

Librela® (bedinvetmab injection) and Solensia® (frunevetmab injection)

Novel medications control the pain of osteoarthritis in dogs and cats

THE PROBLEM

Osteoarthritis (OA) is a painful, progressive, incurable degenerative disease prevalent in dogs and cats. Studies show that as many as 40% of dogs screened for OA had clinical signs, and more than 60% of cats 6 years or older are affected.^{1,2}

OA is a disease of the joint that impacts the entire wellbeing of the patient, including cognitive function, sleep patterns, sensitivity to environmental stimuli and relationships with humans and other animals.^{3,4} Nonsteroidal anti-inflammatory drugs (NSAIDs) were established as a cornerstone of canine OA pain management, yet while these drugs improved the quality of life for millions of dogs, their use has limitations, including:

- **Safety concerns** — NSAIDs can cause liver and kidney damage and are not well-tolerated by some animals.^{5,6}
- **Availability** — No NSAIDs are labeled for chronic OA in the feline species in the United States.
- **Compliance** — Administering oral medications daily can interfere with the human-animal bond and lapse in compliance.⁷

THE SOLUTION

OA is a complex disorder affecting the structure and function of the joint. For dogs, risk factors include poor conformation, genetics, trauma, obesity and age.⁸ The etiology of feline OA is less understood; idiopathic, primary

Sharon L. Campbell, DVM, MS, DACVIM
Dr. Campbell is the Medical Affairs Lead for Canine Chronic Pain at Zoetis. She received her DVM degree from University of Wisconsin and completed a residency in internal medicine and a master's degree at Virginia-Maryland Regional College of Veterinary Medicine. She was a Clinical Instructor at the University of Tennessee and has worked at private referral hospitals. Dr. Campbell is also a diplomate of the ACVIM and Fear Free Certified.

Tracey L. Deiss, DVM
Dr. Deiss is the Veterinary Medical Lead for Feline Anxiety and Pain at Zoetis. She earned her DVM degree at Texas A&M University while gaining experience in laboratory animal medicine and surgery at the MD Anderson Cancer Center. She went on to work at an emergency hospital and small animal practice before joining Zoetis.

OA is the most common form without an obvious risk factor, while secondary OA results from a risk factor like trauma.⁹ When a risk factor affects a joint, tissue damage triggers the immune system's inflammatory response. As the condition progresses, the joint is eventually exposed to low-grade inflammation and a chronic catabolic state.

As a consequence of the inflammatory response, many inflammation mediators and cytokines are released into the joint. One of these is nerve growth factor (NGF), a powerful driver of pain and inflammation. NGF modulates pain and inflammation by interacting with the tropomyosin receptor kinase A (TrkA). TrkA receptors are found on sensory

nerves and immune cells.¹⁰ When NGF binds to TrkA, the complex travels to the cell nucleus in the dorsal root ganglion, resulting in peripheral and central sensitization.¹⁰ Further, NGF stimulates the release of inflammatory mediators, substance P and calcitonin gene-related peptide, back to the joint leading to neurogenic inflammation.¹⁰ Other actions of NGF include binding to TrkA receptors on immune cells, causing release of more inflammatory mediators and NGF, angiogenesis and neuronal sprouting. These actions contribute to the cycle of pain, inflammation and joint destruction.¹⁰

The development teams behind Librela and Solensia saw potential in targeting NGF for controlling OA pain in dogs and cats with

species-specific anti-NGF monoclonal antibodies (mAbs). Anti-NGF mAbs could sequester excess NGF, preventing its binding to TrkA receptors and therefore reduce the NGF cycle.

THE INNOVATION

The mAbs from one species can induce an immune response when used in another species, so for therapeutic purposes, mAbs need to be species-specific to reduce the risk of reactions to the antibody.

To develop the canine-specific anti-NGF therapy for OA, Zoetis researchers immunized dogs with NGF and tested their serum to determine if anti-NGF mAbs were effectively produced. They collected samples from the dogs who produced anti-NGF mAbs and isolated the B cells that produced the antibodies to NGF. Using advanced technology, large amounts of the monovalent anti-NGF mAbs were produced and purified, creating the master bank, which is used to produce therapeutic batches of the mAbs.

