



Solensia™
(frunevetmab injection)

Bonqat® 
(pregabalin oral solution)

Treat feline OA pain with confidence—start with Solensia

Solensia Key Feature #1:

The first and only FDA-approved therapeutic for control of feline osteoarthritis (OA) pain.

Solensia Key Feature #2:

One injection = 1 month of pain control.

Its Benefit:

Gives veterinarians a clear choice – an FDA approved, first tier therapy to start newly diagnosed cats on effective OA pain control.

Its Benefit:

A simple, clinic-administered plan that can help cats return to comfortable movement by controlling OA pain.

Alleviate feline acute anxiety and fear with Bonqat

Bonqat Key Feature #1:

Bonqat helps alleviate vet-visit acute anxiety and fear in cats.

Its Benefit:

Helps remove a common barrier to getting cats into the clinic—making it easier for caregivers to say “yes” to starting Solensia and returning for monthly injections.

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 on page 40.

BONQAT IMPORTANT SAFETY INFORMATION: Not for human use. Do not use in cats with known hypersensitivity to pregabalin. Use with caution in cats with cardiac disease, hypertension, renal disease, or severe systemic disorders. The safe use of BONQAT has not been evaluated in breeding, pregnant, or lactating cats; in cats younger than 7 months of age; in cats with cardiac disease, hypertension, renal disease, or severe systemic disorders; or in conjunction with opioids and other sedatives. The most common side effects are incoordination, lethargy, and vomiting. See full Prescribing Information on page 42.

Solensia: SolensiaVetTeam.com, Bonqat: BonqatVetTeam.com,
Veterinary Medical Information & Product Support: 1-888-963-8471

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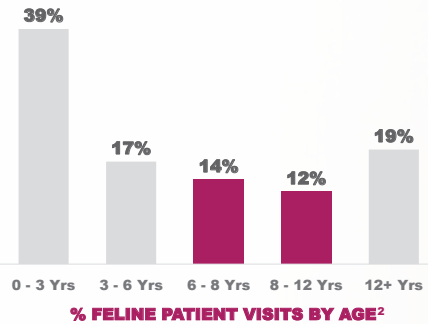
**sound
byte**

zoetis

Feline osteoarthritis (OA) pain is more common than many cat owners think—and cats are experts at hiding it.

Nearly 40% of all cats experience OA pain, and it's still under-recognized and under-discussed.

Nearly **40%** of all cats have clinical signs of OA¹



OA pain isn't just a senior-cat issue—it can affect cats of all ages, including young cats.

Make OA pain a standard part of wellness conversations by asking about 3 quick “red flags”:

- Changes in **jumping** or using stairs
- Less interest in **chasing/running**
- **Litter box** changes or difficulty getting in/out

¹ Enomoto M, Mantyh PW, Murrell J, Innes JF, Lascelles BDX. Anti-nerve growth factor monoclonal antibodies for the control of pain in dogs and cats. Vet Rec. 2019;184(1):23.

² Zoetis Market Research: Feline Visit Growth Age MAT. September 2022.

sound byte

CHECK-OFF &
ECHO NOTES

State the Issue

Based on what you're noticing at home, like changes in jumping, playing/chasing, or the litter box and what I'm seeing on today's exam, I'm concerned your cat may have osteoarthritis (OA) pain. Cats often mask pain, so it can look like subtle behavior changes or 'slowing down'.

State the Solution

The good news is we can control OA pain. Solensia is the first and only FDA-approved therapeutic to control feline OA pain, and one injection provides one month of pain control.

Make Your Recommendation

I recommend we start Solensia today to control your cat's OA pain and help them get back to comfortable movement and normal behaviors. If getting into the carrier or coming to the clinic is stressful, we can also use Bonqat to help alleviate acute vet-visit anxiety and fear so visits are easier for both of you.

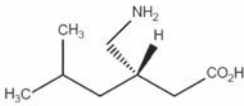
Package Insert

Bonqat[®]
(pregabalin oral solution)

Each mL of BONQAT contains 50 mg pregabalin.
For oral use in cats only.

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

DESCRIPTION:
Each mL of BONQAT contains 50 mg pregabalin. The chemical name of pregabalin is (3S)-3-(aminomethyl)-5-methylhexanoic acid. It is a white or almost white powder having a molecular weight of 159.23g/mol. The molecular formula is C₈H₁₇NO₂ and the structural formula is:



INDICATIONS:
BONQAT is indicated for alleviation of acute anxiety and fear associated with transportation and veterinary visits in cats.

