# TREAT PARVO
# FIGHT PARVO
# STOP PARVO

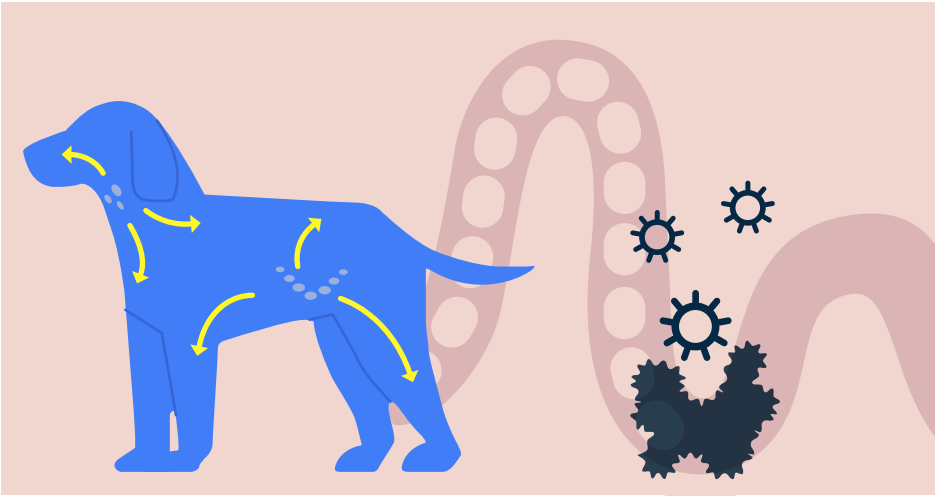
Canine Parvovirus Monoclonal Antibody

**THE FIRST & ONLY MONOCLONAL ANTIBODY**
**treatment that targets canine parvovirus.**

# PARVO KILLS

While canine parvovirus (CPV) vaccinations are highly effective and widely available, CPV is still a real and ever-present threat to all dogs, with unvaccinated and young puppies the most at risk.

## CPV infection can be fast and unpredictable.



CPV initially replicates in oropharyngeal and mesenteric lymph nodes, entering a cell by binding to a viral protein receptor on its surface.[1]

The virus then enters the cell, hijacking its metabolism, and spreads to rapidly dividing cells in the GI tract, bone marrow and lymphoid tissues.[2]

**The effects of the virus are most prominent in the GI tract, causing breakdown of the blood-intestinal barrier.**

- This can lead to GI bleeding, dehydration and hypovolemic shock.
- Viral attack on bone marrow can destroy young immune cells.
- Combined with harmful bacteria entering the bloodstream due to destruction of the intestinal barrier, this can lead to secondary infections and life-threatening sepsis.[2]

## Left untreated, CPV can be deadly for puppies.

Common symptoms include:

- **Lack of appetite**
- **Hemorrhagic diarrhea**
- **Fever or low body temperature**
- **Vomiting**
- **Lethargy**
- **Abdominal pain**

**Traditionally, treatment requires days of labor and worry and long, isolated stays in your clinic. But even then, positive outcomes are hard to predict.**

To effectively treat CPV, there is a need for a targeted solution with a predictable outcome.

# FIGHT PARVO
## with Canine Parvovirus Monoclonal Antibody

Canine Parvovirus Monoclonal Antibody is the first and only USDA-conditionally approved monoclonal antibody (mAb) treatment that targets CPV.

**With just one intravenous dose, Canine Parvovirus Monoclonal Antibody may shorten the course of the disease and improve outcome.**

- Targets parvovirus directly
- Single-dose efficacy
- High safety profile
- Helps decrease burden of supportive care
- Helps reduce emotional stress

Now you can take charge of parvo with a targeted treatment that helps ease the stress of your patients, your clients and your clinic.

**Two components. One powerful product.**


**Canine Parvovirus Monoclonal Antibody is composed of a dog constant region and a rat variable region.**

These two elements work together to neutralize canine parvovirus in vivo by selectively binding and blocking the virus from entering and destroying enterocytes.

