
felycin®-CA1
(sirolimus delayed-release tablets)
Fight back
with Felycin®-CA1.
The first FDA conditionally approved once-weekly drug
for the management of ventricular hypertrophy in cats
with subclinical hypertrophic cardiomyopathy (HCM).
PRN
PHARMACAL

Hypertrophic cardiomyopathy (HCM) is the most prevalent heart disorder in cats.[1]

HCM is associated with marked left ventricular (LV) hypertrophy and decreased LV performance, which leads to secondary left atrial (LA) dilatation and increases the risk of congestive heart failure (CHF), aortic thromboembolism (ATE), and sudden death.

FAST FACTS

PREVALENCE

1 IN 7 CATS HAS HCM *(15%)*.[1,2]

ETIOLOGY

Unknown; however, higher incidence and genetic mutations identified in

MAINE COON AND RAGDOLL BREEDS.[2]

PRESENTATION

HCM often develops

SILENTLY

before signs appear, with many cats remaining symptom-free until complications suddenly emerge.[1,2]

TREATMENT

HISTORICALLY NO DISEASE-MODIFYING TREATMENT.[1,2]

PROGNOSIS

While many cats remain subclinical, some progress to develop left-sided CHF (23.9%) or arterial thromboembolism (11.3%).[4]

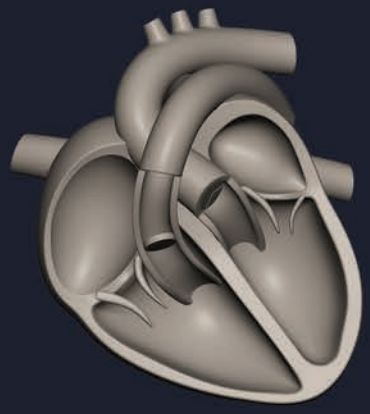
23%

of cats with HCM suffer cardiovascular mortality within 5 years of diagnosis.[1,3]

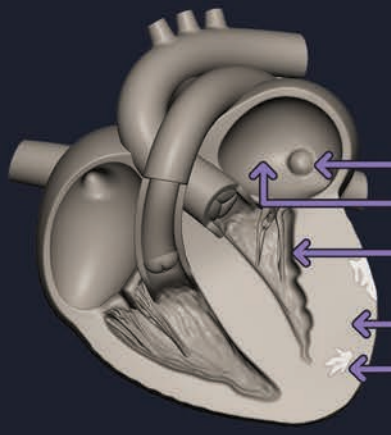
Who is the typical HCM cat?

HCM can occur at any age, in both sexes, and in any breed.[1,2] Older male cats tend to be predisposed to HCM. A higher incidence has been observed in certain breeds, including Maine Coon, Ragdoll, British Shorthair, Persian, Bengal, Sphynx, Norwegian Forest and Birman cats.[1]

NORMAL HEART



HCM HEART



HCM STAGES

A
Predisposed to HCM

B1
Subclinical (low risk)

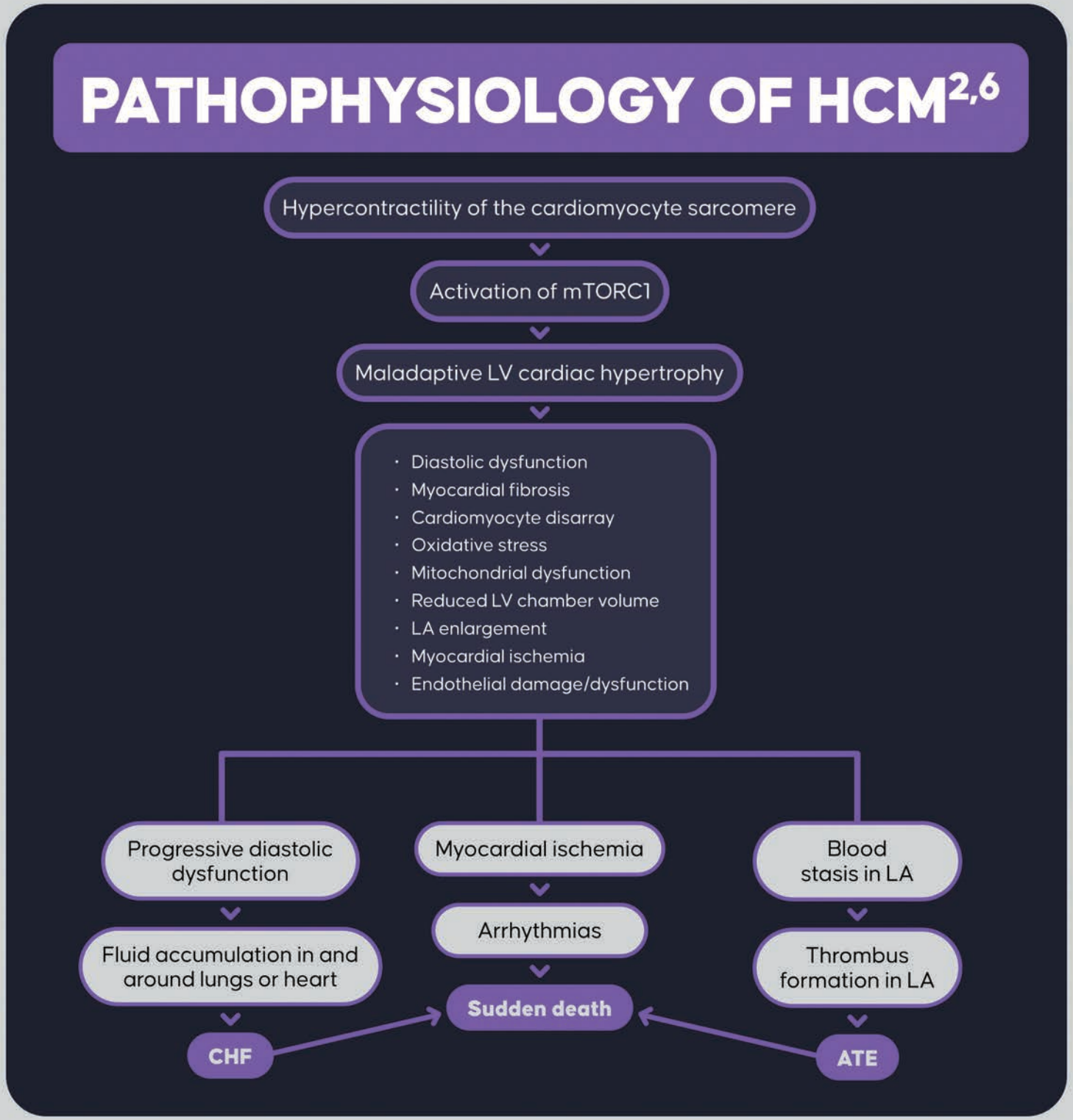
B2
Subclinical (high risk)

C
Current or previous CHF or ATE

D
Refractory (not responding to conventional therapy)

HCM is a silent killer of cats.