The process to develop feline-specific anti-NGF therapy for OA was similar, but the researchers started by immunizing a mouse rather than a cat. They then replaced parts of the mAbs with feline material until the mAbs were mostly feline.¹⁰

Librela and Solensia are innovative treatment options for controlling OA pain. Given as a once-monthly injection, this route of administration can overcome the challenges of other OA pain medications, such as reduced compliance and disruption in the human-animal bond.⁷

SOLENSIA IMPORTANT SAFETY

INFORMATION: For use in cats only. Women who are pregnant, trying to conceive or breastfeeding should take extreme care to avoid self-injection. Hypersensitivity reactions, including anaphylaxis, could potentially occur with self-injection. SOLENSIA should not be used in breeding cats or in pregnant or lactating queens. SOLENSIA should not be administered to cats with known hypersensitivity to frunevetmab. The most common adverse events reported in a clinical study were vomiting and injection site pain. See full Prescribing Information at SolensiaPI.com

LIBRELA IMPORTANT SAFETY

INFORMATION: For use in dogs only. Women who are pregnant, trying to conceive or breastfeeding should take extreme care to avoid self-injection. Hypersensitivity reactions, including anaphylaxis, could potentially occur with self-injection. LIBRELA should not be used in breeding, pregnant or lactating dogs. LIBRELA should not be administered to dogs with known hypersensitivity to bedinvetmab. The most common adverse events reported in a clinical study were urinary tract infections, bacterial skin infections and dermatitis. See full Prescribing Information at LibrelaPI.com

References

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LIBRELA AND SOLENSIA



Brief Summary of full Prescribing Information.

Librela™ (bedinvetmab injection)

Canine anti-nerve growth factor monoclonal antibody for subcutaneous use in dogs only.
Single-Use Vial

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

INDICATION
LIBRELA is indicated for the control of pain associated with osteoarthritis in dogs.

DOSAGE AND ADMINISTRATION
The minimum target dose of LIBRELA is 0.23 mg/lb (0.5 mg/kg) body weight, administered subcutaneously once a month. Dogs should be dosed by weight range according to the specific dosing information below.
The product does not contain a preservative. The full content of each vial is for single-use only. Once punctured, contents of the vial should be used immediately and any remaining solution should be discarded.

Dogs weighing ≥ 11 lb (≥ 5 kg):
Dogs should be dosed by weight range according to the Dosing Table below (Table 1). Dogs are given the full content of 1 or 2 vials of the appropriate concentration based on body weight. Aseptically withdraw the total dose into a single syringe and administer immediately.

Table 1. Dosing Table

Dog Body Weight in Pounds (lb)	Dog Body Weight in Kilograms (kg)	Number and Strength (mg/mL) of LIBRELA Vials to be Administered				
		5 mg/mL orange	10 mg/mL blue	15 mg/mL green	20 mg/mL gold	30 mg/mL purple
11-22.1	5-10	1 vial				
22.2-44.1	10.1-20		1 vial			
44.2-66.1	20.1-30			1 vial		
66.2-88.2	30.1-40				1 vial	
88.3-132.3	40.1-60					1 vial
132.4-176.4	60.1-80				2 vials	
176.5-220.5	80.1-100				1 vial	1 vial
220.6-264.6	100.1-120					2 vials

Dogs < 11 lb:
Aseptically withdraw 0.045 mL/lb (0.1 mL/kg) from a 5 mg/mL vial (orange vial) into a single syringe and administer immediately. Discard the vial after the dose has been withdrawn.
Effectiveness may not be achieved until after the second dose (see **EFFECTIVENESS**).

CONTRAINDICATIONS
LIBRELA should not be administered to dogs with known hypersensitivity to bedinvetmab.
LIBRELA should not be used in breeding dogs or in pregnant or lactating dogs. Immunoglobulin G class antibodies such as LIBRELA can pass through the placental blood barrier and be excreted in milk. Fetal abnormalities, increased rates of stillbirths and increased postpartum fetal mortality were noted in rodents and primates receiving anti-NGF monoclonal antibodies.