DOSAGE AND ADMINISTRATION:
Client Information Sheet is on the reverse of this package insert.
Always provide client information sheet with prescription.

BONQAT is administered orally as a single dose of 5 mg/kg (0.1 mL/kg) approximately 1.5 hours before the start of the transportation or veterinary visit and can be given on two consecutive days. If the cat weighs more than 22 pounds, the total dose will need to be calculated and given in two separate doses as the syringe holds a maximum of 1 mL of solution. A small amount of food can be given with BONQAT.

CONTRAINDICATIONS:
Do not use in case of hypersensitivity to pregabalin or to any of the excipients (sodium benzoate, ethyl maltol, hydrochloric acid, sodium hydroxide).

WARNINGS:
Human Safety Warnings:
Not for human use.

Appropriate precautions should be taken while handling BONQAT. Avoid skin contact, eye contact, or contact with mucous membranes.

Symptoms of exposure to pregabalin include dizziness, sleepiness, blurred vision, weakness, dry mouth, and difficulty with concentration or attention.

In case of accidental eye or mucosal exposure, flush with water for 15 minutes. If wearing contact lenses, eyes should be rinsed first, then remove contact lenses and continue rinsing. Seek medical advice if symptoms occur.

In case of skin contact, wash with soap and water immediately. Remove contaminated clothing. Seek medical advice if symptoms occur.

In case of accidental ingestion, seek medical advice if symptoms occur. Do not drive as sleepiness may occur. In case of ingestion by a child, seek medical attention immediately. Show the package insert or the label to the physician.

Drug Abuse, Addiction, and Diversion
Controlled Substance:
BONQAT contains pregabalin, a Schedule V controlled substance.

Abuse: Abuse is defined as the intentional, non-therapeutic use of a drug, even once, to achieve a desired psychological or physiological effect. Pregabalin is not known to be active at receptor sites associated with drugs of abuse. However, pregabalin is associated with drug liking and is known to be misused and abused in the community, particularly in combination with opioids. Consider the potential risks of misuse or abuse before prescribing this product. Signs of pregabalin misuse or abuse include drug seeking behavior.

Pregabalin should be handled appropriately to minimize the risk of diversion, including restriction of access, the use of accounting procedures, and proper disposal methods, as appropriate to the clinical setting and as required by law.

Note to physician: BONQAT contains pregabalin.

The safety data sheet (SDS) contains more detailed occupational safety information. To report adverse reactions in users or to obtain a copy of the SDS for BONQAT contact Zoetis Inc. at 1-888-963-8471.

Animal Safety Warnings: Some cats may experience hypothermia, depression, drowsiness, muscle tremors, and/or ataxia. These cats should be kept warm and not offered food or water until BONQAT's effects have worn off (usually within 6 hours). (See **TARGET ANIMAL SAFETY**)
Keep BONQAT in a secure location out of reach of dogs, cats, and other animals to prevent accidental ingestion or overdose.

PRECAUTIONS:
Use with caution in cats with concurrent cardiac disease or hypertension because BONQAT may cause bradycardia and reflex hypertension. The safety of BONQAT has not been evaluated in cats with concurrent cardiac disease or hypertension.

The safe use of BONQAT in cats younger than 7 months of age has not been evaluated.

The safe use of BONQAT used in conjunction with opioids and other sedatives has not been evaluated.

Use with caution in cats with pre-existing renal disease (See **Clinical Pharmacology**).

The safe use of BONQAT in cats with severe systemic disorders has not been evaluated. Use with caution in cats with severe systemic disorder.

The safe use of BONQAT in breeding, pregnant, and lactating cats has not been evaluated.

ADVERSE REACTIONS:
In a well-controlled European field study, which included a total of 238 cats (108 treated with BONQAT at the label dose of 5 mg/kg, 29 treated with BONQAT at a dose of 2.5 mg/kg, and 101 administered placebo control), 5 months to 15 years of age and weighing 1.8 to 10.3 kg, the following adverse reactions were reported:

Table 1. Adverse reactions

Adverse reaction	Pregabalin 5 mg/kg N=108	Pregabalin 2.5 mg/kg N=29	Placebo N=101
Ataxia	5 (4.6%)	1 (3.4%)	0
Lethargy	3 (2.8%)	2 (6.9%)	0
Emesis	2 (1.9%)	0	0
Proprioception abnormality	1 (0.9%)	1 (3.4%)	0
Muscle tremor	1 (0.9%)	0	0
Anorexia	1 (0.9%)	0	0
Weight loss	1 (0.9%)	0	0
Mydriasis	0	1 (3.4%)	0

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

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

INFORMATION FOR CAT OWNERS:
Possible side effects on BONQAT include incoordination, tiredness, and vomiting. Some cats might be more sensitive to BONQAT; if the cat appears to be uncoordinated or overly tired, it should be kept warm and not offered food or water until the effect of BONQAT has worn off. This will normally happen within a few hours. If there are further concerns related to side effects after dosing the veterinarian should be contacted.