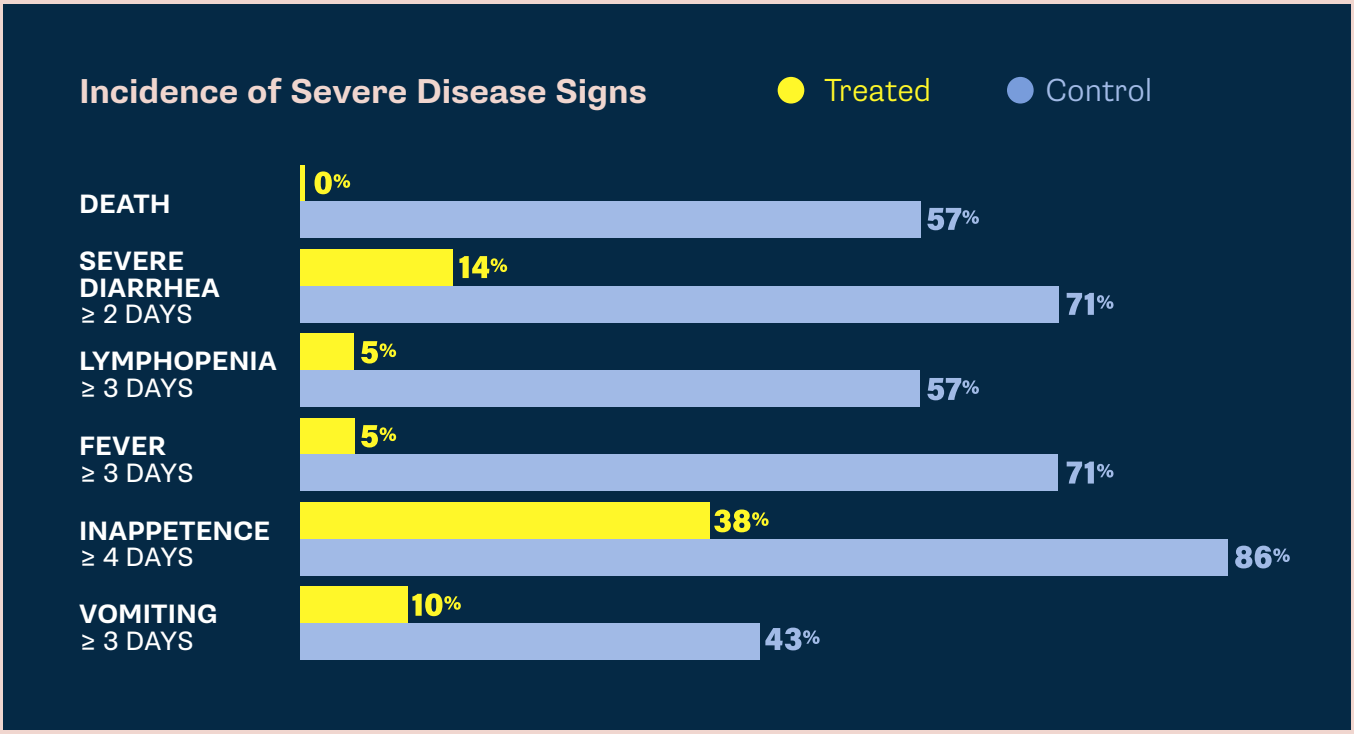
# STOP PARVO
## with targeted efficacy

In a treatment efficacy study, **no dogs treated with Canine Parvovirus Monoclonal Antibody died after challenged with virulent CPV-2b**. The prevented fraction for mortality in treated dogs compared to controls was 1.00 (95% Confidence Interval 0.73, 1.00).[3]

CPMA-treated dogs also had significantly faster times to resolution of:[3]