WARNINGS
User Safety Warnings
Not for use in humans. Keep this and all drugs out of reach of children. For use in dogs only.
Hypersensitivity reactions, including anaphylaxis, could potentially occur in the case of accidental self-injection.
In case of accidental self-injection, seek medical advice immediately and show the package leaflet, vial or carton to the physician.
Pregnant women, women trying to conceive, and breastfeeding women should take extreme care to avoid accidental self-injection.
The importance of Nerve Growth Factor in ensuring normal fetal nervous system development is well-established and laboratory studies conducted on nonhuman primates with human anti-NGF antibodies have shown evidence of reproductive and developmental toxicity.

PRECAUTIONS
Administration of monoclonal antibodies may be associated with hypersensitivity reactions and delayed hypersensitivity reactions. If anaphylaxis or other hypersensitivity reaction occurs, discontinue use and institute appropriate therapy.
The safe use of this product with other monoclonal antibodies has not been evaluated. Use with caution in dogs with known hypersensitivity to other immunoglobulin therapy.
Evaluations were not made to determine if interactions occurred between LIBRELA and veterinary vaccines.
Treatment with LIBRELA may result in the formation of anti-bedinvetmab antibodies and potentially the loss of product effectiveness (see **IMMUNOGENICITY**).
The safe use of anti-NGF monoclonal antibodies with concurrent non-steroidal anti-inflammatory drugs (NSAIDs) has not been established in dogs. In human clinical trials, rapidly progressing osteoarthritis (RPOA) has been reported in a small number of patients receiving humanized anti-NGF monoclonal antibody therapy. The incidence of these events increased in human patients receiving NSAID treatment long-term in combination with an anti-NGF monoclonal antibody. RPOA has not been characterized or reported in dogs.

The safety and effectiveness of LIBRELA has not been evaluated in dogs less than 12 months of age.
LIBRELA has not been studied in dogs that have a history of cruciate ligament rupture within six months before initial product use as these cases were excluded from the field studies.
Long term effects which may occur more than 9 months after the use of LIBRELA have not been evaluated.
NGF is expressed within the heart and vasculature, and the long-term effects of reduced NGF in dogs with cardiac disease are unknown.

Primates receiving high doses of anti-NGF monoclonal antibodies had anatomical changes in postganglionic cell bodies (reduced size and number of neurons). The change in cell body size returned to normal after anti-NGF monoclonal antibody administration was discontinued. NGF is involved in the normal development of sensory and sympathetic nerve fibers in developing animals. This may be important with use of LIBRELA in young growing dogs.

ADVERSE REACTIONS
The safety of LIBRELA was assessed in a masked, controlled 84-day US field study evaluating the effectiveness of LIBRELA for the control of pain associated with osteoarthritis. Enrollment included 272 dogs, 135 dogs treated with LIBRELA and 137 dogs treated with a negative control (sterile saline). The enrolled dogs were at least 1 year of age (1 to 17 years old), weighed between 1.8 to 62.7 kg and were of various breeds or non-purebred. Dogs were dosed at 28-day intervals and received up to three injections. The most common adverse reactions reported during the study are summarized in Table 2 below.

Table 2. Number (%) of Dogs with Adverse Reactions Reported in the US Field Study

Adverse Reaction*	LIBRELA n (%) (Total N = 135)	Negative Control n (%) (Total N = 137)
Urinary tract infection	15 (11.1)	11 (8.0)
Bacterial skin infection	11 (8.1)	9 (6.6)
Dermatitis	10 (7.4)	8 (5.8)
Dermal mass	8 (5.9)	5 (3.6)
Erythema	6 (4.4)	5 (3.6)
Dermal cyst(s)	4 (3.0)	2 (1.5)
Pain on injection	4 (3.0)	2 (1.5)
Inappropriate urination**	4 (3.0)	1 (0.7)
Histiocytoma	3 (2.2)	0 (0.0)
*An adverse reaction may have occurred more than once in a dog; only the first occurrence was counted. ** Of these, two dogs treated with LIBRELA were among those reported with a urinary tract infection.		