BONQAT must not be re-dosed if the cat spits part of the dose, vomits after treatment, or in case of hypersalivation, or if BONQAT does not seem to have any effect.

Always provide the Client Information Sheet with prescription.

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

CLINICAL PHARMACOLOGY:

Absorption
BONQAT is rapidly absorbed after oral administration in cats. Following oral administration of 5 mg/kg to fasted cats the maximum observed concentration (C_{max}) in plasma was 10.1 ± 0.8 (SD) µg/mL and occurred at 0.5-1.0 hours post-dose. The area under plasma concentration time curve from time zero to the last quantifiable time point (AUC_{last}) was 199±27 µg²h/mL. The mean absolute oral bioavailability was 94.3%.

Distribution
BONQAT has a relatively large volume of distribution. After intravenous (IV) bolus administration of 2.5 mg/kg, the volume of distribution at the steady state (V_{ss}) was 0.4±0.02 L/kg in cats. BONQAT is not known to bind to plasma proteins in other species, but this has not been studied in cats.

Metabolism and excretion
BONQAT is slowly eliminated from the body of cats. After IV bolus administration of 2.5 mg/kg, total plasma clearance was 0.03±0.008 L/h/kg. The mean half-life of elimination from circulation was 12.3±3.1 hours after IV administration of 2.5 mg/kg and 14.7±2.7 hours after oral administration of 5 mg/kg.

Elimination of the parent compound as well as the methylation metabolite from circulation occurs almost exclusively by renal excretion in other species. This has not been studied in cats.

Mechanism of Action
Pregabalin is a ligand of alpha2-delta subunit of voltage-gated calcium channels. It reduces the presynaptic calcium influx in neurons and thereby the release of various neurotransmitters, including glutamate, norepinephrine, serotonin, dopamine, substance P and calcitonin gene-related peptide.

EFFECTIVENESS:
The effectiveness of BONQAT was demonstrated in a well-controlled multi-center field study conducted in Europe. A total of 238 cats with a history of being anxious and/or fearful when transported by a car and during veterinary visits were allocated to 1 of 3 treatment groups: 108 cats received BONQAT orally at a dose of 5 mg/kg, 29 cats received BONQAT at a dose of 2.5 mg/kg and 101 cats received placebo (vehicle oral solution containing no active ingredient). The study included assessments during transportation and veterinary examination at a screening visit and a treatment visit. To keep both study visits as similar as possible, all cats were administered tap water prior to the screening visit. Prior to the treatment visit, each cat was administered its randomized treatment. The treatment visit was conducted 5-10 days after the screening visit in a similar manner as the screening visit. Doses were administered approximately 1.5 hours before the cat was put into the carrier and starting of the transportation to the visits. The cats were between 5 months and 15 years of age and weighed 1.8 to 10.3 kg.

Treatment success was defined with 2 primary effectiveness endpoints: the owner's assessment of the treatment effect based on the cat's anxiety and/or fear during transportation in a car and the veterinarian's assessment of the treatment effect based on the cat's anxiety and/or fear during physical examination at the clinic. These endpoints were based on the following scale (1- Excellent, 2- Good, 3- Fair, 4- Poor, 5- Very Poor).

The treatment effect was statistically significant for both primary effectiveness variables (p < 0.0010) in the group administered BONQAT at the dose 5 mg/kg compared to the placebo group. In the 5 mg/kg group, cat owners assessed the response as excellent or good during the transportation in 54.3% of cases; the corresponding proportion in the placebo group was 27.1%. In the 5 mg/kg group, the veterinarians assessed the response as excellent or good during the clinical examination in 52% of cases; the corresponding proportion in the placebo group was 30%. The 2.5 mg/kg group was not statistically different than placebo for both primary variables.