- **Vomiting**
- **Lethargy**
- **Abnormal attitude**
- **Inappetence**

## After challenged with virulent CPV-2b, **ZERO DOGS DIED** when treated with Canine Parvovirus Monoclonal Antibody[3]

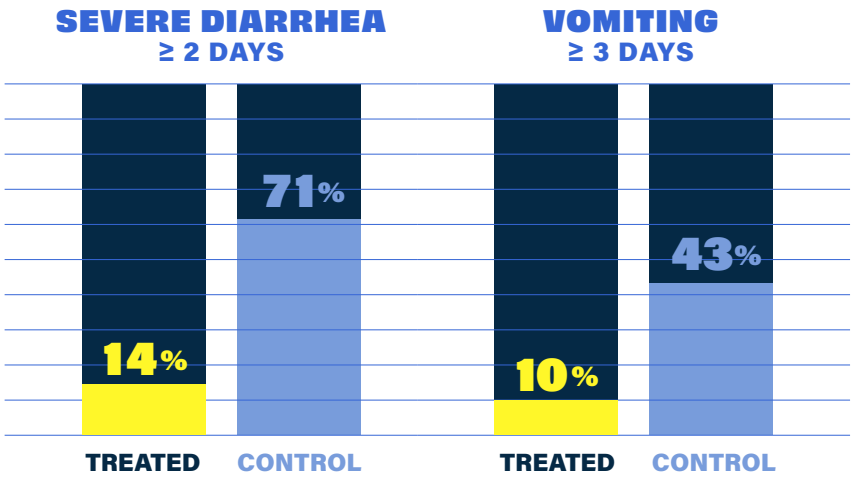


# Canine Parvovirus Monoclonal Antibody helps puppies go home sooner[3]

## Less time. Less worry. In just one dose.

We anticipate Canine Parvovirus Monoclonal Antibody will help greatly decrease the burden of supportive care for CPV.

You may be able to save days of labor and stress associated with managing the symptoms of this potentially deadly disease.




## Expected Outcomes Compared to Traditional Treatment

**Expected outcomes with Canine Parvovirus Monoclonal Antibody treatment:**

- ✔ One intravenous dose
- ✔ Highly effective
- ✔ Faster resolution of clinical signs or severe disease
- ✔ May reduce hospitalization
- ✔ Puppies may feel better faster, go home sooner

**Traditional parvo treatment can consist of:**

- ✘ 24/7 care
- ✘ 3-5 days of hospitalization
- ✘ Emotional stress for staff
- ✘ Risk of cross-contamination
- ✘ Unpredictable outcomes with potentially high pet owner costs

Advantages of

# **Canine Parvovirus Monoclonal Antibody**

vs. current plasma treatment

| | **Canine Parvovirus Monoclonal Antibody** | Hyperimmune Plasma |
|---|---|---|
| USDA Conditionally Approved | ✔ | – |
| Selectively binds and neutralizes canine parvovirus | ✔ | – |
| Proven efficacy in parvoviral enteritis cases | ✔ | – |
| Can simplify and streamline treatment protocol | ✔ | – |
| Stored frozen | ✔ | ✔ |
| Special supplies for administration required | – | ✔ |

Well tolerated in **puppies as young as 6 weeks of age.**[3]

# Storage and administration

Canine Parvovirus Monoclonal Antibody is delivered in unique packaging designed to keep it at ≤ -15° C or ≤ 5° F and should be stored frozen.

This innovative freezer box is environmentally safe and sustainable, containing Enviro Ice™ gel packs – the only eco-friendly ice packs that are 100% drain-safe and easily recyclable into plant food.

