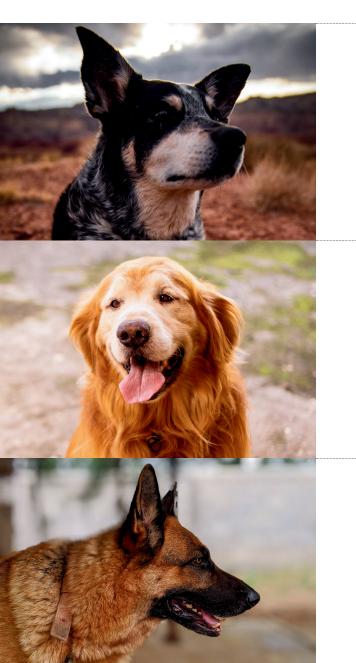
A novel treatment option for canine lymphoma



Patient Status:

Declined Referral

Sadie 12 year old Spayed Female Aussie / Lab mix

- Chief Complaint: Rapid onset of symptoms including lethargy and loss of appetite.
- Diagnosis: Diffuse, large, B-cell lymphoma.
- Client Perspective: Concerned that aggressive treatment may further decrease
 quality of life, family opted not to pursue chemotherapy.
- Treatment: LAVERDIA-CA1 prescribed as a single agent treatment.

Patient Status

Waiting for Specialist Appointment

Scout 10 year old Neutered Male Golden Retriever

- Chief Complaint: Owner noticed "swelling" in neck, otherwise happy and healthy.
- Diagnosis: Peripheral T-cell lymphoma.
- Client Perspective: Immediately confident about pursuing chemotherapy, client learns there's a 3-week wait to see a specialist.
- Treatment: Consulting with specialist, you prescribe LAVERDIA-CA1 to help slow lymphoma progression.

Patient Status:

Stopped Chemotherapy

Pepper 9 year old Neutered Male German Shepherd

- Chief Complaint: Patient completed CHOP 8 months ago, client recognized enlarged lymph node.
- Diagnosis: Relapse, diffuse, large, T-cell lymphoma.
- Client Perspective: Client can't manage another round of chemotherapy, concerned about quality of life and cost.
- Treatment: LAVERDIA-CA1 offers another treatment option, with the convenience of at-home administration.

What does Conditional Approval Mean?

For a veterinary drug to receive conditional approval, it must be shown to be safe when used according to the label. It must also demonstrate a "reasonable expectation of effectiveness," but has not yet proven that it meets the "substantial evidence" standard of effectiveness for full approval. While a drug is conditionally approved it is not to be used for any off-label species or indications.

First-in-class SINE technology



Targeted

Kills cancer cells at the nuclear core, generally sparing healthy ones¹





Convenient

Twice weekly at-home oral administration





Affordable

Priced to expand your options and treat more patients



For technical questions contact **Dechra Veterinary Technical Support** at (866)-933-2472

IMPORTANT SAFETY INFORMATION

For use in dogs only. LaverdiaTM-CA1 (verdinexor tablets) is conditionally approved for the treatment of lymphoma in dogs. NOT FOR USE IN HUMANS. KEEP THIS AND ALL MEDICATIONS OUT OF THE REACH OF CHILDREN. CHILDREN SHOULD NOT COME INTO CONTACT WITH LAVERDIA-CA1. Pregnant women, women who may become pregnant, nursing women and children should not handle or administer Laverdia-CA1 or come into contact with the feces, urine, saliva, or vomit of treated dogs for 3 days following treatment. Laverdia-CA1 can affect male fertility based on animal studies and studies in humans. Wear protective disposable chemotherapy resistant gloves when handling Laverdia-CA1 to avoid direct exposure to moistened, broken or crushed tablets or biological waste from the treated dog (feces, urine, saliva, or vomit). Do not use in dogs that are pregnant, lactating or intended for breeding. Laverdia-CA1 is a possible teratogen and can affect female and male fertility. Dogs should be frequently monitored for hematologic and serum chemistry abnormalities. The most commonly reported adverse reactions in dogs include anorexia, weight loss, vomiting, diarrhea, lethargy, polyuria, polydipsia, elevated liver enzymes and thrombocytopenia. Please see package insert or visit dechra-us.com for full prescribing information.

CAUTION: Federal (USA) 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.

1. Etchin J, Sun Q, Kentsis A, Farmer A, Zhang ZC, et al. (2013) Antileukemic activity of nuclear export inhibitors that spare normal hematopoietic cells. Leukemia 27: 66–74.

