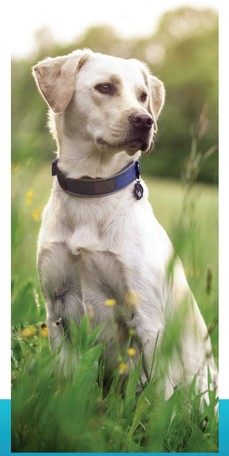
TANOVEA®-CA1
WAS GENERALLY WELL TOLERATED IN CLINICAL STUDIES

In two multi-institutional field studies, 22 dogs with untreated, relapsed or refractory lymphoma received single-agent TANOVEA-CA1 as an intravenous infusion at doses of 0.66 to 1.2 mg/kg administered once every three weeks for one to six doses.

The majority of adverse reactions were Veterinary Cooperative Oncology Group (VCOG)[5] grade 1 or 2.[6]

- Most common adverse reactions included diarrhea, neutropenia, weight loss, hyporexia, and lethargy. Dermatologic changes, such as otitis externa, alopecia, dermatitis, pyoderma, ulcerations, and excoriations have also been observed.
- Less frequent but more serious adverse reactions included grade 3 anorexia/hyporexia, weight loss, vomiting, diarrhea, otitis externa, dehydration, aspiration pneumonia, neutropenia, thrombocytopenia, anemia, hyperbilirubinemia, and hypertriglyceridemia; grade 4 tachypnea and neutropenia; and grade 5 dyspnea (secondary to pulmonary fibrosis).

Most adverse reactions resolved spontaneously, with supportive treatment, dose modification, or dose delay.[6]



Contraindications, Warnings, and Precautions:

Do not use TANOVEA-CA1 in dogs with pulmonary fibrosis or a history of chronic pulmonary disease that could lead to fibrosis, such as chronic bronchitis. Do not use in West Highland White Terriers, and use with caution in other terrier breeds. Do not use in dogs that are pregnant, lactating, or intended for breeding.

TANOVEA-CA1 has been associated with an infrequent, but potentially life-threatening or fatal pulmonary fibrosis, which may be an idiosyncratic toxicity. Monitoring for signs of pulmonary dysfunction and/or radiographic changes consistent with pulmonary fibrosis is recommended.

TANOVEA-CA1 is not for use in humans and should be kept out of the reach of children. Wear chemotherapy-resistant gloves to prevent contact with feces, urine, vomit, and saliva of treated dogs for five days following treatment. TANOVEA-CA1 is cytotoxic and can cause birth defects, and affect female and male fertility. Pregnant and breast-feeding women should not prepare or administer the product.

The safety and effectiveness of TANOVEA-CA1 has not been evaluated in conjunction with other chemotherapeutic agents or other treatments. The effect of concomitant medications on the metabolism of TANOVEA-CA1 has not been evaluated.

Please see the accompanying TANOVEA-CA1 package insert for full prescribing information.

CAUTION: Federal (US) 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.

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TANOVEA®-CA1
DEMONSTRATED A REASONABLE EXPECTATION OF EFFECTIVENESS IN CLINICAL STUDIES

TANOVEA-CA1 can be used in dogs with naïve and relapsed/refractory lymphoma.[3,6]

77% overall response rate (ORR).

100% of naïve dogs and **64%** of relapsed/refractory dogs responded to treatment.

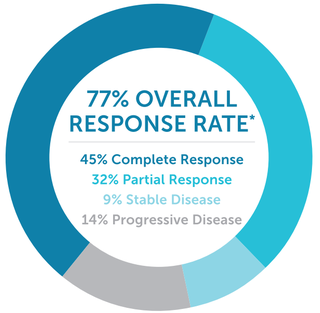
134 day overall median progression free survival time (PFS) in responding dogs.

TANOVEA-CA1 can also be used for re-induction.[3,6]

60% ORR in dogs re-induced with TANOVEA-CA1 upon relapse following their initial TANOVEA-CA1 treatment.

50% of those dogs had a complete response and **10%** had a partial response.

PFS in responding dogs ranged from **43 to 99 days.**



*In two field studies evaluating 65 dogs with lymphoma, 22 dogs received TANOVEA-CA1 once every three weeks; 8 dogs were treatment-naïve and 14 dogs had failed previous therapy.