The safety of LIBRELA was also evaluated in a masked, controlled 84-day European field study evaluating the effectiveness of LIBRELA for the control of pain associated with osteoarthritis. Enrollment included 281 dogs, 138 dogs were treated with LIBRELA and 143 treated with a negative control (sterile saline). The enrolled dogs were at least 1 year of age (1 to 17.5 years old), weighed between 1.7 to 66 kg and were of various breeds or non-purebred. Dogs were dosed at 28-day intervals and received up to three injections. The most common adverse reactions reported during the study are summarized in Table 3 below.

Table 3. Number (%) of dogs with Adverse Reactions Reported in the European Field Study

Adverse Event Reported*	LIBRELA n (%) (Total N = 138)	Negative Control n (%) (Total N = 143)
Increased Blood Urea Nitrogen (BUN)**	19 (13.8)	7 (4.9)
Lethargy	5 (3.6)	0 (0.0)
Emesis	4 (2.9)	1 (0.7)
Anorexia	3 (2.2)	0 (0.0)
Lameness	3 (2.2)	1 (0.7)
Cough	3 (2.2)	1 (0.7)

*An adverse reaction may have occurred more than once in a dog; only the first occurrence was counted.
** Two dogs treated with LIBRELA suffered serious adverse events and were euthanized during or after study completion: A 13-year old Bichon Frise had pre-existing increased urine protein-creatinine ratio and heart failure that worsened during study; the dog also had an increase in creatinine during the study and was diagnosed with renal failure and was euthanized 3 days after completing the study. An 8-year-old mixed breed dog had pancreatitis and was euthanized on Day 74. The remainder of the dogs that had elevations in the BUN did not have any obvious adverse events associated with this finding.

One dog in the LIBRELA group was diagnosed with pyelonephritis on Day 15; this dog had pre-existing increased serum BUN and creatinine and a recent history of urinary tract infection that was not confirmed resolved prior to enrollment. Non-steroidal anti-inflammatory drugs (NSAIDs) and acetaminophen were initiated on Day 7 for osteoarthritis-associated joint pain but NSAIDs were discontinued on Day 10 due to anorexia and gastroenteritis; azotemia worsened at Day 13 and the dog received no further LIBRELA treatment.

One dog in the LIBRELA group with a history of atopy, developed mild alopecia and mild erythema on the injection site on Days 5 and 23. Both episodes of alopecia and erythema resolved with treatment.

A total of 89 dogs were enrolled in a 6-month, single arm, open labeled, uncontrolled continuation of the EU field study and received monthly subcutaneous injections of LIBRELA. The study provided additional field safety information.

One dog experienced acute gastroenteritis and recovered following treatment for abdominal pain, fever, vomiting, and anorexia. One large breed dog enrolled for stiffl osteoarthritis developed acute forelimb lameness that was diagnosed as elbow dysplasia. Two dogs presented with rear limb paresis of unknown etiology, one of whom responded to ongoing NSAID treatment and one who did not.

CONTACT INFORMATION
To report suspected adverse drug events, for technical assistance or to obtain a copy of the Safety Data Sheet (SDS), contact Zoetis Inc. at 1-888-963-8471.

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

TARGET ANIMAL SAFETY
6 Month Margin of Safety Study:
LIBRELA (bedinvetmab injection) 15 mg/mL and 30 mg/mL concentrations were administered subcutaneously to 11 to 12-month old, healthy Beagles (8 dogs per group) at doses of 1 mg/kg (1X), 3 mg/kg (3X), and 10 mg/kg (10X) every 28 days for seven consecutive doses. The control group (8 dogs) received sterile saline injections. Dogs weighed 5.6-11.7 kg at study initiation.

There were no clinically significant changes noted in neurological examinations, body temperature, heart and respiratory rate, blood pressure, electrocardiography, and organ weights. Detailed pathology evaluation of the shoulder, elbow, hip, and knee joints were conducted.