*Conditionally approved by FDA pending a full demonstration of effectiveness under application number 141-526 14SD-LAV22011-0322



LAVERDIA CA1

(verdinexor tablets)

Conditionally approved by FDA pending a full demonstration of effectiveness under application number 141-526

The Power To Treat Lymphoma,







Phone - 800.233.0210

www.pennvet.com

Lymphoma Cells Overproduce XPO1

XPO1 enables cancer cells to grow uncontrolled by exporting TSPs out of the cell nucleus



Cytoplasm

Nucleus

Exportin 1 (XPO1)

p27 among others.

Verdinexor

XPO1 is the sole nuclear exporter of several

regulatory proteins, including p53, Rb1, and

major tumor suppressor and growth

Binds to XPO1 and selectively inhibits

nuclear export of TSPs. This binding

functionally inactivates XPO1 and targets

the protein for proteasome degradation,

resulting in restoration of TSP cellular

localization and function. The binding is

low toxicity for healthy cells.

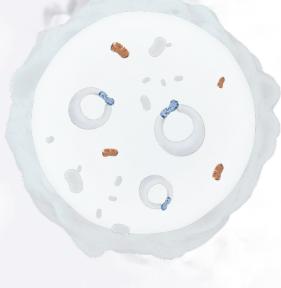
TSPs act inside the cell nucleus

to suppress tumor growth.

slowly reversible, contributing to relatively



XPO1 inhibition results in nuclear retention and reactivation of TSPs, leading to selective induction of apoptosis of lymphoma cells





Healthy cells are generally spared in this process while TSPs accumulate in lymphoma cells and cause apoptosis



LAVERDIA CA1 (verdinexor tablets)

Conditionally approved by FDA pending a full demonstration of effectiveness under application number 141-526

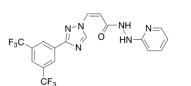
2.5 mg · 10 mg · 50 mg

Coated Tablets Antineoplastic For oral use in dogs only

CAUTION: Federal (USA) law restricts this drug to Dosing Restrictions. use by or on the order of a licensed veterinaria law to use this product other than as directed dosed or undergo dose adjustments. in the labeling.

blocks chromosome region maintenance 1 (CRM1). the same.

LAVERDIA-CA1 has the following structural formula:



Chemical Formula: C10H12F6N6O

Molecular Weight: 442.33

treatment of lymphoma in dogs.

INDICATION: LAVERDIA-CA1 is indicated for the

DOSAGE AND ADMINISTRATION: Always provide the Client Information Sheet to the dog owner with each prescription.

1. Feed the dog immediately before giving **Tumor Suppressor Protein (TSP)** LAVERDIA-CA1.

Dosina Instructions:

2. Wear protective disposable chemotherapy resistant gloves when handling LAVERDIA-CA1 (see USER SAFETY WARNINGS).

3. Administer LAVERDIA-CA1 at an initial dose of 1.25 mg/kg administered orally twice per week (e.g., Monday and Thursday or Tuesday and Friday) with at least 72 hours between doses (see Table 1).

4. If tolerated after 2 weeks, increase the dose of LAVERDIA-CA1 to 1.5 mg/kg twice per week with at least 72 hours between doses (see Table 2).

5. Dose reductions of 0.25 mg/kg to a minimum dose of 1 mg/kg twice per week with at least 72 hours between doses (see Table 3) or dose interruptions may be considered as a result of adverse reactions (See ANIMAL SAFETY WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS).

6. Do not split or crush tablets

Use only as directed. It is a violation of Federal Dogs weighing less than 9 kg may not be accurately

LAVERDIA-CA1 cannot be accurately increased in **DESCRIPTION:** LAVERDIA-CA1 (verdinexor tablets) dose from 1.25 mg/kg to 1.5 mg/kg in dogs weighing is a selective inhibitor of nuclear export (SINE) that 9 to 9.6 kg because the dose administered remains

Dog weight

(kg)