Although many cats with HCM remain free of clinical signs, some experience serious complications, including CHF, arterial thromboembolism, and sudden death.[3,5]



YOU MAY NOT HAVE SEEN HCM THIS WEEK, BUT IT PROBABLY SAW YOU.

Clinical signs of HCM are vague and nonspecific, occurring late in the course of the disease, and are typically related to CHF or ATE.[1,2] Approximately 23% of cats with HCM will progress to develop one or more serious sequelae within 5 years, including CHF (20%), arterial thromboembolism (10%), or sudden death (3%).[3] More than 50% of cats with subclinical HCM will die of cardiovascular disease.[3]

Cats developing CHF or ATE are unlikely to survive to

1 YEAR.[3]

ABOUT 80%

of cats with ATE die or are euthanized upon presentation.[2]

	Cardiac Biomarkers[1,5]	Cardiac Auscultation[1,3]
Subclinical HCM	Elevated NT-proBNP by SNAP or quantitative analysis	• None • Parasternal systolic murmur • Third heart sounds (gallop) • Arrhythmias
Increased risk of developing CHF or ATE if they exhibit any of the following	• Gallop sound • Arrhythmia • Moderate to severe LA enlargement • Reduced LA or LV function	• Extreme LV hypertrophy • Higher levels of NT-proBNP or cardiac troponin I • History of syncope
		5-year progression rate for cats with HCM[3]
Congestive heart failure (CHF)	• Tachypnea • Labored breathing	20%
Aortic thromboembolism (ATE)	Hindlimb paralysis	10%
Sudden death		3%

SCREEN TO INTERVENE

The diagnosis of HCM in cats is challenging, but a lack of screening is a missed opportunity to catch subclinical cases early enough for treatment.

15%

of cats have HCM.[1]

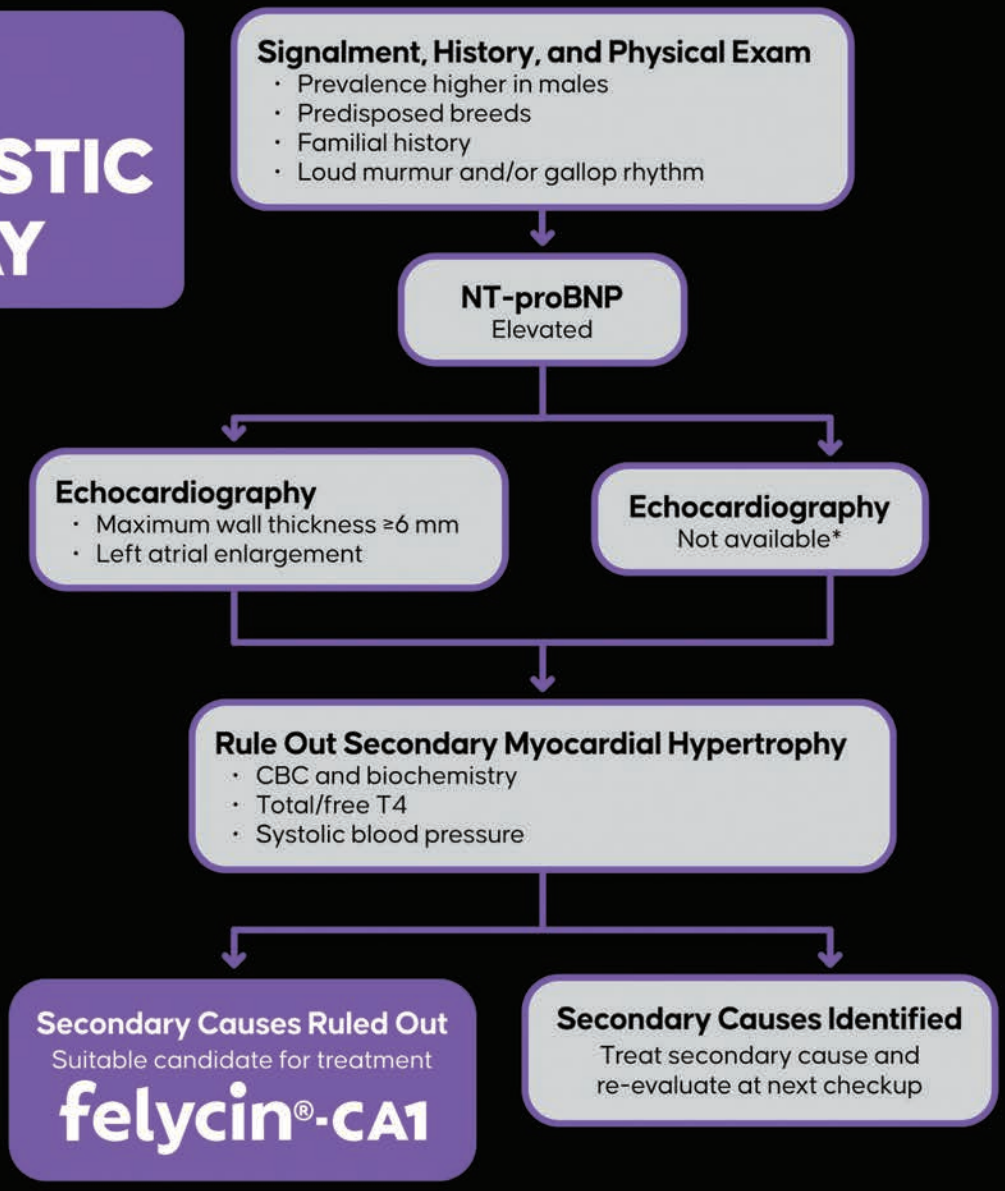
IF YOU AREN'T DIAGNOSING HCM IN 1 OF EVERY 7 CATS YOU SEE ***YOU MAY BE MISSING AN OPPORTUNITY TO INTERVENE.***