Vomiting and soft stool were noted across all groups throughout the study. Scabbing on the face, neck and thorax was seen across all groups except the 1 mg/kg group. Injection site redness was noted sporadically for 1 control dog, 2 dogs in the 1 mg/kg treatment group, 5 dogs in the 3 mg/kg treatment group, and 5 dogs in the 10 mg/kg treatment group. One dog in the 3 mg/kg treatment group had a temporary, mild swollen facial area 26 days after the first dose that resolved spontaneously. Two dogs in the 3 mg/kg treatment group had lymphadenopathy on the last study day with no related histopathology findings. One dog in the 10 mg/kg treatment group had an approximately 2.5 cm X 3.5 cm circular raised firm erythematous lesion with slight serosanguinous discharge and mild scabs of the shaved cervical area that resolved over 14 days.

One dog in the 1 mg/kg treatment group had an increasing ALP value over the course of the study that increased threefold above the high end of the reference range at study completion. There was no gross or histopathology correlate.

One dog in the 1 mg/kg treatment group had mild cartilage necrosis in the left ulna and an erosion in the cartilage of the right ulna. One dog in the 3 mg/kg treatment group had mild bilateral, femoral neck enthesophytes observed on radiographs pre-treatment. On end of study radiography and pathology evaluation, this dog had an osteophyte of the left acetabulum, mild left acetabulum remodeling and severe left femoral neck enthesophytes. Microscopically, mild to moderate cartilage degeneration with erosion and proteoglycan depletion was also noted in the left proximal femur and acetabulum. The mild right femoral neck enthesophytes were the same grade as pre-treatment. The findings may be progression of an underlying musculoskeletal condition; however, a potential relation to treatment cannot be ruled out.

None of the LIBRELA-treated dogs developed anti-drug antibodies due to bedinvetmab administration.

Additional Safety Studies:

In a two-week laboratory safety study, eight dogs concurrently received one subcutaneous injection of LIBRELA at the high end of the inherent dose band (1 mg/kg) and fourteen days of an injectable NSAID. This limited laboratory study did not provide sufficient data to support a conclusion on the safety of concurrent use of LIBRELA and NSAIDs.

In a 3-month exploratory laboratory safety study using a non-final formulation of bedinvetmab administered by subcutaneous injection monthly for four doses, a dog administered a 4 mg/kg dose had a reddened and/or swollen muzzle abrasion, with an elevated white blood cell count, and elevated globulin level and fibrinogen level. At one of the injection administrations, one dog administered a 4 mg/kg dose had a 4 cm X 2 cm injection site erythema with an eschar that resolved; and one dog administered a 1 mg/kg dose had 3 cm X 1 cm injection site erythema that resolved. Another dog administered a 1 mg/kg dose had injection site erythema, scabbing, and mucopurulent discharge for 18 days.

STORAGE CONDITIONS
LIBRELA (bedinvetmab injection) should be stored in a refrigerator, 2° – 8°C (36° – 46° F). Do not freeze. Store vials in their boxes to protect from prolonged exposure to light. Once punctured, contents of the vial should be used immediately and any remaining solution should be discarded.

HOW SUPPLIED
LIBRELA is available in 5 strengths packaged in 4 mL glass vials containing an extractable volume of 1 mL of clear solution. Each strength is available in cartons containing 2 or 6 vials.

Approved by FDA under NADA # 141-562

zoetis

Distributed by:
Zoetis Inc.
Kalamazoo, MI 49007
March 2023

40042787A&P

Brief Summary of full Prescribing Information.

Solensia™ (frunevetmab injection)

7 mg/mL

Feline anti-nerve growth factor monoclonal antibody for subcutaneous injection in cats only.
Single-Use Vial

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

INDICATION
SOLENSIA is indicated for the control of pain associated with osteoarthritis in cats.

DOSAGE AND ADMINISTRATION
Cats should be dosed by weight range according to the Dosing Chart (Table 1) below. Cats are given the full content of 1 or 2 vials based on body weight to target a minimum dosage of 0.45 mg/lb. (1 mg/kg) body weight, administered subcutaneously once a month. Aseptically withdraw the total dose into a single syringe and administer immediately.