9 — 11.5

11.6 — 13.5

156 - 175

13.6 — 15.5 | 17.5

17.6 — 19.5 22.5

19.6 — 21.5 25

21.6 — 23.5 27.5

23.6 — 25.5 30

256 - 275 325

29.6 — 31.5 | 37.5

336 - 355 425

35.6 — 37.5 | 45

37.6 — 39.5 | 47.5

41.6 — 43.5 52.5

45.6 — 47.5 | 57.5

47.6 — 49.5 60

49.6 — 51.5 62.5

51.6 - 53.5 65

53.6 - 55.5 67.5

55.6 — 57.5 70

57.6 — 59.5 72.5

59.6 — 61.5 75

27.6 — 29.5

31.6 — 33.5

39.6 — 41.5

436 - 455

Table 1. LAVERDIA-CA1 dose table for the 1.25 mg/kg dose*

mg to

12.5

Number of Tablets

2.5 mg | 10 mg | 50 mg

2 1 - ** Use an appropriate combination of to dose dogs over 61.3 kg. - 2 - Table 3. LAVERDIA-CA1 dose table for the 1 mg/kg dose***	for		
- 2 - Table 3. LAVERDIA-CA1 dose table f			
- Idbic o. EAVENDIA OAT dosc table t			
the 1 mg/kg dece***	lata		
1 2 - the ring/kg dose	lata		
2 2 - Number of Table	Number of Tablets		
3 2 - Total			
Dog weight mg to 2.5 mg 10 mg 5	50 mg ablets		
1 3 - 3 - 10 10			
2 3 - 10 144 105	-		
3 3 - 145 160 15			
14.5 10.5 10 2 1	-		
105 010 00	-		
1 4 - 2	-		
2 4 - 22 - 24.4 22.5 1 2	-		
3 4 - 24.5 - 26.9 25 2 2	-		
1 27 - 29.4 27.5 3 2	-		
29.5 — 31.9 30 - 3	-		
32 - 34.4 32.5 1 3	-		
34.5 - 36.9 35 2 3	-		
37 — 39.4 37.5 3 3	-		
39.5 – 41.9 40 - 4	-		
1 1 1 42 - 44.4 42.5 1 4	-		
2 1 1 44.5 – 46.9 45 2 4	-		
3 1 1 47 - 49.4 47.5 3 4	-		
- 2 1 49.5 - 51.9 50	1		
1 2 1 52 - 54.4 52.5 1 -	1		
2 2 1 54.5 - 56.9 55 2 -	1		
ombination of tablets 57 – 59.4 57.5 3 -	1		
kg. 59.5 - 61.9 60 - 1	1		

^{*} Use an appropriate co to dose doas over 61.5 kg

*** Use an appropriate combination of tablets

• Remove contact lenses to dose doas over 61.9 kg.

CONTRAINDICATIONS:

Do not use in dogs that are pregnant, lactating or intended for breeding, LAVERDIA-CA1 is a possible teratogen and can affect female and male fertility. Laboratory studies in the rat have shown reduced fertility, embryotoxicity, teratogenicity, and maternal toxicity. Administration of LAVERDIA-CA1 caused degeneration/atrophy and vacuolation in the seminiferous tubules and oligospermia in the enididymides in male dogs in the margin of safety study (see TARGET ANIMAL SAFETY).

Table 2. LAVERDIA-CA1 dose table for

Total

11.4 — 12.9 | 17.5 | 3 | 1 |

16.4 — 17.9 | 25 | 2 | 2 |

30

18 — 19.6 | 27.5 | 3 | 2 | -

21.4 — 22.9 | 32.5 | 1 | 3 | -

23 – 24.6 | 35 | 2 | 3

24.7 — 26.3 | 37.5 | 3 | 3

26.4 — 27.9 | 40 | - | 4

28 — 29.6 | 42.5 | 1 | 4 | -

29.7 — 31.3 | 45 | 2 | 4 | -

31.4 – 32.9 | 47.5 | 3 | 4 | -

33 — 34.6 50 - - 1

41.4 - 42.9 | 62.5 | 1 | 1 | 1

43 — 44.6 | 65 | 2 | 1 | 1

44.7 — 46.3 | 67.5 | 3 | 1 | 1

48 – 49.6 72.5 1 2 1

51.4 - 52.9 77.5 3 2 1

54.7 — 56.3 | 82.5 | 1 | 3 | 1

59.7 — 61.3 | 90 | - | 4 | 1

80

75 | 2 | 2 | 1

85 2 3 1

- 3 1

34.7 — 36.3 | 52.5 | 1 | -

36.4 — 37.9 | 55 | 2

38 — 39.6 57.5 3

39.7 — 41.3 | 60 |

46.4 — 47.9

49.7 — 51.3

53 - 54 6

56.4 - 57.9

58 — 59.6 | 87.5 |

20

mg to

Number of Tablets

2.5 mg | 10 mg | 50 mg

tablets tablets tablets

- 2

the 1.5 mg/kg dose*

9.7 - 11.3

13 — 14.6

19.7 — 21.3

14.7 — 16.3 22.5

USER SAFETY WARNINGS

NOT FOR USE IN HUMANS KEEP THIS AND ALL MEDICATIONS OUT OF THE REACH OF CHILDREN, CHILDREN SHOULD NOT COME INTO CONTACT WITH LAVERDIA-CA1. Children should not come in contact with the feces, urine, vomit, or aliva of treated dogs.