**Thaw at room temperature and immediately administer intravenously at a dose of 0.2 ml/ kg (0.2 ml/ 2.2 lb) of the dog's body weight.**


| Dosage Chart | | |
|---|---|---|
| Dog's body weight **Pounds** | Dog's body weight **Kilograms** | Volume to administer |
| 2.2 | 1 | **0.2 mL** |
| 11 | 5 | **1 mL** |
| 22 | 10 | **2 mL** |
| 33 | 15 | **3 mL** |
| 44 | 20 | **4 mL** |
| 55 | 25 | **5 mL** |

**STORE FROZEN**
At ≤ -15° C (≤ 5° F)

**THAW & ADMINISTER**
IV administration

**WELL-TOLERATED**
in healthy puppies as young as 6 weeks of age[3]

Canine Parvovirus Monoclonal Antibody

# PARVO KILLS

## Now you can fight back.

Canine Parvovirus Monoclonal Antibody is the first and only USDA-conditionally approved treatment approved for parvovirus infection.

- One intravenous dose
- Highly effective
- Faster resolution of clinical signs or severe disease
- May reduce hospitalization
- Puppies may feel better faster and go home sooner

**Contact your Elanco sales representative or visit www.FightParvo.com**

[1]Mazzaferro EM. Update on canine parvoviral enteritis. *Vet Clin North Am Small Anim Pract*. 2020 Nov;50(6):1307-25.

[2]Zachary JF. In: Zachary JF, editor. Mechanisms of microbial infections. Pathologic basis of veterinary disease. 6th ed. Elsevier;2017:132-241.

[3]Elanco Animal Health. Data on file.

# STAY AHEAD OF PARVO

## with our comprehensive portfolio

### VACCINATE

with TruCan™ and TruCan™ Ultra lines that offer 1 mL and ½ mL options (and combos) for parvo vaccine needs.

### SUPPLEMENT TREATMENT PROTOCOLS

with Entyce® (capromorelin oral solution) to increase appetite, leading to increased food consumption.

**INDICATION FOR ENTYCE:** For appetite stimulation in dogs.
**IMPORTANT SAFETY INFORMATION FOR ENTYCE:** For use in dogs only. Do not use in dogs that have a hypersensitivity to capromorelin. Use with caution in dogs with hepatic dysfunction or renal insufficiency. The safe use of Entyce has not been evaluated in breeding, pregnant or lactating dogs. The most common adverse reactions included diarrhea, vomiting, elevated blood urea nitrogen, polydipsia, and hypersalivation. Please see attached Entyce product label for full prescribing information.



Elanco

# Entyce™
## (capromorelin oral solution)

**30 mg/mL**

**For oral use in dogs only**

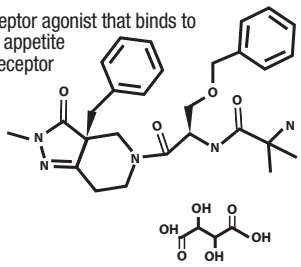
**Appetite Stimulant**

**Caution:**

Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

**Description:**

ENTYCE (capromorelin oral solution) is a selective ghrelin receptor agonist that binds to receptors and affects signaling in the hypothalamus to cause appetite stimulation and binds to the growth hormone secretagogue receptor in the pituitary gland to increase growth hormone secretion. The empirical formula is $C_{28}H_{35}N_5O_4 \cdot C_4H_6O_6$ and the molecular weight 655.70.
The chemical name is 2-amino-N-[2-(3aR-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl)-1R-benzyloxymethyl-2-oxo-ethyl]-isobutyramide L-tartrate.



The chemical structure of capromorelin tartrate is:

**Indication:**

ENTYCE (capromorelin oral solution) is indicated for appetite stimulation in dogs.

**Dosage and Administration:**

Administer ENTYCE orally at a dose of 3 mg/kg (1.4 mg/lb) body weight once daily.

To administer ENTYCE, gently shake the bottle, and then withdraw the appropriate amount of solution using the provided syringe.

Rinse syringe between treatment doses.

The effectiveness of ENTYCE has not been evaluated beyond 4 days of treatment in the clinical field study (See Effectiveness).

**Contraindications:**

ENTYCE should not be used in dogs that have a hypersensitivity to capromorelin.

**Warnings:**

Not for use in humans. Keep this and all medications out of reach of children and pets.