The product does not contain a preservative. The full content of each vial is for single use only. Once punctured, contents of the vial should be used immediately and any remaining solution should be discarded.

Table 1. Dosing Chart

Weight of Cat (lb.)	Weight of Cat (kg)	Volume	Number of Vials*
5.5-15.4	2.5-7 kg	1 mL	1
15.5-30.8	7.1-14 kg	2 mL	2

*1 mL frunevetmab injection per vial

CONTRAINDICATIONS
SOLENSIA should not be administered to cats with known hypersensitivity to frunevetmab.
SOLENSIA should not be used in breeding cats or in pregnant or lactating queens because it may pass through the placental blood barrier and be excreted in milk. Fetal abnormalities, increased rates of stillbirths and increased postpartum fetal mortality were noted in rodents and primates receiving anti-NGF mAbs.

WARNINGS
User Safety Warnings
Not for use in humans. Keep out of reach of children.

Hypersensitivity reactions, including anaphylaxis, could potentially occur in the case of accidental self-injection.

In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.

Pregnant women, women trying to conceive, and breastfeeding women should take extreme care to avoid accidental self-injection.

The importance of NGF in ensuring normal fetal nervous system development is well-established and laboratory studies conducted on nonhuman primates with human anti-NGF antibodies have shown evidence of reproductive and developmental toxicity.

PRECAUTIONS
Administration of mAbs may be associated with hypersensitivity reactions and delayed hypersensitivity reactions. If anaphylaxis or other hypersensitivity reaction occurs, discontinue use and institute appropriate therapy.

Administration of SOLENSIA may be associated with scabbing on the head and neck, dermatitis, and pruritus; however, pre-approval data suggest that these signs do not require cessation of SOLENSIA administration (see **ADVERSE REACTIONS** and **TARGET ANIMAL SAFETY**).

Evaluations were not made to determine if interactions occurred between SOLENSIA and veterinary vaccines.

Treatment with SOLENSIA may result in the formation of anti-frunevetmab antibodies and potentially the loss of product effectiveness (see **Immunogenicity**).

The safe use of SOLENSIA with concurrent non-steroidal anti-inflammatory drugs (NSAIDs) has not been established in cats. In human clinical trials, rapidly progressing osteoarthritis (RPOA) has been reported in a small number of patients receiving humanized anti-NGF mAb therapy. The incidence of these events increased in human patients receiving NSAID treatment long term in combination with an anti-NGF mAb. RPOA has not been characterized or reported in cats.

SOLENSIA has not been evaluated in cats less than 7 months or 5.5 lbs.

Long term effects, which may occur more than 6 months after the use of SOLENSIA, have not been evaluated. Primates receiving high doses of anti-NGF mAbs had reduced cell size in postganglionic neuronal cell bodies. The change in cell body size returned to normal after anti-NGF mAb administration was discontinued. NGF is involved in the normal development of sensory and sympathetic nerve fibers in developing animals. This may be important with use of SOLENSIA in young growing cats.

The safe use of this product with other mAbs has not been evaluated.

ADVERSE REACTIONS
The safety of SOLENSIA was evaluated in a masked, controlled 112-day field study to evaluate the effectiveness of SOLENSIA for the control of pain associated with osteoarthritis in cats. Enrollment included 275 cats weighing 2.5-to 11.4 kg and 1.6-to 22.4 years old; 182 cats were treated with SOLENSIA and 93 cats were administered a vehicle control. Cats were dosed at 28-day intervals and received up to three injections. The most common adverse reactions reported during the field study are presented below.