Pregnant women, women who may become pregnant, and nursing women should not handle or administer LAVERDIA-CA1 or come in contact with the feces, urine, vomit, or saliva from LAVERDIA-CA1-treated dogs. LAVERDIA-CA1 may cause birth defects and can affect female fertility based on animal studies.

LAVERDIA-CA1 can affect male fertility based on animal studies and studies in humans. Wear protective disposable chemotherapy resistant

gloves when handling LAVERDIA-CA1 to avoid exposure to drug. Wear protective disposable chemotherapy resistant

gloves to prevent direct contact with moistened. broken or crushed LAVERDIA-CA1 tablets

Wear protective disposable chemotherapy resistant gloves to prevent contact with feces, urine, vomit, and saliva during treatment and for 3 days after the dog has received the last treatment. Place all waste material in a plastic bag and seal before general disposal. Wash hands immediately and thoroughly with soap and water if contact occurs with the feces, urine, vomit, or saliva om LAVERDIA-CA1 treated dogs.

Any items that come in contact with feces, urine vomit, or saliva should not be washed with other laundry during treatment and for 3 days after the last treatment with LAVERDIA-CA1.

Wear protective disposable chemotherapy resistant gloves when handling the dog's toys, food bowl, and water bowl. Wash food and water bowls separately rom other items during treatment and for 3 days

after the dog has received the last treatment.

If LAVERDIA-CA1 is accidentally ingested, or if 2.5 mg 10 mg 50 mg there is significant contact with feces, urine, vomit. or saliva of dogs during treatment or within 3 days after the last treatment without proper precautions. seek medical advice immediately. It is important to show the treating physician a copy of the package insert, label, or client information sheet.

> Special instructions for handling and administering the product

• It is recommended that LAVERDIA-CA1 be administered under the supervision of, or in consultation with, a veterinarian experienced in the use of cancer therapeutic agents.

. Use standard measures for the safe handling of all chemotherapeutic drugs. Refer to Occupational Safety and Health Administration (OSHA) for appropriate guidelines, recommendations, and egulations for handling antineoplastic agents.

· Do not eat, drink, or smoke while handling the • Do not store near food, in or near a food preparation

area, or with medications intended for use in humans.

 In case of contact with the skin, wash the affected area immediately and thoroughly with soap and water.

Accidental eye exposure Rinse the eves with large amounts of tap wate

(use eyewash station if present) for 10 minutes while olding back the eyelid

package insert or label to the physician.

Accidental oral exposure or ingestion

· Seek medical advice immediately and show the hypoalbuminemia, prolonged prothrombin time Neurologic: seizure, tremor, disorientation

· Ocular: corneal opacity

Protein losing nephropathy

CONTACT INFORMATION:

www.fda.gov/reportanimalae

INFORMATION FOR DOG OWNERS:

Always provide the Client Information Sheet with each

accidental human exposure to LAVERDIA-CA1.

quantifiable plasma concentration (AUClast) and

as assessed by dose normalized AUClast and

evaluation days.

both evaluation days. The increase in exposure gastrointestinal motility modifiers, and opioids

· Skin: bruising, erythema, alopecia

· Other: nasal discharge, epistaxis, lymphadenitis

package insert or label to the physician.

ANIMAL SAFETY WARNINGS

LAVERDIA-CA1 can cause severe anorexia. Patients should be carefully monitored for inappetence vomiting, diarrhea and dehydration, and supportive ADVERSE REACTIONS). In the study used to 2) was observed in verdinexor treated dogs in pharmacokinetic differences or trends observed. support reasonable expectation of effectiveness, low the study supporting reasonable expectation of doses of corticosteroids (prednisone) were found to effectiveness. Two dogs with thrombocytopenia Following oral administration of a preliminary

adverse reactions associated with verdinexor.

accidental ingestion or overdose.