The diagnosis of HCM is one of exclusion due to other systemic diseases that may exhibit a similar cardiac morphology, including hyperthyroidism, systemic hypertension, acromegaly, and dehydration.[2,4] In the case of another systemic disease in a cat with severe LV hypertrophy, HCM should still be considered, as comorbidities may exist.[2]

SYSTEMIC DISEASES WITH SIMILAR CARDIAC MORPHOLOGY

DISEASE	RULE IN/OUT
Hyperthyroidism	Total T4
Systemic hypertension	Doppler to measure blood pressure
Acromegaly	Rare: Exclude diabetes
Dehydration	Physical exam, CBC/UA

HCM DIAGNOSTIC PATHWAY



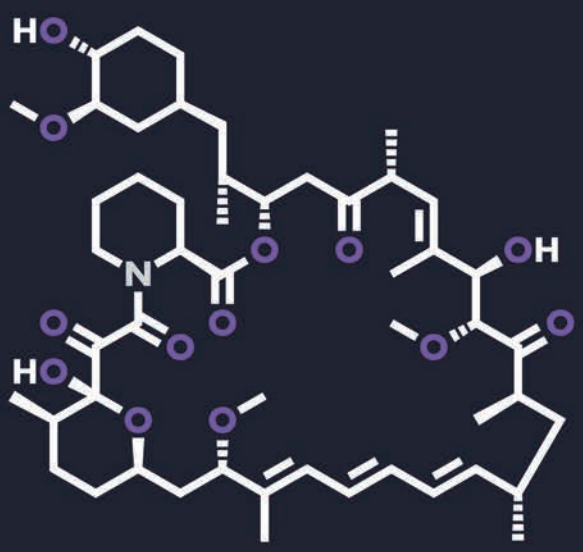
What About Radiographs?

While less accurate, radiographs are yet another tool for diagnosis. They can identify substantial LA enlargement in severe cases;[2] however, they cannot distinguish from other cardiomyopathies.

Until now, little therapeutic advancement has been made in the treatment of HCM to delay the progression of disease, possibly improve the quality of life for patients and families, or show a survival benefit in subclinical cats.[4] Treatment has been limited to the management of clinical signs with loop diuretics, antithrombotic drugs, antiarrhythmic agents, ACE inhibitors, and diet. Proper diagnosis, followed by treatment, could potentially slow the cardiomyopathic changes—or even reverse the hypertrophy.

IF ONLY YOU HAD A TREATMENT TO OFFER THESE PATIENTS ...

*Echocardiographic examination is recommended in all cases to diagnose subclinical HCM.



SEEKING A SOLUTION IN SIROLIMUS.

SIROLIMUS, ALSO KNOWN AS RAPAMYCIN, is a macrolide that has been used to help prevent organ rejection in human allograft patients for more than 25 years.

Sirolimus targets the mTOR protein kinase, which is hyperactivated in cardiovascular diseases, including HCM. **mTOR promotes anabolic processes, downregulates catabolic processes, and signals adaptive cardiac remodeling in response to mechanical overload.**[7] Studies show that mTORC1 activation caused by hemodynamic stressors may be detrimental to the heart, leading to pathologic hypertrophy.[4]

Sirolimus inhibits the mTORC1 protein complex.[4,8,9,10] Long-term treatment with sirolimus has been shown to inhibit a second mTOR complex, mTORC2, with possible resultant side effects (e.g., glucose intolerance, hepatic insulin resistance). These deleterious effects are mitigated using intermittent dosing,[4,8,11] such as once-weekly delayed-release sirolimus, which was found to be well-tolerated in cats with subclinical HCM.

Overview of mTORC1 & mTORC2

	mTORC1	mTORC2
Sensitivity to sirolimus	Acutely sensitive	Comparatively insensitive
Pathophysiological relevance	mTORC1 activation is required for necessary cell functions. Overactivation of mTORC1 is associated with pathologic cardiac hypertrophy. mTORC1 inhibition attenuates cardiac hypertrophy by promoting autophagy, attenuating oxidative stress, and blocking pro-inflammatory responses.	Chronic/frequent administration of sirolimus results in inhibition of mTORC2, which is associated with negative metabolic and immunological consequences including glucose intolerance and hepatic insulin resistance.
Intermittent use of sirolimus	Provides transient inhibition of mTORC1. Inhibition of mTORC1 has been shown to: • Reduce pathologic LV hypertrophy • Improve diastolic and systolic indices of heart function	Mitigates the risk of mTORC2 inhibition.

The inhibition of mTORC1 was shown to prevent and reverse maladaptive hypertrophy with pressure overload in rodent disease models.[9,10] Sirolimus has also been associated with reduced cardiac wall thickness in human allograft patients.[12]

SCAN THE QR CODE TO SEE SIROLIMUS' MODE OF ACTION.

Screen at-risk patients with purpose.
Put an end to feeling powerless.

A disease-modifying drug is now available
for patients diagnosed with subclinical HCM!

INTRODUCING FELYCIN®-CA1

This first-in-class FDA conditionally approved once-weekly drug may prevent and delay progressive LV hypertrophy in cats with subclinical HCM, empowering you to proactively diagnose and manage subclinical HCM in your feline patients.