Consult a physician in case of accidental ingestion by humans. **For use in dogs only**

**Precautions:**

Use with caution in dogs with hepatic dysfunction. ENTYCE is metabolized by CYP3A4 and CYP3A5 enzymes (See Clinical Pharmacology).

Use with caution in dogs with renal insufficiency. ENTYCE is excreted approximately 37% in urine and 62% in feces (See Adverse Reactions and Clinical Pharmacology).

The safe use of ENTYCE has not been evaluated in dogs used for breeding or pregnant or lactating bitches.

**Adverse Reactions:**

In a controlled field study, 244 dogs were evaluated for safety when administered either ENTYCE or a vehicle control (solution minus capromorelin) at a dose of 3 mg/kg once daily for 4 days. Enrolled dogs had a reduced or absent appetite for a minimum of 2 days prior to day 0 and had various medical conditions: arthritis (40); gastrointestinal disease (24); allergy (22); dental disease (22); cardiovascular disease (16); renal disease (13); and others. Some dogs may have experienced more than one of the adverse reactions during the study.

The following adverse reactions were observed:

**Table 1: Adverse Reactions reported in dogs administered ENTYCE oral solution compared to vehicle control**

| Adverse Reactions | ENTYCE (n = 171) n (%) | Vehicle Control (n = 73) n (%) |
|---|---|---|
| **GASTROINTESTINAL** | | |
| Diarrhea | 12 (7.0 %) | 5 (6.8 %) |
| Vomiting | 11 (6.4 %) | 4 (5.5 %) |
| Hypersalivation | 4 (2.3 %) | 0 (0.0 %) |
| Abdominal discomfort | 2 (1.2 %) | 0 (0.0 %) |
| Flatulence | 2 (1.2 %) | 0 (0.0 %) |
| Nausea | 2 (1.2 %) | 0 (0.0 %) |
| **CLINICAL PATHOLOGY** | | |
| Elevated blood urea nitrogen | 7 (4.1 %) | 2 (2.7 %) |
| Elevated phosphorus | 4 (2.3 %) | 1 (1.4 %) |
| Elevated creatinine | 1 (0.6 %) | 1 (1.4 %) |
| **OTHER** | | |
| Polydipsia | 7 (4.1 %) | 1 (1.4 %) |
| Lethargy/depression | 2 (1.2 %) | 0 (0.0 %) |

The following adverse reactions were reported in < 1% of dogs administered ENTYCE: hyperactivity, increase fecal volume, increase gut sounds, and polyuria.

To report suspected adverse events, for technical assistance or to obtain a copy of the Safety Data Sheet (SDS), contact Elanco US Inc. at 1-888-545-5973. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or http://www.fda.gov/reportanimalae.

**Clinical Pharmacology:**

Following oral administration of ENTYCE at a dose of 3 mg/kg to 12 Beagle dogs, absorption of capromorelin was rapid with the maximum concentration ($C_{max}$) reached within 0.83 hr ($T_{max}$). After $C_{max}$, the plasma concentrations declined mono-exponentially with a short terminal half-life ($T_{½}$) of approximately 1.19 hrs. There were no gender differences in capromorelin pharmacokinetics. The exposure ($C_{max}$ and AUC) of capromorelin increased with dose, but the increases were not dose proportional following single and repeat once daily administrations of capromorelin. There was no drug accumulation following repeat oral administration.

