Diagnosi precoce dell'insufficienza renale cronica nel cane*. Waltham Focus 2005;12(1):6-13
- Malberti F, Surian M, Poggio F, Minoia C, Salvadeo A. *Efficacy and safety of long-term treatment with calcium carbonate as a phosphate binder*. *Am J Kidney Dis*. 1998 Dec;12(6):487-91
- Michell AR. *Management of renal diseases: have we progressed?* Proceedings of 4° European FECAVA SCIVAC Congress.
- Nagode La, Chew DJ, Podell M. *Benefits of calcitriol therapy and serum phosphorus control in dogs and cats with chronic renal failure. Both are essential to prevent or suppress toxic hyperparathyroidism*. *Vet Clin North Am Small Anim Pract*. 1996 Nov;26(6):1293-330
- Nikolic J, Cvetkovic T, Sokolovic D. *Role of quercetin on hepatic urea production in acute renal failure*. *Ren Fail*. 2003 Mar;25(2):149-55
- Pastoor FJH, Opitz R, Van 't Klooster AT. *Dietary calcium chloride vs. calcium carbonate reduces urinary pH and phosphorus concentration, improves bone mineralization and depresses kidney calcium level in cats*. *J Nutr*. 1994;124:2212-2222
- Phillips SL, Polzin DJ. *Clinical disorders of potassium homeostasis. Hyperkalemia and hypokalemia*. *Vet Clin North Am Small Anim Pract*. 1998 May;28(3):545-64
- Pollen SM. *Renal disease in small animals: a review of conditions and potential nutrient and botanical interventions*. *Alt Med Rev*. 2001;6:546-561
- Polzin DJ, Osborne CA, Adams LD, O'Brien TD. *Dietary management of canine and feline chronic renal failure*. *Vet Clin North Am Small Anim Pract*. 1989 May;19(3):539-60
- Polzin DJ, Osborne CA, Ross S, Jacob F. *Dietary management of feline chronic renal failure: where are we now? In what direction are we headed?* *Journal of Feline Medicine and Surgery* 2000 Jun;2(2):75-82
- Pozet N, Traeger J. *Study on the clinical pharmacology of a lyophilized extract of Lespedeza capitata*. *Lyon Med*. 1972 Jan;227(2):175-82
- Ranganathan N, Patel B, Ranganathan P, Marczyk J, Dheer R, Chordia T, Dunn SR, Friedman EA. *Probiotic amelioration of azotemia in 5/6th nephrectomized Sprague-Dawley rats*. *Scientific World Journal*. 2005 Aug 24;5:652-60
- Ross LA. *Fluid therapy for acute and chronic renal failure*. *Vet Clin North Am Small Anim Pract*. 1989 Mar;19(2):343-59
- Rubin SI. *Chronic renal failure and its management and nephrolithiasis*. *Vet Clin North Am Small Anim Pract*. 1997 Nov;27(6):1331-54
- Sparkes AH. *Chronic renal failure in the cat*. Proceedings of 2007 European Veterinary Conference. Amsterdam
- Tsakamoto Y, Moriya R, Nagaba Y, Morishita T, Izumida I, Okubo M. *Effect of administering calcium carbonate to treat secondary hyperparathyroidism in non dialyzed patients with chronic renal failure*. *Am J Kidney Dis*. 1995 Jun;25(6):879-86
- Tylicki L, Rutkowski B, Horl WH. *Antioxidants: a possible role in kidney protection*. *Kidney Blood Press Res*. 2003;26:303-314
- Yarnell E. *Botanical medicines for the urinary tract*. *World J Urol*. 2002 Nov;20(5):285-93
- Wagner H, Elbl G. *ACE-inhibitory procyanidins from Lespedeza capitata*. *Planta Med*. 1992 Jun;58(3):297
- Wagner E, Schwendenwein I, Zentek J. *Effects of a dietary chitosan and calcium supplement on Ca and P metabolism in cats*. *Berl Munch Tierarztl Wochenschr*. 2004 Jul-Aug;117(7-8):310-5
- Willard MD. *Disorders of potassium homeostasis*. *Vet Clin North Am Small Anim Pract*. 1989 Mar;19(2):241-63
- Zayachkivska OS, Konturek SJ, Drozdowicz D, Konturek PC, Brzozowski T, Ghegotsky MR. *Gastroprotective effects of flavonoids in plant extracts*. *J Physiol and*