PRECAUTIONS:

in dogs with concurrent serious infections; concurrent nephropathy (PLN). Two additional dogs, though not (1.1-2.5 hours). renal, cardiovascular, or hepatic disease; in dogs reported, may have had a PLN. One dog was reported

LAVERDIA-CA1 can cause hematologic and serum day 7 which persisted (and worsened) to the end of chemistry abnormalities. Dogs should be frequently the study (study day 105). At the start of the study Additional information for Conditional Approvals to moderate vacuolation, and minimal Leydig cell chemistry abnormalities when initiating and maintaining the dog had hypoalbuminemia. treatment with LAVERDIA-CA1 (see ADVERSE REACTIONS and TARGET ANIMAL SAFETY).

has not been evaluated in conjunction with other Sheet (SDS) contact Dechra Veterinary Products at chemotherapeutic agents or other treatment (866) 933-2472. modalities for lymphoma

The effect of concomitant medications on the experience reporting for animal drugs, contact FDA metabolism of LAVERDIA-CA1 has not been evaluated. at 1-888-FDA-VETS or at

The safe use of LAVERDIA-CA1 has not been evaluated in dogs younger than 7 months of age.

administration of LAVERDIA-CA1 with drugs veterinarian, how to handle and administer the product, (mg/kg) and dosing frequency (2 versus 3 times per acetaminophen) should be minimized.

ADVERSE REACTIONS:

In the field study supporting reasonable expectation of effectiveness, 58 dogs were treated with verdinexor (not commercial formulation) at doses CLINICAL PHARMACOLOGY: between 1.0 mg/kg and 1.75 mg/kg administered Mechanism of action 2 to 3 times a week (see REASONABLE Verdinexor is a reversible, selective inhibitor of CRM1-EXPECTATION OF EFFECTIVENESS)

All dogs experienced at least one adverse reaction, also known as XPO1). Verdinexor inhibits the export response rate (best response of partial or complete lymphoma in dogs (v1.0)—a veterinary cooperative The most common adverse reactions across all of Tumor Suppressor Proteins (TSP) and Growth response) for all dogs was 34.5% (20/58), distributed oncology group (VCOG) consensus document. Vet dose groups included; anorexia, vomiting, diarrhea. Regulatory Proteins (GRP) from the nucleus where proportionately between the naïve (12/35, 34.3%) Compar Onco, 2010, Vol.8(1), p.28-37. weight loss and lethargy. Most adverse reactions were they carry out their normal functions; it is selectively and first relapse (8/23, 34.8%) subgroups. Among considered Veterinary Cooperative Oncology Group cytotoxic for cells with genomic damage (i.e. for dogs with objective response, the median duration LAVERDIA is a trademark of Dechra Limited. Dechra common terminology criteria for adverse events tumor cells). (VCOG-CTCAE)1 Grade 1 (mild) or 2 (moderate). Pharmacokinetics Twenty-one dogs experienced a VCOG-CTCAE Verdinexor administered orally is well absorbed were noted when comparing dose groups. A subset Manufactured by: Grade 3 (severe), 4 (life-threatening), or 5 (death) in dogs and achieves therapeutic levels (>0.5 (n=17, 29%) of the overall enrolled population had a Halo Pharmaceutical, Inc. adverse reaction.

Of the 58 dogs treated with verdinexor, adverse of verdinexor three times per week for 13 weeks had T-cell lymphoma and 12 had B-cell lymphoma reactions occurring in ≥10% of dogs associated with to fed healthy young adult Beagle dogs, overall Three dogs, 2 dogs with T-cell lymphoma (1 naïve <u>Distributed by:</u> verdinexor treatment included:

- · General: lethargy, fever, weakness, generalized · Gastrointestinal: anorexia, vomiting, diarrhea
- Renal: polyuria, polydipsia, hematuria, proteinuria, low urine specific gravity, urinary tract infection
- Hepatic: elevated liver enzymes, bilirubinuria
- Cardiorespiratory: cough/dyspnea
- Metabolic: weight loss

• Hematologic: thrombocytopenia, anemia, dose normalized Cmax was approximately dose TARGET ANIMAL SAFETY: lymphopenia, neutrophilia, leukopenia, eosinopenia, proportional from 1.25 mg/kg to 1.5 mg/kg and In a 13-week margin of safety study, 32 healthy number 141-526 neutropenia, monocytosis, leukocytosis, prolonged less than dose proportional from 1.5 mg/kg to Beagle dogs (4/sex/group), approximately 7 partial thromboplastin time, elevated blood urea 1.75 mg/kg in males on both evaluation days. In months old at study initiation, were administered nitrogen, hypercalcemia, hyperphosphatemia