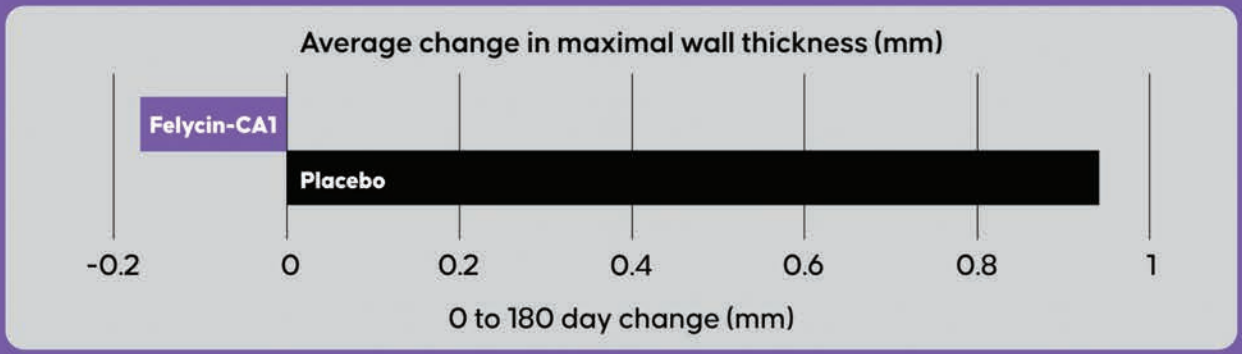
What does "conditional approval" mean?

Felycin®-CA1 is conditionally approved by the FDA. This means that the product has been demonstrated to be safe and that there is a reasonable expectation of effectiveness, which means that the product is reasonably expected to provide the intended effect when used under the conditions of use described in the labeling. The sponsor will continue to collect the evidence of effectiveness needed for the product to receive full approval. It is a violation of Federal Law to use this product other than as directed in the labeling. Additional information on conditional approval can be found by searching fda.gov for "conditional approval."

RAPACAT STUDY[4]

OBJECTIVE	Evaluate the effects of once-weekly Felycin®-CA1 (sirolimus delayed-release tablets) over 6 months in cats with subclinical HCM.
ANIMALS	Forty-three client-owned cats with subclinical HCM ranging from 1 to 12 years of age. Thirty-six cats completed the study after 180 days.
METHODS	Cats enrolled in a double-blind, multi-centered, randomized, placebo-controlled clinical trial were given Felycin-CA1 at the label dose, high dose, or a placebo once a week for 6 months.
RESULTS	**Efficacy:** At Day 180, maximum LV myocardial wall thickness was significantly lower in the label dose Felycin-CA1 group compared to the placebo group. **Safety:** Oral Felycin-CA1 was well tolerated with no significant differences in adverse events between groups.
CLINICAL RELEVANCE	Felycin-CA1 was well tolerated and may prevent or delay progressive LV hypertrophy in cats with subclinical HCM.

FELYCIN-CA1-TREATED CATS HAD A REDUCTION IN LV MAXIMAL WALL THICKNESS.



Thirty-six client-owned cats with subclinical HCM were administered Felycin-CA1 or placebo. At day 180, cats treated with the recommended label dose of Felycin-CA1 had a significantly lower maximal wall thickness, showing an average **reduction** of 0.17mm in comparison with a 0.94mm **increase** for cats receiving placebo.

Felycin®-CA1 underwent extensive safety studies.

Three safety studies were conducted by the sponsor, including a laboratory margin of safety study, a pilot safety study, and a vaccine response study. Some cats receiving sirolimus had elevated transaminase liver enzymes, including alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST). All affected cats remained clinically normal. There was no evidence of liver pathology in cats undergoing postmortem examination.

At Day 56 cats who were administered Felycin-CA1 demonstrated an adequate immune response to a killed rabies vaccine administered on Day 29.*

3
unique safety studies

84
healthy male and female cats in total

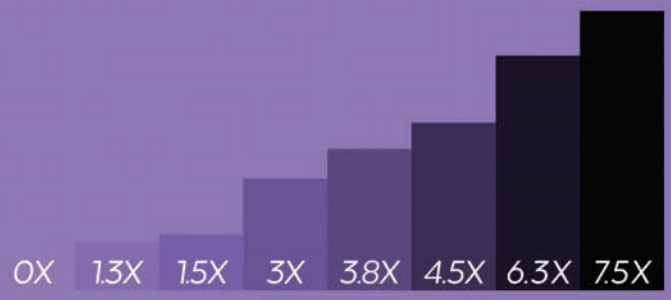
VACCINE-NAÏVE CATS USED*

Study duration of up to

24
weeks and dosing intervals up to

3x
per week

FELYCIN-CA1 DOSED AT



THE LABEL DOSE OF 0.3 MG/KG DOSED WEEKLY ACROSS ALL THREE STUDIES

3
KEY TAKEAWAYS

1. Felycin-CA1's once-weekly dosing regimen demonstrated a favorable safety profile.
2. Regular monitoring of liver function is essential for patient management.
3. Felycin-CA1 does not impact a cat's ability to mount an immune response to rabies vaccine administration.

Precautions

- Most common precaution associated with use relates to the progression of the HCM disease process (arrhythmia, CHF, syncope, pericardial effusion, and sudden death).
- Other reported side effects include liver enzyme elevation (ALT, AST), lethargy, vomiting, diarrhea, and inappetence.
- A serum biochemical profile should be performed in cats prior to starting treatment to assess liver function.
- Liver enzymes should be evaluated 1-2 months after starting treatment and every 6-12 months thereafter. Discontinue use of medication if ALT and AST levels become >2x upper limit of normal.
- The impact of concurrent administration of Felycin-CA1 on vaccination for FHV-1, FCV, FPV, and FeLV has not been evaluated.

*Vaccine response study only.

IMPORTANT SAFETY INFORMATION: Do not use Felycin®-CA1 in cats with diabetes mellitus. Discontinue immediately if a cat receiving Felycin-CA1 is diagnosed with diabetes mellitus. Do not administer in cats with pre-existing liver disease. Administration of Felycin-CA1 with drugs that inhibit cytochrome P-450 3A4 or P-glycoprotein, such as calcium channel blockers, amiodarone, azoles, or cyclosporine, may increase risk for toxicity. Use caution when administering in cats with the MDR1 mutation or when administering concomitantly with another P-gp substrate. Treatment with Felycin-CA1 could impact the cat's ability to mount an adequate immune response to vaccinations.

The use of Felycin-CA1 in cats with viral disease like feline viral rhinotracheitis has not been evaluated. The safety and effectiveness of Felycin-CA1 has not been evaluated in cats with other cardiomyopathy phenotypes, in cats receiving beta blockers or corticosteroids, in cats with kidney disease, hyperthyroidism, or other significant systemic disease. The effectiveness of Felycin-CA1 has not been evaluated in sexually intact cats, therefore, should not be used in animals intended for breeding.