The owner's assessment of ability to place the cat into the carrier was improved from screening to treatment visit in the group administered BONQAT at the dose of 5 mg/kg compared to the placebo group. The owner-assessed signs of anxiety and/or fear decreased from screening to treatment visit in the 5 mg/kg group compared to the placebo group. Based on the owners' observations, vocalization, panting/intense breathing, activity, resistance, and freezing were the signs with the greatest improvement between screening and treatment visits in the 5 mg/kg group. The majority of the cat owners assessed administration of BONQAT as either very easy or easy.

TARGET ANIMAL SAFETY:

In a margin of safety study, 32 healthy, 7-month-old Domestic shorthair cats (4/sex/group) were administered a negative control or BONQAT for six consecutive days by once daily oral administration at dose levels of 5, 15, and 25 mg/kg/day.

At 5 mg/kg/day, observed signs of sedation included: abnormal gait, slight to moderate uncoordinated behavior, decreased activity, slightly limited usage of hind limbs, lying on side, hypothermia and/or drowsy appearance (i.e. depression, drowsiness, and/or ataxia). Clinical signs of sedation were resolved at the four-hour clinical observation. One male and one female cat had hypothermia observed two to four hours post-dose respectively, the lowest body temperature value was 99°F. Cats had a decrease in heart rate with maximum effect at six hours, but the heart rates stayed within normal range. All adverse observations were resolved by six hours after dosing on the first day of treatment.

At 15 and 25 mg/kg/day, signs of sedation were observed in all cats and included ataxia, lethargy, slightly to moderately limited usage of hind limbs, slight to severe uncoordinated behavior, partially to completely closed eyes, lying on side, dilated pupils, hypothermia, and/or drowsy appearance (i.e. depression, drowsiness, and/or ataxia). On Day 1, all cats had a decreased body temperature at one or more timepoints, the lowest values were 97.8°F when dosed at 15 mg/kg/day and 98.2°F when dosed at 25 mg/kg/day. One cat dosed at 25 mg/kg/day had a loss of consciousness, abnormal gait, eyes closed, decreased activity, lying on side, sedation, salivation, vomiting, hypothermia, and uncoordinated behavior. This cat recovered by the four-hour observation. Directly after dosing, slight to severe salivation was observed in multiple cats on one or more days. Cats had decreased heart rate with maximum effect at two to six hours, some cats had bradycardia (120-130 bpm). The majority of cats maintained a normal blood pressure, but a few cats with bradycardia had a reflexive hypertension. Most adverse observations resolved by eight hours after treatment administration.

In a second margin of safety study, 32 healthy, 1 to 3 years old Domestic shorthair cats (4/sex/group) were administered a negative control or BONQAT for 3 consecutive days by once daily oral administration at dose levels of 5, 15 and 25 mg/kg/day. Directly after dosing, slight to severe hypersalivation was noted in all dose groups.

At 5 mg/kg/day, signs of sedation were observed in 6 of 8 cats, and included: abnormal gait, hypothermia, decreased respiratory rate and/or lethargy. These signs were observed between 1 and 6 hours after dosing on the first day of treatment. On Day 2, at six hours post-dose, one cat had muscle tremors that resolved without treatment by the 8-hour observation. Three cats had bradycardia (120-128 bpm) with maximum effect from two to six hours post-dose, but the heart rate remained within the normal range for the other five cats.

At 15 and 25 mg/kg/day, signs of sedation observed in all cats included: ataxia, hypothermia, lethargy, uncoordinated behavior, decreased respiratory rate, and/or they were cold to the touch. The signs of sedation were observed for 12 hours after dosing. One cat in the 15 mg/kg/day dose group had muscle tremors at four hours post-dosing as well as ataxia, lethargy, hypothermia, and a decrease in heart rate. Cats had a decrease in heart rate with maximum effect at two to six hours, a few cats had bradycardia (106-122 bpm). The majority of cats maintained a normal blood pressure, but a few cats with bradycardia had a reflex hypertension. One cat in the 15 mg/kg/day dose group had bradycardia with reflex hypertension at two hours post-dose followed by a reflex tachycardia at six- and eight-hours post-dose.

STORAGE INFORMATION:

Store the bottle in a refrigerator at 2-8°C (36-46°F). Use bottle contents within six months after the first opening of the bottle. Up to one month of this time the bottle can be stored at or below 25°C (77°F).

HOW SUPPLIED:

BONQAT is packed in a clear 5 mL glass bottle containing 2 mL of BONQAT (pregabalin oral solution) at 50 mg/mL. The bottle has a child resistant closure and an oral dosing syringe adapter. The bottle is further packed into a carton with a package insert and an oral dosing syringe (1 mL).