• Skin: subcutaneous edema/swelling, pyoderma greater than dose proportional from 1.25 mg/kg of body weight 3 times a week (Monday, Wednesday, 1894-02

Adverse reactions occurring in <10% of dogs exposure from 1.5 mg/kg to 1.75 mg/kg on both dosed. Dogs were fed prior to dosing. All dogs

associated with verdinexor treatment included: · Renal: protein losing nephropathy, urinary incontinence

 Seek medical advice immediately and show the
 Hepatic: hepatomegaly, elevated bilirubin, icterus
 Time to maximum plasma concentration (Tmax)
 Dose-dependent LAVERDIA-CA1-related clinical • Cardiorespiratory: heart murmur, arrhythmia, heart was typically reached between 1.1 and 2.5 hours findings included vomiting, inappetence, decreased • Hematologic: hypoglubulinemia, hypoproteinemia,

post-dose under fed conditions and there were body condition, decreased body weight, loss of skin no differences in Tmax related to sex, dosage, or elasticity, lacrimation, slight depression, and slight evaluation day. In general, the terminal elimination decrease of forelimb strength. Non-dose-dependent half-life for all dose groups was similar, regardless LAVERDIA-CA1-related findings included abnormal

approximately 2.0 to 4.0 hours. Inter-animal variability was relatively high in all Dogs in the 1.0 mg/kg group and dogs in the 1.5 and

of sex, dosage, or evaluation day and ranged from feces (soft, watery, or mucoid feces), excessive

shedding, and sparse hair.

LAVERDIA-CA1 treated dogs included lower testes,

thymus, and thyroid/parathyroid gland weights

the testes and epididymides (moderate to marked

seminiferous tubules degeneration/atrophy, minimal

germ cell debris in the epididymides) and in the

thymus (minimal to mild cortical lymphoid depletion)

LAVERDIA-CA1 is presented as immediate release

coated tablets in three dosage strengths, 2.5 mg, 10

dose groups (%CV ranging from 16% to 81% for 1.75 mg/kg groups had lower body weight values, care should be provided as clinically indicated (see Thrombocytopenia (VCOG-CTCAE Grade 1 and AUClast), so care should be taken in assessing actual starting on study days 28 and 21 respectively, that continued to the end of the study compared to

reduce the incidence of anorexia and gastrointestinal during the study were reported with bruising and formulation of verdinexor to fed and fasted Dose-dependent LAVERDIA-CA1-related clinical one dog with thrombocytopenia was reported with dogs, there was a significant food effect on the pathology findings included decreases in chloride epistaxis. In human studies of a closely related pharmacokinetics of verdinexor with a 3-fold and and increases in fibrinogen. Non-dose-dependent Keep LAVERDIA-CA1 in a secure location out of compound, idiosyncratic reductions in platelets 5-fold increase in AUC and Cmax, respectively, LAVERDIA-CA1-related clinical pathology findings reach of dogs, cats, and other animals to prevent (severe or medically significant but not immediately when verdinexor was administered orally in the included decreases in lymphocytes, eosinophilis, life-threatening in 10-20% of patients) were reported. presence of food. Time to reach Cmax (Tmax) was and monocytes, and increases in albumin and markedly more variable (1-18 hours) when dogs were blood urea nitrogen. dosed under fasted conditions as compared to when Safe use of LAVERDIA-CA1 has not been evaluated One dog was reported with a protein losing verdinexor was administered under fed conditions Dose-dependent organ weight findings in the

with diabetes mellitus; in dogs with clinically relevant with hypoalbuminemia and proteinuria on study day REASONABLE EXPECTATION OF EFFECTIVENESS: Dose-dependent histopathological findings in the hypercalcemia; or in dogs with concurrent malignancy. 21 which progressed until study end (study day 194). LAVERDIA-CA1 is conditionally approved pending LAVERDIA-CA1 treated dogs included lesions in Another dog was reported with proteinuria at study a full demonstration of effectiveness.

monitored for evidence of hematologic and serum the dog had hyperalbuminemia; by study day 105 can be found by searching https://www.fda.gov for hypertrophy in the testes; and severe oligospermia/ "animal conditional approval".