Treatment with Felycin-CA1 has been associated with the elevation of the transaminase enzymes, which include alanine aminotransferase (ALT) and aspartate aminotransferase (AST). Bloodwork should be repeated 1 to 2 months following initiation of treatment, and every 6-12 months thereafter. Discontinue treatment if transaminase values exceed 2X the upper limit of normal (ULN), if other liver enzymes besides ALT or AST are elevated, or if clinical signs of liver dysfunction are noted.

The most frequently observed adverse reactions in cats treated with Felycin-CA1 were cardiovascular in nature, relating to the progression of HCM, and included arrhythmia, congestive heart failure, syncope, and pericardial effusion. Other adverse reactions observed were lethargy, vomiting, diarrhea, and inappetence.

For use only in otherwise healthy cats with subclinical HCM in the absence of other causes of compensatory myocardial hypertrophy (e.g. systemic hypertension), current or historic symptoms of congestive heart failure, arterial thromboembolism, and severe LV outflow tract obstruction.

Not for human use. Keep out of reach of children. Contact a physician in case of accidental ingestion by humans. Pregnant and breastfeeding women should avoid contact with Felycin-CA1. People with known hypersensitivity to sirolimus should administer Felycin-CA1 with caution.

Keep Felycin-CA1 in a secure location out of reach of dogs, cats and other animals to prevent accidental ingestion or overdose.

Felycin-CA1 is conditionally approved by FDA pending a full demonstration of effectiveness under application number 141-604. See prescribing information for complete details regarding adverse events, warnings, and precautions.

4-2025

References

[1]Fuentes VL, Abbott J, Chetboul V, et al. ACVIM consensus statement guidelines for the classification, diagnosis, and management of cardiomyopathies in cats. *JVIM* 2020;34:1062-1077.

[2]Kittleson MD, Cote E. The feline cardiomyopathies: Hypertrophic cardiomyopathy. *JFMS* 2021;23:1028-1051.

[3]Fox PR, Keene BW, Lamb K, et al. International collaborative study to assess cardiovascular risk and evaluate long-term health in cats with preclinical hypertrophic cardiomyopathy and apparently healthy cats: The REVEAL Study. *JVIM* 2018;32:930-943.

[4]Kaplan JL, Rivas VN, Walker AL, et al. Delayed-release rapamycin halts progression of left ventricular hypertrophy in subclinical feline hypertrophic cardiomyopathy: results of the RAPACAT trial. *JAVMA* 2023;261(11):1628-1637.

[5]Ironside VA, Tricklebank PR, Boswood A. Risk indicators in cats with preclinical hypertrophic cardiomyopathy: a prospective cohort study. *JFSM* 2021;23(2):149-159.

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[7]Sciarretta S, Forte M, Frati G, Sadoshima J. New Insights Into the Role of mTOR Signaling in the Cardiovascular System. *Circ Res.* 2018 Feb 2;122(3):489-505.

[8]Arriola Apelo SI, Neuman JC, Baar EL, et al. Alternative rapamycin treatment regimens mitigate the impact of rapamycin on glucose homeostasis and the immune system. *Aging Cell* 2016;15:28-38.

[9]Gu J, Hu W, Song ZP, et al. Rapamycin inhibits cardiac hypertrophy by promoting autophagy via the MEK/ERK/Beclin-1 pathway. *Frontiers in Physiology* 2016;7(104).

[10]McMullen JR, Sherwood MC, Tarnavski O, et al. Inhibition of mTOR signaling with rapamycin regresses established cardiac hypertrophy induced by pressure overload. *Circulation* 2004;109:3050-3055.

[11]Lamming DW. Inhibition of the mechanistic target of rapamycin (mTOR) – Rapamycin and beyond. *Cold Spring Harb Perspect Med* 2016;6:a025924.

[12]Raichlin E, Chandrasekaran K, Kremers WK, et al. Sirolimus as primary immunosuppressant reduces left ventricular mass and improves diastolic function of the cardiac allograft. *Transplantation* 2008;86(10):1395-1400.

felycin®-CA1

(sirolimus delayed-release tablets)

Cardiac drug for oral use in cats only

Conditionally approved by FDA pending a full demonstration of effectiveness under application number 141-604.

It is a violation of Federal law to use this product other than as directed in the labeling.

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION:
FELYCIN®-CA1 (sirolimus delayed-release tablets) contains the active ingredient sirolimus. FELYCIN®-CA1 is available in 0.4 mg, 1.2 mg, and 2.4 mg tablet strengths.

FELYCIN®-CA1 are enteric film-coated biconvex tablets, plain on both sides. The 0.4 mg tablet is orange, the 1.2 mg tablet is blue, and the 2.4 mg tablet is white.

INDICATION:
FELYCIN®-CA1 (sirolimus delayed-release tablets) is indicated for the management of ventricular hypertrophy in cats with subclinical hypertrophic cardiomyopathy (HCM).

Subclinical HCM refers to cats with left ventricular (LV) hypertrophy (LV wall thickness of ≥6 mm at end diastole by 2D or M-mode assessment) in the absence of systemic hypertension, other causes of compensatory myocardial hypertrophy, current or historic symptoms of congestive heart failure, arterial thromboembolism, and severe LV outflow tract obstruction.

DOSAGE AND ADMINISTRATION:
Administer FELYCIN®-CA1 at a target dosage of 0.3 mg/kg orally once weekly (see Table 1).

FELYCIN®-CA1 should be swallowed whole and not chewed. Do not split or crush tablets.

FELYCIN®-CA1 should be administered in conjunction with a meal.

Table 1. Dosing table (0.3 mg/kg once per week)

Body Weight (kg)	Number of Tablets		
	0.4 mg	1.2 mg	2.4 mg
2.5 – 3.2	2	0	0
3.3 – 4.8	0	1	0
4.9 – 6.4	1	1	0
6.5 – 9.6	0	0	1
>9.6	0	1	1

Due to the available tablet strengths, cats weighing less than 2.5 kg cannot be accurately dosed.