TANOVEA-CA1 IS CONVENIENT FOR VETERINARIANS AND PET OWNERS

- ☑ One dose every three weeks
- ☑ Only five doses for full treatment
- ☑ Simple, 30-minute intravenous infusion of 1 mg/kg
- ☑ Stepwise dose reductions or dose delays can help manage adverse reactions

TANOVEA®-CA1 (rabacfosadine for injection)

VETDC

REFERENCES: 1. Reiser H, Wang J, Chong L, et al. GS-9219—A novel acyclic nucleotide analogue with potent antineoplastic activity in dogs with spontaneous non-Hodgkin's lymphoma. *Clin Cancer Res* 2008;14:2824–2832. **2.** Kramata P, Downey KM, Paborsky LR. Incorporation and excision of 9-[2-phosphonylmethoxyethyl]guanine (PMEG) by DNA polymerase delta and epsilon in vitro. *J Biol Chem* 1998;273:21966–21971. **3.** Vail DM, Thamm DH, Reiser H, Ray AS, Wolfgang GHI, Watkins WJ, Babusis D, Henne IN, Hawkins MJ, Kurzman ID, Jeraj R, Vanderhoek M, Plaza S. Assessment of GS-9219 in a pet dog model of non-Hodgkin's lymphoma. *Clin Cancer Res* 2009 May 15;15(10):3503–10. **4.** Lawrence J, Vanderhoek M, Barbee D, et al. Use of 3'-deoxy-3'-[18F]fluorothymidine PET/CT for evaluating response to cytotoxic chemotherapy in dogs with non-Hodgkin's lymphoma. *Vet Radiol Ultrasound* 2009;50:660–668. **5.** Veterinary Cooperative Oncology Group – common terminology criteria for adverse events (VCOG-CTCAE) following chemotherapy or biologic antineoplastic therapy in dogs and cats v1.1. *Vet Comp Oncol.* 20 Jul 2011. DOI: 10.1111/j.1476-5829.2011.00283.x. **6.** TANOVEA-CA1 [package insert]. VetDC Inc., May 2019.

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THE FIRST FDA CONDITIONALLY APPROVED DRUG FOR CANINE LYMPHOMA

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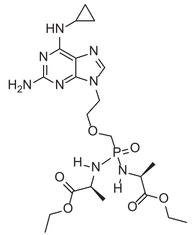
TANOVEA-CA1 is indicated for the treatment of lymphoma in dogs
Conditionally approved by FDA pending a full demonstration of effectiveness under application number 141-475

TANOVEA®-CA1

IS A NOVEL, ANTI-PROLIFERATIVE, SMALL MOLECULE DESIGNED TO TARGET AND KILL LYMPHOMA CELLS



TANOVEA-CA1 is a double prodrug of 9-(2-phosphonylmethoxyethyl) guanine (PMEG), a potent inhibitor of DNA synthesis.

TANOVEA-CA1 is hydrolyzed intracellularly, subsequently deaminated to PMEG and phosphorylated to the active form.[1]

TANOVEA-CA1 inhibits the proliferation of lymphocytes and lymphoma/leukemia cell lines *in vitro* and has demonstrated inhibition of DNA polymerases α, δ and ε, resulting in S phase arrest and induction of apoptosis.[2]

Data from studies in healthy dogs and in dogs with lymphoma demonstrated that administration of TANOVEA-CA1 results in accumulation of PMEG in lymphoid cells, with markedly reduced PMEG concentrations in plasma and non-target organs.[3]

TANOVEA-CA1 inhibits lymphocyte proliferation *in vivo*.

Uptake of the 18F-fluorothymidine tracer via positron emission tomography/computed tomography (PET/CT) following TANOVEA-CA1 treatment.[3,4]

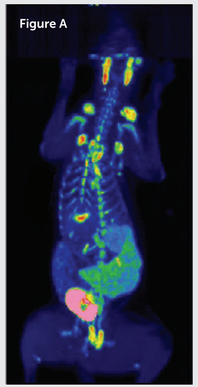


Figure A depicts the tracer present in lymph nodes, bone marrow, bladder, kidneys and spleen of a dog with lymphoma prior to treatment.

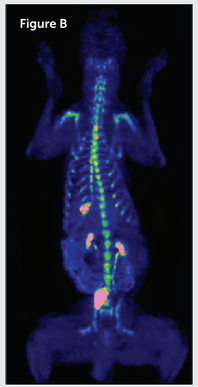


Figure B shows the same dog nine weeks after TANOVEA-CA1 treatment, with markedly reduced tracer uptake in the lymph nodes, which correlated with a complete response in this dog.