A field study was used to demonstrate a reasonable To report suspected adverse events, for technical expectation of effectiveness for LAVERDIA-CA1 for HOW SUPPLIED: The safety and effectiveness of LAVERDIA-CA1 assistance, or to obtain a copy of the Safety Data the treatment of lymphoma in dogs.

lymphoma in dogs (v1.0).2

survived to study termination.

clinically significant differences in treatment benefit

mg and 50 mg. The 2.5 mg tablets are supplied in An open-label, single arm, multicenter field study was conducted to evaluate the effectiveness and safety 10-count and 50-count, the 10 mg tablets are supplied For additional information about adverse drug of verdinexor tablets (not commercial formulation). in 10-count and 50-count, and the 50 mg tablets are The study enrolled 58 client-owned dogs with supplied in 16-count and 50-count in an HDPE bottle lymphoma either newly diagnosed (n=35), or in first with a heat sealed, child-resistant cap and a desiccant relapse following completion of one chemotherapy included in each bottle. The bottles are individually regimen (n=23). Treatment groups were designated by packaged into cartons. the following verdinexor dose regimens: 1.5 mg/kg 3 times weekly: 1.25 mg/kg 3 times weekly: or 1.25 DISPOSA The primary metabolism of LAVERDIA-CA1 in prescription and review it with the dog owner or person mg/kg 2 times weekly then increased to 1.5 mg/kg Dispose of any unused product or waste materials vitro and in vivo is thought to be inactivation responsible for care of the dog. Advise dog owners twice weekly if well-tolerated. Dose increases and in accordance with proper procedures for by glutathione (GSH) conjugation. Therefore, about possible adverse reactions, when to contact a decreases, including changes in dosing amount cytotoxic drugs. which undergo substantial GSH conjugation (e.g., and how to clean up any feces, urine, vomit, or saliva week) were allowed based on drug tolerability and STORAGE INFORMATION

from dogs treated with LAVERDIA-CA1 (verdinexor response to treatment. Response to treatment was Store the bottles at controlled room temperature 20° tablets). The Client Information Sheet also contains evaluated using Veterinary Cooperative Oncology to 25°C (68° - 77°F).

warnings for humans and what to do in case of Group (VCOG) response criteria for periphera 1. Veterinary co-operative oncology group - common For all dogs enrolled, median time to progression terminology criteria for adverse events (VCOG-(TTP) was 29.5 days (range 7-244 days). The CTCAE) following chemotherapy or biological

median TTP for the naïve and first relapse cases antineoplastic therapy in dogs and cats v1.1. Vet mediated nuclear export (SINE) that specifically was 36.5 days (range 7-244 days) and 22 days. Compar Onco. 2016. Vol.14(4), p.417-446. blocks Chromosome Region Maintenance 1 (CRM1, (range 7-194 days), respectively. The objective 2. Response evaluation criteria for peripheral nodal

of response was 18 days (range 7-187 days). No is a registered trademark of Dechra Limited to 1.0 µM) with doses of 1 to 3 mg/kg. Following TTP of at least 56 days. Of these 17 dogs, 11 were (d/b/a Cambrex Whippany)

oral administration of a preliminary formulation naïve to treatment and 6 had relapsed lymphoma; 5 Whippany, NJ USA

mean exposure in terms of area under the plasma and 1 relapsed) and 1 dog with B-cell lymphoma Dechra Veterinary Products concentration time curve from time zero to the last naïve to treatment had TTP of 182 days or longer. 7015 College Boulevard, Suite 525 Overland Park, KS 66211 maximum plasma concentration (Cmax) showed an During the study, verdinexor was administered (866) 933-2472

increase from 1.25 mg/kg to 1.5 mg/kg; however, concomitantly with other medications such as exposure at 1.75 mg/kg was either similar or lower corticosteroids (prednisone, 39 dogs), proton pump Product inquiries should be directed to than exposure for the 1.5 mg/kg dose group on inhibitors, antibiotics, H2 blockers, anti-emetics, Dechra Veterinary Products, (866) 933-2472.

> Conditionally approved by FDA pending a full demonstration of effectiveness under application

females, the increase in AUClast and Cmax was LAVERDIA-CA1 at either 0, 1.0, 1.5, or 1.75 mg/kg

to 1.5 mg/kg and there was minimal increase in and Friday). Dogs in the control group were sham- PIN-7001-05