CONTRAINDICATIONS:
Do not use FELYCIN®-CA1 in cats with diabetes mellitus. Discontinue immediately if a cat receiving FELYCIN®-CA1 is diagnosed with diabetes mellitus. The administration of FELYCIN®-CA1 to a cat that developed diabetes mellitus was associated with the development of diabetic ketoacidosis and death (see **Adverse Reactions).**

Do not administer FELYCIN®-CA1 in cats with pre-existing liver disease (see **Adverse Reactions, Precautions,** and **Target Animal Safety).**

WARNINGS:
User Safety Warnings: Not for use in humans. Keep out of reach of children. Contact a physician in case of accidental ingestion by humans.

Accidental Ingestion of FELYCIN®-CA1:
In case of accidental ingestion seek medical advice immediately and show the package insert or the label to the physician.

Sirolimus can cause a range of adverse effects including fever, hypertension, headache, and adverse gastrointestinal effects.

Drug Handling and Administration:
Pregnant and breastfeeding women should avoid contact with FELYCIN®-CA1. People with known hypersensitivity to sirolimus should administer FELYCIN®-CA1 with caution.
Always store tablets in the original packaging and only remove the required number of tablets from the blister at the time of dosing.

Ensure that any tablets that are not swallowed by the cat are disposed of immediately.

Avoid direct contact with vomit, saliva, and tablet remnants. When cleaning up vomit, saliva, or tablet remnants, wear gloves and wash hands afterwards.

During normal handling of FELYCIN®-CA1, the coating on the tablets will prevent contact with the active ingredient, sirolimus. However, if the coating is broken down through ingestion or vomiting by the cat, exposure to sirolimus can occur.

To obtain a copy of the Safety Data Sheet (SDS), contact PRN Pharmacal at 1-800-874-9764.

Animal Safety Warnings:
Sirolimus is a known substrate for cytochrome P-450 3A4 (CYP3A4) and P-glycoprotein (P-gp) in humans. Administration of FELYCIN®-CA1 with drugs that inhibit CYP 3A4 or P-gp, such as calcium channel blockers, amiodarone, azoles (e.g., ketoconazole), or cyclosporine, may increase risk for toxicity. Use caution when administering FELYCIN®-CA1 in cats with the MDR1 mutation or when administering concomitantly with another P-gp substrate (e.g., eprinomectin and emodepside). Treatment with FELYCIN®-CA1 could impact the cat's ability to mount an adequate immune response to vaccinations.

Concurrent administration of FELYCIN®-CA1 did not impact the cat's ability to mount an adequate immune response to a killed rabies vaccine (see **Clinical Pharmacology** and **Target Animal Safety).** The impact of concurrent administration of FELYCIN®-CA1 on vaccination for FHV-1, FCV, FPV, and FeLV has not been evaluated.

Keep FELYCIN®-CA1 in a secure location out of reach of dogs, cats, and other animals to prevent accidental ingestion or overdose.

PRECAUTIONS:
For use only in otherwise healthy cats with subclinical HCM in the absence of other causes of compensatory myocardial hypertrophy (e.g., systemic hypertension), current or historic symptoms of congestive heart failure, arterial thromboembolism, and severe LV outflow tract obstruction.

A diagnosis of subclinical HCM should be made by means of a comprehensive physical examination including blood pressure measurement to rule out systemic hypertension, and cardiac examination which should include echocardiography to confirm the presence of LV hypertrophy and radiography to rule out congestive heart failure.

Echocardiographic examination is recommended in all cases to diagnose subclinical HCM. A diagnosis of subclinical HCM is based on an end-diastolic left ventricular wall thickness of ≥6 mm measured by 2D or M-mode assessment.

Sirolimus undergoes extensive hepatic metabolism in humans. Prior to initiation of treatment with FELYCIN®-CA1, a comprehensive physical examination and screening bloodwork including a serum biochemical profile should be conducted to rule out pre-existing liver dysfunction.

Treatment with FELYCIN®-CA1 has been associated with the elevation of the transaminase enzymes, which include alanine aminotransferase (ALT) and aspartate aminotransferase (AST).

Bloodwork should be repeated 1 to 2 months following initiation of treatment, and every 6 to 12 months thereafter. If mild transaminase elevations are observed (up to 2X the upper limit of normal (ULN)), bloodwork should be repeated in 2 months. If these values remain elevated, discontinue treatment with FELYCIN®-CA1.

Discontinue treatment with FELYCIN®-CA1 if transaminase values exceed 2X the upper limit of normal (ULN), if other liver enzymes besides ALT or AST are elevated, or if clinical signs of liver dysfunction are noted.

Available information does not indicate that FELYCIN®-CA1 is immunosuppressive at the doses administered. The use of FELYCIN®-CA1 in cats with chronic viral diseases like feline viral rhinotracheitis has not been evaluated.

The safety and effectiveness of FELYCIN®-CA1 has not been evaluated in cats with other cardiomyopathy phenotypes.

The safety and effectiveness of FELYCIN®-CA1 has not been evaluated in cats receiving beta blockers or corticosteroids.

The safety and effectiveness of FELYCIN®-CA1 has not been evaluated in cats with chronic kidney disease, hyperthyroidism, or other significant systemic disease.

The effectiveness of FELYCIN®-CA1 has not been evaluated in sexually intact cats. Therefore, FELYCIN®-CA1 should not be used in animals intended for breeding.

ADVERSE REACTIONS:
In a well-controlled pilot field study, 43 cats with subclinical HCM were administered either the label dose of FELYCIN®-CA1 (0.3 mg/kg once weekly; n=15), twice the label dose (0.6 mg/kg once weekly; n=15), or a placebo control tablet (n=13). Cats were followed for 180 days or until removal from the study (see **Reasonable Expectation of Effectiveness**).

Cardiac: The most frequently observed adverse reactions in cats treated with FELYCIN®-CA1 were cardiovascular in nature, relating to the progression of HCM, and included arrhythmia, congestive heart failure, syncope, and pericardial effusion.

Three of the cats receiving twice the label dose of FELYCIN®-CA1 (0.6 mg/kg) progressed to congestive heart failure or sudden death. Two of these cats had severe pre-existing structural disease. The third cat did not have severe structural disease at enrollment but had markedly elevated serum N-terminal pro-brain natriuretic peptide (NT-proBNP) at enrollment (1344 pmol/L, normal <100 pmol/L), which can indicate an increased risk of disease progression. The relationship to treatment with FELYCIN®-CA1 is unknown due to the small sample size of this study and the variable disease progression of HCM.