Table 2. Adverse Reactions Reported in the Field Study¹

Adverse Reaction	Solensia N=182 (%)	Vehicle Control N=93 (%)
Vomiting	24 (13.2%)	10 (10.8%)
Injection site pain ²	20 (10.9%)	13 (14%)
Diarrhea	12 (6.6%)	5 (5.4%)
Abnormal behavior and behavioral disorders ³	12 (6.6%) ⁴	5 (5.4%) ⁵
Renal insufficiency ⁶	12 (6.6%)	4 (4.3%)
Anorexia	12 (6.6%)	4 (4.3%)
Lethargy	11 (6.0%)	3 (3.2%)
Dermatitis	11 (6.0%)	1 (1.1%)
Alopecia	10 (5.5%)	2 (2.2%)
Dehydration	8 (4.4%)	0 (0.0%)
Lameness ⁷	8 (4.4%)	2 (2.2%)
Pruritus	7 (3.8%)	0 (0.0%)
Weight loss	6 (3.3%)	5 (5.4%)
Scabbing on head/neck	6 (3.3%)	1 (1.1%)
Gingival disorder	5 (2.7%)	0 (0.0%)
Bacterial skin infection	4 (2.2%)	1 (1.1%)
Otitis externa	4 (2.2%)	0 (0.0%)

¹ If a cat experienced the same event more than once, only the first occurrence is reported
² The control product was the vehicle without active ingredient
³ Behavior abnormal for the individual cat
⁴ Individual cats had at least one of the following behavior changes: anxiety (1), hiding (1), hypersomnia (1), inappropriate urination (5), sleeping with owner (1), vocalization (3), increased aggressive behavior (1)
⁵ Individual cats had at least one of the following behavior changes: anxiety (2), disorientation (1), inappropriate urination (2), and vocalization (1)
⁶ Worsening of existing disease
⁷ New lameness or worsening of previous lameness

The safety of SOLENSIA was also evaluated in a masked, controlled 56-day exploratory field study to evaluate the effectiveness of SOLENSIA for the control of pain associated with osteoarthritis in cats. Enrollment included 126 cats; 85 cats were treated with frunevetmab injection manufactured similar to SOLENSIA and 41 cats were administered a vehicle control. Cats were dosed at 28-day intervals and received up to two injections. The most frequently reported adverse reactions were digestive tract disorders, including vomiting and diarrhea, and skin disorders, including dermatitis/eczema and alopecia that were mostly attributed to irritation by an activity monitor collar required for the study.

Immunogenicity
All therapeutic proteins, including monoclonal antibodies, have the potential for immunogenicity, including the production of antibodies that bind to the therapeutic protein and may decrease effectiveness. Such host-derived antibodies are termed anti-drug antibodies (ADA). SOLENSIA, therefore has the potential to cause the cat to produce ADAs against frunevetmab.

The presence of binding antibodies to frunevetmab in cats was assessed using a screening and confirmatory assay approach. In controlled field effectiveness studies in cats with osteoarthritis (see **EFFECTIVENESS**), four out of 259 cats that received SOLENSIA once monthly developed anti-drug antibodies (ADAs). One cat tested positive for ADAs on Days 0, 28, 56, and 84. This cat had non-detectable plasma drug concentration levels of SOLENSIA on Days 28 and 56, and was a treatment failure in the effectiveness analysis, suggesting that the ADAs may have clinical significance. No assessment for neutralizing antibodies was performed.

The observed incidence of antibody positivity in an assay is highly dependent on several factors including assay sensitivity and specificity, assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to SOLENSIA with the incidence of antibodies to other products may not be appropriate.

CONTACT INFORMATION
To report suspected adverse drug events, for technical assistance or to obtain a copy of the Safety Data Sheet (SDS), contact Zoetis Inc. at 1-888-963-8471.

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

STORAGE CONDITIONS
SOLENSIA should be stored upright in a refrigerator, between 35°– 46°F (2°– 8°C). Do not freeze. Protect from light. See in-use instructions provided in the **DOSAGE AND ADMINISTRATION** section.

HOW SUPPLIED
SOLENSIA is supplied as a sterile buffered solution of 7mg/mL of frunevetmab in single-use 4 mL glass vials containing an extractable volume of 1mL of clear solution with a butyl rubber stopper and aluminum overseal. Vials are available in cartons containing 2 or 6 vials.

Approved by FDA under NADA # 141-546

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Distributed by:
Zoetis Inc.
Kalamazoo, MI 49007

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