Approved by FDA under NADA # 141-580

BONQAT® is a trademark of Orion Corporation.

Manufactured by:

ORION PHARMA
Orion Corporation
Turku, Finland

Distributed by:

zoetis
Zoetis Inc.
Kalamazoo, MI 49007

Issued: November 2023



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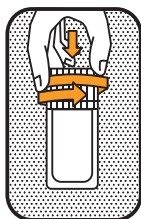
Bonqat® (pregabalin oral solution)

CLIENT INFORMATION SHEET FOR OWNER/HANDLER USE AND SAFETY

This sheet summarizes the basic information about BONQAT and does not replace the instructions from your veterinarian.

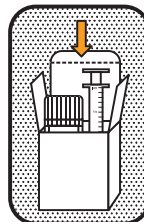
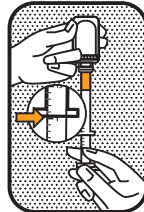
Talk to your veterinarian if you have questions regarding any part of this information or if you want to know more about BONQAT.

INSTRUCTIONS FOR USE



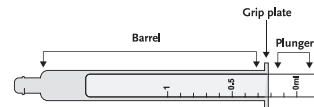
1. REMOVE CAP

Remove the cap from the bottle (press down and twist). Save the cap for reclosure.



2. CONNECT SYRINGE

Push the syringe tightly into the adapter located at the top of the bottle. Use only the syringe provided with the product.



3. SELECT DOSE

Turn the bottle with the syringe in place upside down. Pull the plunger out until the black line of correct dose (mL) (prescribed by your veterinarian) can be seen under the grip plate of the syringe barrel.

If the cat weighs more than 22 pounds, the total dose will need to be calculated and given in two separate doses as the syringe holds maximally only 1 mL of solution.

Don't leave the filled dosing syringe unattended while preparing the cat for administration.

4. GIVE DOSE

Gently place the syringe in the mouth of the cat and administer the dose to the base of the tongue by gradually pressing the plunger until the syringe is empty.

If the dose cannot be given directly into the mouth the dose can be mixed with a small amount of the cat's favorite food. Do not leave additional food available for the cat after the dose has been administered as extra food may delay the onset of effect.

5. BACK TO PACKAGE

Screw the bottle cap back on tightly and rinse the syringe with water. Dry the syringe and put it, the bottle, and this Client Information Sheet back into the carton.

Store the carton in the refrigerator. Wash your hands when finished.

What is BONQAT?

BONQAT is a prescription medicine containing pregabalin. It is used to treat cats afraid of travelling and veterinary visits. BONQAT is a colorless or slightly reddish solution packaged in a clear glass bottle.

Can BONQAT be given with food?

The product can be given with a small amount of food (e.g. teaspoon of moist food or about ten kibbles of dry food). Water can be freely available.

When should I administer BONQAT and what should I expect after administering BONQAT?

BONQAT should be given approximately 1.5 hours before the start of transportation. Your cat should be more relaxed and easier to handle when put into the carrier, during car travel and at the veterinary visit.

Can I give my cat more than one dose of BONQAT?

Do not repeat the dose of BONQAT. If the cat spits out part of the dose, vomits after treatment, drools excessively, or if BONQAT does not seem to have any effect, contact your veterinarian to discuss further treatment options.

What are the possible side effects that may occur in my cat after being given BONQAT?

Possible side effects include incoordination, tiredness, and vomiting. Some cats might be more sensitive to BONQAT; if your cat appears to be uncoordinated or overly tired, keep it warm and do not offer food or water until the effect of BONQAT has worn off. This will normally happen within a few hours. Contact your veterinarian if you have concerns.

What should I do if I have accidentally given my cat too much BONQAT?

Contact your veterinarian immediately.

What if I get BONQAT in my eyes, nose or mouth?

BONQAT can be absorbed into your body through your eyes or mucous membranes (such as your nose and mouth). If BONQAT comes in contact with your eyes or mucous membranes, flush with plenty of water for 15 minutes. If wearing contact lenses, eyes should be rinsed first, then remove contact lenses and continue rinsing. Seek medical advice if symptoms occur. Symptoms of exposure to BONQAT can include dizziness, sleepiness, blurred vision, weakness, dry mouth, and difficulty with concentration or attention.

What if I get BONQAT on my skin?