Non-Cardiac: Other adverse reactions observed in cats treated with FELYCIN®-CA1 were lethargy, vomiting, diarrhea, and inappetence.

Diabetes Mellitus: One cat receiving the label dose (0.3 mg/kg) of FELYCIN®-CA1 developed diabetes mellitus during the study, manifesting as hypercholesterolemia, hyperglycemia, and glucosuria with prior evidence of urinary tract infection at scheduled visits. Treatment for

diabetes was not initiated and the cat continued on the study. Subsequently, the cat presented in diabetic ketoacidosis, and despite intensive medical management, the cat died of acute cardiac arrest.

Pre-Existing Liver Disease: In a separate pilot field study conducted in cats with chronic kidney disease (CKD), one cat was enrolled with a history of elevated alkaline phosphatase (ALP). After treatment with the label dose (0.3 mg/kg) of FELYCIN®-CA1, this cat experienced a progressive decline in appetite, elevation of liver enzymes, including ALP, ALT, and AST, and icterus, and was euthanized approximately 4 months after exiting the study.

CONTACT INFORMATION:
To report suspected adverse drug experiences or for technical assistance contact PRN Pharmacal at 1-800-874-9764.

For additional information about reporting adverse drug experiences for animal drugs, contact FDA at 1-888-FDA-VETS or online at www.fda.gov/reportanimalae.

CLINICAL PHARMACOLOGY:
Mode of action: Sirolimus is an immunosuppressant that targets and inhibits the mammalian target of rapamycin C1 (mTORC1) protein complex, a central regulator of cell growth and nutrient response. Studies in rodent models suggest mTOR inhibition by sirolimus attenuates cardiac hypertrophy by promoting autophagy, attenuating oxidative stress and blocking pro-inflammatory responses, thereby resulting in an improvement in cardiac function in rodents.

Pharmacokinetics: In a laboratory safety study in healthy adult cats after repeat oral dosing of FELYCIN®-CA1 once per week for 24 weeks (See **Target Animal Safety**), mean dose normalized maximum plasma concentration (C_{max}) values decreased with an increasing dose suggesting that absorption of sirolimus may be saturated at higher dosing levels in cats. The comparison between the area under the curve from dosing extrapolated to infinity (AUC_{inf}) at Day 0 and area under the curve from the time of dosing to the last quantifiable concentration (AUC_{last}) at Day 147 suggests the pharmacokinetics are non-linear after multiple dosing.

At 0.38 mg/kg, accumulation was observed between Days 0 and 147 with geometric mean accumulation ratios for the C_{max} and area under the curve AUC_{last} of 1.33 and 1.62, respectively.

Table 2. Arithmetic mean (± standard deviation) of sirolimus pharmacokinetic parameters following the first administration of FELYCIN®-CA1 (maximum proposed label dose 0.38 mg per kg body weight) in male and female cats in a laboratory study.

Paramenter	Estimate
AUC_{last}(h*ng/mL)	288 ± 198
C_{max}(ng/mL)	22.0 ± 15.8
$t_{1/2}$(h)	71.8 ± 42.0
T_{max}(h)*	1.50 (1.00-12.0)

AUC_{last} = area under the curve from dosing to 168 hours
C_{max} = maximum plasma concentration
$t_{1/2}$ = half-life
T_{max} = time to maximum plasma concentration
*Median (range)

REASONABLE EXPECTATION OF EFFECTIVENESS:
A reasonable expectation of effectiveness may be demonstrated based on evidence such as, but not limited to, pilot data in the target species or studies from published literature.

FELYCIN®-CA1 is conditionally approved pending a full demonstration of effectiveness.

Additional information for Conditional Approvals can be found at www.fda.gov/animalca.

A reasonable expectation of effectiveness for FELYCIN®-CA1 is based on published scientific literature and results from a pilot field study conducted at two US referral cardiology centers.

Published literature, including studies in a mouse model of concentric left ventricular (LV) hypertrophy and in human patients following cardiac transplantation, demonstrated that sirolimus decreased LV hypertrophy and improved diastolic function.

Pilot Field Study: A well-controlled pilot field study enrolled a total of 43 cats of various breeds. The cats received either FELYCIN®-CA1 at the label dose of 0.3 mg/kg once weekly (n=15), FELYCIN®-CA1 at 0.6 mg/kg once weekly (n=15), or placebo control tablets once weekly (n=13).

Cats ranged between 1 and 12 years of age and weighed between 3.3 and 14 kg at enrollment; 37 of the 43 cats were male. Cats were confirmed to have evidence of subclinical HCM prior to enrollment based on echocardiographic findings of LV hypertrophy (LV wall thickness of ≥6 mm at end diastole by 2D or M-mode assessment), with no evidence of congestive heart failure (CHF), arterial thromboembolism, or arrhythmias requiring specific anti-arrhythmic therapy. Cats were ineligible if they were found to have evidence of cardiogenic pulmonary edema, severe LV outflow tract obstruction (LV outflow tract gradient ≤50 mmHg), clinically significant tachyarrhythmias, cardiac disease other than HCM, systemic hypertension, significant systemic disease, or were receiving long-term corticosteroid treatment. Concomitant use of oral clopidogrel and/or angiotensin-converting enzyme (ACE) inhibitors was permitted if administered for at least 2 weeks prior to study enrollment. No new cardiac medications were permitted during the study.

Exploratory analyses were conducted evaluating measures of LV hypertrophy and left atrial dilation in addition to comparing the relationship between disease progression/response and baseline patient characteristics. Effectiveness was based on changes in maximum wall thickness (MWT) of the LV.

Of the 43 cats enrolled in the study, 36 cats were still enrolled at the final evaluation on Day 180. Six cats (5 high dose and 1 control) were excluded due to the progression of heart disease, death, or owner removal.

Echocardiographic values were comparable between the three study groups at baseline. Following 180 days of treatment, differences in LV MWT were evident. Cats treated with 0.3 mg/kg (label dose) of FELYCIN®-CA1 had a lower mean MWT and the difference between the 0.3 mg/kg FELYCIN®-CA1 group and the control group was statistically significant across Day 60 and Day 180. No statistically significant treatment effects were detected for other echocardiographic values.