**Table 2. Plasma PK parameters following oral administration of 3 mg/kg of ENTYCE**

| Parameter | Mean | SD |
|---|---|---|
| $T_{max}$ (hr) | 0.83 | 0.58 |
| $C_{max}$ (ng/mL) | 330 | 143 |
| $AUC_t$ (ng*hr/mL) | 655 | 276 |
| $AUC_{inf}$ (ng*hr/mL) | 695 | 262 |
| $T_{½}$ (hr) | 1.19 | 0.17 |

The mean absolute oral bioavailability of capromorelin was 44%. The mean total plasma clearance and volume of distribution was 18.9 mL/min/kg and 2.0 L/kg, respectively. Capromorelin was not highly bound (unbound fraction 51%) to plasma protein. The protein binding was concentration-independent over the range of 10 to 1000 ng/mL. *In vitro* (human liver microsomes) and *in vivo* (rats) metabolism studies suggest that capromorelin is metabolized by hepatic enzymes, mainly CYP3A4 and CYP3A5. Therefore, drugs that inhibit CYP3A4 and CYP3A5 activity may affect capromorelin metabolism. Following oral administration of radio-labelled capromorelin to dogs, capromorelin was excreted in urine (37%) and in feces (62%) within 72 hours.

**Effectiveness:**

Laboratory Effectiveness Study: Twenty four healthy Beagle dogs (6 dogs per sex in each group) with normal appetite were randomized into two groups and dosed daily with ENTYCE (capromorelin oral solution) at 3 mg/kg/day or vehicle control (solution minus capromorelin) to compare food intake over a 4-day period. The dogs were 13 months of age and weighed between 6.5 and 12.5 kg at the time of randomization. Six dogs administered ENTYCE repeatedly exhibited salivation post dosing and two dogs administered vehicle control exhibited salivation only one time on study day 0. Emesis was observed in one dog administered ENTYCE on study day 1. Dogs administered ENTYCE at a dose of 3 mg/kg/day for 4 consecutive days had statistically significantly increased food consumption compared to the vehicle control group ($p < 0.001$).

Clinical Field Study: Effectiveness was evaluated in 177 dogs (121 dogs in the ENTYCE group and 56 dogs in the vehicle control group) in a double-masked, vehicle controlled field study. Dogs with a reduced appetite or no appetite, with various medical conditions, for a minimum of 2 days prior to day 0 were enrolled in the study. The dogs ranged in age from 4 months to 18 years. Dogs were randomized to treatment group and dosed once daily for 4 days with ENTYCE at 3 mg/kg or vehicle control. Dogs were assessed for appetite by owners on day 0 and day 3 ± 1 using an "increased", "no change" or "decreased" scoring system. Dogs were classified as a treatment success if the owner scored their dog's appetite as "increased" on day 3 ± 1. The success rates of the two groups were significantly different ($p = 0.0078$); 68.6% (n = 83) of dogs administered ENTYCE were successes, compared to 44.6% (n = 25) of the dogs in the vehicle control group.

**Animal Safety:**

In a 12-month laboratory safety study, 32 healthy Beagle dogs (4 dogs per sex per group) approximately 11-12 months of age and weighing 9-13.6 kg were dosed orally with capromorelin in deionized water daily at 0X (placebo), 0.3 (0.13X), 7 (3.07X), and 40 (17.5X) mg/kg/day. Administration of capromorelin was associated with increased salivation and reddening/swollen paws, increased liver weights and hepatocellular cytoplasmic vacuolation. Treatment related decreases were seen in red blood cell count, hemoglobin and hematocrit in the 40 mg/kg group. Pale skin, pale gums, and decreased red blood cell count, hemoglobin and hematocrit were observed in one dog administered 40 mg/kg/day. Increases were seen in cholesterol, high density lipoproteins, and the liver specific isozyme of serum alkaline phosphatase in the 40 mg/kg group. Growth hormone and insulin-like growth factor 1 plasma levels were increased in all groups administered capromorelin. There were no effects noted on gross necropsy. Capromorelin levels were similar in plasma collected on days 90, 181, and 349 indicating no accumulation of drug.

**Storage Conditions:**

Store at or below 86° F (30° C)

**How Supplied:**

30 mg/mL flavored solution in 10 mL, 15 mL and 30 mL bottles with measuring syringe

Approved by FDA under NADA # 141-457

Manufactured for:
Elanco US Inc.
Greenfield, IN 46140, USA
Revised: September 2020



Elanco™