BONQAT does not absorb through intact skin, but if you have cuts or chapped skin, the drug can be absorbed into your body. In case of skin contact, wash immediately with large amounts of water. Remove contaminated clothing. Contact your physician if you have any questions or concerns.

To report side effects, call Zoetis Inc. at 1-888-963-8471.

What else should I know about BONQAT?

BONQAT should only be given to the cat for which it was prescribed. This sheet provides a summary of information about BONQAT. If you have any questions or concerns about BONQAT or its effects on your cat, talk to your veterinarian.

How do I store BONQAT?

Store the bottle with the dosing syringe and this Client Information Sheet in the carton inside a refrigerator at 2-8°C (36-46°F). Use bottle contents within six months after the first time you open the bottle. Up to one month of this time the bottle can be stored at room temperature (below 25°C (77°F)).

Keep BONQAT out of sight and reach of children and pets at all times.

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.

DESCRIPTION
SOLENSIA (frunevetmab injection) is a sterile injectable solution containing 7mg/mL of frunevetmab in histidine buffer (10 mM L-histidine monohydrochloride, 5% D-sorbitol, 0.01% polysorbate 20, adjusted to pH 6.0 by HCl/NaOH, quantity sufficient to 1 mL by Water for Injection.). Frunevetmab is a felinized immunoglobulin G monoclonal antibody (mAb), a murine antibody in which all regions of the mouse antibody are replaced with feline counterparts except for the complementarity-determining regions. Frunevetmab binds to nerve growth factor (NGF) to block NGF's effects. Such mAbs are commonly referred to as anti-NGF mAbs.

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.

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 SafetyWarnings
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.

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>.

CLINICAL PHARMACOLOGY
Mechanism of Action
Frunevetmab is a felinized monoclonal antibody that binds to nerve growth factor (NGF), reduces NGF binding to the tropomyosin receptor kinase A (TrkA) and p75^{NTR} receptors, and decreases signal transduction in cell types involved in pain. *In vitro* binding studies suggest that frunevetmab binds with high affinity to NGF, but does not bind to other neurotrophins, including human neurotrophin-3 (NT-3), feline and human neurotrophin-4 (NT-4), and human brain-derived neurotrophic factor (BDNF).
NGF has been found to be elevated in osteoarthritic joints of multiple species. Following a noxious stimulus, inflammatory cytokines and NGF are released by tissues of the joint. NGF binds to TrkA/p75^{NTR} receptors found on peripheral nerves, immune cells, endothelial cells, synoviocytes, and chondrocytes to induce peripheral sensitization, neurogenic inflammation, and increased pain perception.
Frunevetmab binds to NGF and prevents NGF/TrkA/p75^{NTR} cellular signaling. In *in vitro* studies, frunevetmab potentially inhibits NGF-mediated signaling as measured by reducing proliferation of TF-1 cells, a human erythroleukemia cell line, and functionally blocks NGF-induced neurite outgrowth in rat PC-12 neuronal cells.
NGF binds to TrkA receptors located on immune cells to elicit the release of additional proinflammatory mediators, including NGF itself. These inflammatory mediators lead to further peripheral sensitization involved in pain perception. Frunevetmab reduces the expression of these inflammatory mediators in rat PC-12 neuronal cells.
Pharmacokinetics
In a laboratory safety study in healthy cats administered SOLENSIA (frunevetmab injection) subcutaneously once every twenty-eight days for six consecutive doses (2.8 mg/kg), area under the plasma concentration time curve from time zero to the end of the dose interval (AUC) and maximum plasma concentration (C_{max}) increased in a less than dose proportional manner. Dosing every 28 days resulted in minimal accumulation over the course of five consecutive SOLENSIA doses of 2.8 mg/kg.

Table 3. Mean ± Standard Deviation frunevetmab pharmacokinetic parameters following subcutaneous dosing to laboratory and osteoarthritic cats.

Parameter	Laboratory Cats	Osteoarthritic Cats
Dose (mg/kg)	2.8	3.0
C _{max} (µg/mL)	42.8 ± 10.4	30.2 ± 5.5
T _{max} [#] (day)	3.5 (1-7)	7.0 (3-7)
AUC (day*µg/mL)	596 ± 245	653.0 ± 132
t _{1/2} (day)	9.8 ± 3.1	11.0 ± 2.5
Bioavailability (%)	Not determined	73.2 ± 14.8

[#]Median and range

In a cross-study comparison of the pharmacokinetics in healthy laboratory cats and cats with naturally occurring osteoarthritis, the median time to maximum concentration (T_{max}) was approximately 3.5 days longer in cats with osteoarthritis compared to healthy cats. C_{max} was greater in healthy cats compared to cats with osteoarthritis. Overall drug exposure (AUC) and half-life were similar between healthy cats and cats with osteoarthritis. Compared to an intravenous dose, subcutaneously-administered frunevetmab had a bioavailability of approximately 73% in cats with osteoarthritis.