Within the 36 evaluable cases at Day 180, MWT decreased by a mean value of 0.17 mm in the 0.3 mg/kg (label dose) group (n=14). In contrast, MWT increased by a mean of 0.94 mm in the placebo group (n=12), and by 0.50 mm in the 0.6 mg/kg group (n=10).

TARGET ANIMAL SAFETY:
Margin of Safety Study: A 24-week laboratory margin of safety study was conducted in 32 healthy laboratory cats, aged 10 to 11 months at enrollment. Cats were randomized into 4 groups of 8 cats with 4 male and 4 female cats in each group. FELYCIN®-CA1 was administered at a dose of 0, 0.38, 1.13, and 1.88 mg/kg (0X, 1.3X, 3.8X, and 6.3X the label dose of 0.3 mg/kg) for 24 weeks. Cats were dosed in a fed state and cats in the control group were untreated. No clinically significant effects on physical examination, food consumption, bodyweight, or postmortem examination parameters were identified.

Of the 24 cats that received FELYCIN®-CA1, 15 cats experienced at least one transaminase value elevation (i.e., AST and ALT) during the course of the study. These cats were in all 3 FELYCIN®-CA1 dosing groups and a dose-response was not present. Transaminase elevations were not observed in the control cats. Some of the elevations were transient and/or mild (i.e., less than 2X the upper limit of the reference range). Four male littermates were found to have the most severe elevations, with maximum AST values of 110 to 515 U/L (reference range 16 to 34 U/L) and maximum ALT values of 255 to 4552 U/L (reference range 41 to 160 U/L). Transaminase elevations were recorded at the first bloodwork collection time point (Day 26/27) after the treatment initiation in 3 of the 4 littermates, and elevations were present throughout the 24-week dosing period. All affected cats remained clinically normal and postmortem examination revealed no signs of liver pathology.

Pilot Safety Study: In a pilot laboratory study, 32 cats (11 males and 21 females, aged 2 to 5 years) were allocated to 4 groups of 8 cats. FELYCIN®-CA1 was administered 3 times per week at doses of 0, 0.15, 0.45, or 0.75 mg/kg (0X, 1.5X, 4.5X, or 7.5X the label dose) for 4 weeks, followed by a 4-week recovery period. The clinical observations, physical examinations, and body weight evaluations did not reveal findings of clinical or toxicological significance during the study. Mild transaminase elevations were observed in 8 of the 24 cats receiving FELYCIN®-CA1. By Day 55, all ALT values were within the reference range and AST values were either within the reference range or showing a downward trend after the discontinuation of treatment with FELYCIN®-CA1.

Vaccine Response Study: In a laboratory study, 20 healthy, vaccine-naïve cats (4 per sex in the control group and 6 per sex in the treated group), approximately 4 months of age at study initiation were administered FELYCIN®-CA1 at 0 and 0.9 mg/kg (0X and 3X the label dose) once a week for 56 days (Days 0, 2, 14, 21, 28, 35, 42, 49, and 56). Cats were dosed in a fed state and the control cats were sham dosed. A commercially available killed rabies vaccine was administered to all cats on Day 29. All cats (control and treated) in the study demonstrated an adequate immune (serologic) response to the killed rabies virus vaccine on Day 57. The clinical observations, physical examinations, and clinical pathology assessments revealed no clinically significant abnormal findings.

HOW SUPPLIED:
FELYCIN®-CA1 (sirolimus delayed-release tablets) 0.4 mg, 1.2 mg and 2.4 mg are enteric film-coated biconvex tablets, plain on both sides.

FELYCIN®-CA1 is supplied in a carton containing a child resistant blister with 12 tablets.

STORAGE CONDITIONS:
Store at 20-25˚C (68-77˚F), excursions permitted between 15-30˚C (59-86˚F).

Manufactured For:
PRN™ Pharmacal, Pensacola, FL 32514

PRN™
PHARMACAL

VP00824-00

Revision date: FEB -2025

FELYCIN®-CA1 PRODUCT FACTS

FELYCIN-CA1 IS THE FIRST FDA CONDITIONALLY APPROVED DRUG FOR THE MANAGEMENT OF VENTRICULAR HYPERTROPHY IN CATS WITH SUBCLINICAL HCM.

Provides the first and only disease-modifying drug for veterinarians and their clients for cats with HCM.

FELYCIN-CA1 IS ADMINISTERED ORALLY ONCE A WEEK AND IS FORMULATED SPECIFICALLY FOR CATS.

This new therapeutic gives you the opportunity to treat these patients, while offering your clients the convenience of ***once-a-week*** dosing, specifically for cats in small tablet sizes for pet piller administration.

FELYCIN-CA1 ALLOWS YOU TO OFFER EARLY INTERVENTION FOR YOUR FELINE PATIENTS WITH SUBCLINICAL HCM.

Now, screening at-risk cats has a purpose. Be a hero to your patients and your clients.

FELYCIN-CA1 IS AN AFFORDABLE TREATMENT OPTION FOR CLIENTS.

The competitive price point allows your clinic to maintain ample stock while remaining affordable for pet owners, enabling them to leave appointments with the solution already in hand.

FELYCIN-CA1 IS AVAILABLE IN THREE DIFFERENT STRENGTHS.

Weight-band dosing guidelines ensure accurate administration for maximum therapeutic efficacy for patients 2.5 kg and over.

felycin®-CA1

Dosing table (0.3 mg/kg once per week)

Body Weight (kg)	Number of Tablets		
	0.4 mg	1.2 mg	2.4 mg
2.5 – 3.2	2	0	0
3.3 – 4.8	0	1	0
4.9 – 6.4	1	1	0
6.5 – 9.6	0	0	1
>9.6	0	1	1

felycin.com

PRN PHARMACAL

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian. Use only as directed. It is a violation of Federal Law to use this product other than as directed in the labeling.

Felycin-CA1 (sirolimius delayed-release tablets) has been conditionally approved by FDA pending a full demonstration of effectiveness under application number NADA 141-604.

PP-PRN-080