In a field effectiveness study at the label dose in cats with osteoarthritis, steady-state was achieved after approximately 2 doses.

EFFECTIVENESS

Because of the limitations currently inherent in studies designed to assess chronic pain and the response to drugs intended to control chronic pain in cats, a weight of evidence approach was employed to determine if the overall evidence supported the conclusion that SOLENSIA was effective for the control of pain associated with osteoarthritis in cats. Based on current thinking, the endpoints used to evaluate the effectiveness of SOLENSIA for the control of osteoarthritic pain in cats are observer-reported measures conducted by either owners or veterinarians. When taken together, the results of the two studies described below demonstrate the effectiveness of SOLENSIA for the control of pain associated with osteoarthritis in cats. Additional information related to the evaluation of these studies, including the study endpoints, is available in the Freedom of Information Summary available at <https://animaldrugsatfda.fda.gov>.

Field Effectiveness Study #1

A 56-day, masked, randomized, controlled field study was conducted at 14 U.S. veterinary clinics. The study enrolled 126 client-owned cats with clinical signs of osteoarthritis (OA) confirmed by radiography and orthopedic examination; enrolled cats weighed 3.3 to 10.5 kg and were over 6 months old. The enrolled cats were randomized to treatment with frunevetmab injection (n=85) manufactured similar to SOLENSIA or vehicle control (n=41), administered subcutaneously on Days 0 and 28 or intravenously on Day 0 and subcutaneously on Day 28. Cats were dosed with frunevetmab injection or vehicle control based on body weight (2.5-7 kg cats received 1 mL, 7.1-14 kg cats received 2 mL).

Outcome measures for the control of pain associated with OA included comparison of the owner's evaluation of Client Specific Outcomes Measures (CSOM) at Days 14, 28, 42, and 56 compared to baseline (Day 0, before treatment); Owner Global Assessments on Days 28 and 56; and total orthopedic pain score completed by the veterinarian at screening and on Days 28 and 56. For the CSOM, treatment success was defined as a reduction of at least 2 in the total CSOM score compared with the score at baseline. Cats that had an increase in any individual CSOM activity score (regardless of the total CSOM score) were considered treatment failures. For the Owner Global Assessment, success was defined as an owner's impression of the response to treatment as Good or Excellent (versus Fair or Poor). Success was not defined for the veterinarian-assessed total orthopedic pain score. The proportion of cats considered treatment successes based on the owner CSOM assessment and the Owner Global Assessment was greater in the frunevetmab injection group compared to the control group for all assessments. The mean total orthopedic pain score was lower in the frunevetmab injection group compared to the control group at all post-dosing assessments.

Table 4. Percent CSOM Success by Assessment Day

Study Day	Frunevetmab Injection (%)	Vehicle Control (%)
14	61.8	60.6
28	68.6	55.9
42	73.5	55.9
56	80.0	47.1

Table 5. Percent Owner Global Assessment Success by Assessment Day

Study Day	Frunevetmab Injection (%)	Vehicle Control (%)
28	63.2	26.3
56	71.1	32.4

Table 6. Mean Veterinarian-Assessed Total Orthopedic Pain Score by Assessment Day

Study Day	Frunevetmab Injection (change from baseline)	Vehicle Control (change from baseline)
Screening	31.88	32.25
28	27.08 (-4.8)	28.03 (-4.22)
56	25.69 (-6.19)	27.75 (-4.5)

Field Effectiveness Study #2

A 112-day, masked, randomized, controlled field study was conducted at 21 U.S. veterinary clinics. The study enrolled 275 client-owned cats with clinical signs of osteoarthritis (OA) confirmed by radiography and orthopedic examination; enrolled cats weighed 2.5 to 11.4 kg and were 1.6 to 22.4 years old. The enrolled cats were randomized to treatment with SOLENSIA (n=182) or vehicle control (n=93), administered subcutaneously on Days 0, 28, and 56. Cats were dosed with SOLENSIA (frunevetmab injection) or vehicle control based on body weight (2.5-7 kg cats received 1 mL, 7.1-14 kg cats received 2 mL).

The primary outcome measure for success for the control of pain associated with OA was comparison of the owner's evaluation of CSOM at Day 56 compared to baseline (Day 0, before treatment). Treatment success was defined as a reduction of at least 2 in the total CSOM score at Day 56 compared with the score at baseline. Cats that had an increase in any individual CSOM activity score (regardless of the total CSOM score) or that received rescue analgesia prior to Day 56 were considered treatment failures. Secondary outcome measures included the total CSOM score on Days 28 and 84; Owner Global Assessments on Days 28, 56, and 84; and total orthopedic pain score completed by the veterinarian on Days 28, 56, and 84. For the Owner Global Assessment, success was defined as an owner's impression of the response to treatment as Good or Excellent (versus Fair or Poor). Success was not defined for the veterinary-assessed total orthopedic pain score. The proportion of cats considered treatment successes based on the owner CSOM assessment and the Owner Global Assessment was greater in the SOLENSIA group compared to the control group for all assessments. The mean total orthopedic pain score was lower in the SOLENSIA group compared to the control group at all post-dosing assessments.

Table 7. Percent CSOM Success by Assessment Day

Study Day	Solensia (%)	Vehicle Control (%)
28	66.9	51.6
56	75.1	64.8
84	76.5	67.3

Table 8. Percent Owner Global Assessment Success by Assessment Day

Study Day	Solensia (%)	Vehicle Control (%)
28	39.3	30.4
56	59.3	48.3
84	64.6	57.8

Table 9. Mean Veterinarian-Assessed Total Orthopedic Pain Score by Assessment Day

Study Day	Solensia (change from baseline)	Vehicle Control (change from baseline)
Screening	34.11	33.6
28	28.68 (-5.43)	29.1 (-4.5)
56	27.52 (-6.59)	28.67 (-4.93)
84	27.29 (-6.82)	28.54 (-5.06)

TARGET ANIMAL SAFETY

Frunevetmab injection was administered subcutaneously to healthy seven to eight-month-old cats (8 cats per group) at doses of 2.8 mg/kg (1X), 8.4 mg/kg (3X), and 14 mg/kg (5X) every 28 days for six consecutive doses. The control group (8 cats) received vehicle control injections. No clinically significant changes related to frunevetmab were observed among the cats for physical examination, lameness evaluation, and body weight.

The most common findings included vomiting and diarrhea observed sporadically in all groups. The highest frequency of vomiting occurred in the 1X group. Clinically relevant skin findings included abrasions, alopecia, or scabs mostly around the face and ears. These findings were noted in three 1X cats, three 3X cats, and one 5X cat. Another 1X cat developed a 2 cm ventral neck lesion following clipping and blood collection on Day 87. Although the initial irritation appeared related to the clipping, the unexpectedly severe and persistent pruritus and prolonged recovery were deemed possibly drug-related. The ulcerated skin lesion healed when self-trauma was prevented including the placement of an e-collar for the remainder of the study.

Flinching was occasionally associated with injections, most frequently noted during the first dosing in all dosing groups. Occasionally, scabs, small abrasions, or spot of alopecia were observed at the injection sites in all dosing groups. A few cats had transient swelling at injection sites.

Body tremors and shivering were noted in one 3X cat on Day 28.

Serum creatinine values in females were significantly higher in the 5X group compared to controls (P < 0.10). Creatinine values on Day 28 were significantly higher (P= 0.0239) in the 1X group compared to the control group. On Day 112, values were significantly higher (P = 0.0443) in the 5X group compared to the control group. Creatinine values did not exceed the reference ranges in cats of either sex at any time point.

There was one 1X cat with mild focal discoloration of the left tibiofemoral joint cruciate ligament on gross pathology. There was no correlative pathology on microscopic examination. No lameness was reported in this cat or any cat over the course of this study.

One 1X cat had a small amount of bilirubinuria on Day 43. This cat had dark urine and hematuria on Days 43-45 with no evidence of UTI on urinalysis. The cat responded to a canned prescription urinary diet and recovered. This cat also vomited food, bile or hair on three days and had diarrhea or dark, tarry stools on two days. Another 3X cat had a small amount of bilirubinuria on Day 83 and orange colored urine. This cat also had elevated serum lactate dehydrogenase activity at three time points.

There was one 5X cat that had a small amount of bilirubinuria at the end of the study with lipid sediment. This cat also had focal hepatic lipidosis on histopathology.

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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