

nocita[®]
(bupivacaine liposome injectable suspension)

REIMAGINE THE **LOOK** OF RECOVERY



Control your patient's post-operative pain with **the only FDA-approved long-acting local anesthetic** to keep them comfortable even after going home

See Prescribing Information for
full Product Information.

ALL SURGICAL PROCEDURES RESULT IN SOME DEGREE OF TISSUE TRAUMA AND ASSOCIATED PAIN

There are 3 main reasons to minimize acute, post-surgical pain¹:

- Ethical obligation to minimize pain and suffering
- Pain delays healing and return to function
- Unmanaged, acute pain can lead to chronic, maladaptive pain

Most patients are discharged from the hospital within 24-48 hours after surgery

- Need to provide analgesia for pain relief through the post-operative period at home

THE MOST EFFECTIVE CLASS OF ANALGESICS FOR PERI-OPERATIVE PAIN CONTROL

Local anesthetics (LAs) are one of the most effective means of preventing transduction and transmission of pain signals

- Block sodium channels on the nerve cell membrane
- Prevent propagation of action potentials (pain signals)
- Considered safe, with side effects generally limited to very high doses, and do not appear to delay tissue healing¹

Previous formulations have some limitations:

- Short duration of action (<8 hours) of available LAs
- Technical difficulty associated with some nerve and epidural blocks
- Complications of indwelling soaker catheters

Current guidelines advocate use of LAs for post-operative pain.^{1,2}

Effective pain management generally involves a balanced or multimodal strategy... Local Anesthetics (LAs) are the only class of drug that renders complete analgesia.

– 2015 AAHA/AAFP Pain Management Guidelines¹

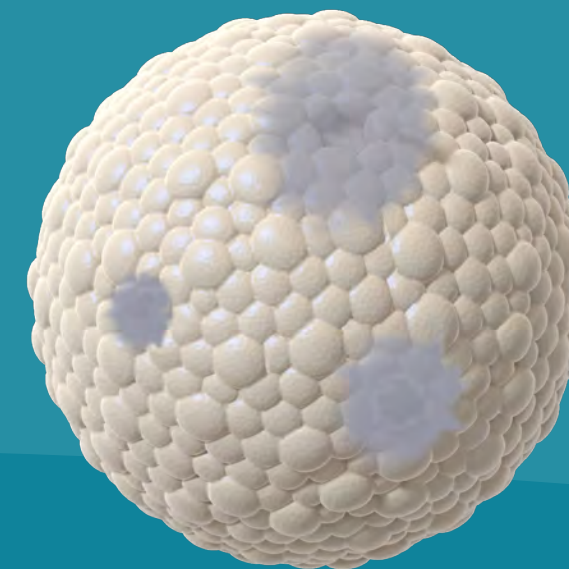


RAISING THE STANDARD OF CARE

Recovery care begins with NOCITA® (bupivacaine liposome injectable suspension)

NOCITA is a long-acting local anesthetic providing up to **72 hours of post-operative pain relief** with one dose for cranial cruciate ligament surgery in dogs and onychectomy in cats.

- Extended duration of action assists in preventing analgesic gaps in the first 72 hours post-surgery
- Provides consistent control after patient is discharged



Multivesicular liposomes

WHAT MAKES NOCITA DIFFERENT?

The extended-release bupivacaine technology used in NOCITA consists of multivesicular liposomes composed of hundreds to thousands of chambers encapsulating aqueous bupivacaine. The liposomes are microscopic structures designed such that bupivacaine is gradually released from vesicles over a period of time.

- Liposomes do not diffuse readily from where they are deposited
- Bupivacaine diffuses locally into surrounding tissues when it is gradually released from individual liposome vesicles

Please see Prescribing Information for full Product Information.

UP TO 72 HOURS POST-OPERATIVE PAIN CONTROL IN A SINGLE DOSE

NOCITA® (bupivacaine liposome injectable suspension) is the only long-acting, local anesthetic that controls post-op pain for up to 72 hours to help dogs undergoing cranial cruciate ligament (CCL) surgery recover comfortably, even after going home.

“In our hospital, we use fewer narcotics and plan our day to utilize the full vial, which allows for less ICU technician workload and improved hospital stay of the pet.”

– Andrew Jackson, DVM, DACVS



DOG INDICATION: For single-dose infiltration into the surgical site to provide local postoperative analgesia for cranial cruciate ligament surgery in dogs.

IMPORTANT SAFETY INFORMATION FOR DOGS: NOCITA® (bupivacaine liposome injectable suspension) is for local infiltration injection in dogs only. Do not use in dogs younger than 5 months of age, dogs that are pregnant, lactating or intended for breeding. Do not administer by intravenous or intra-arterial injection. Adverse reactions in dogs may include discharge from incision, incisional inflammation and vomiting. Avoid concurrent use with bupivacaine HCl, lidocaine or other amide local anesthetics. Please see the full Prescribing Information for more detail.

CLINICAL EFFICACY IN DOGS

NOCITA® (bupivacaine liposome injectable suspension):
Proven pain control for up to 72 hours following canine CCL* surgery

Clinical efficacy study design³

- 182 client-owned dogs undergoing knee surgery
- Randomized, prospective, blinded, placebo-controlled, multicenter study
- 5.3 mg/kg by infiltration injection during surgical closure
- Time intervals for evaluating treatment success were 0-24 hours, 0-48 hours and 0-72 hours
- Success ($P < 0.05$) was defined as no pain intervention**

EFFECTIVENESS RESULTS IN DOGS

	NOCITA®	Saline	p-value
Primary endpoint 0-24 hours	68.8%	36.5%	0.0322
Secondary endpoint [†] 0-48 hours	64.3%	34.6%	0.0402
Secondary endpoint [†] 0-72 hours	61.6%	32.7%	0.0432

*Cranial cruciate ligament

**Pain intervention = rescue analgesia or score of ≥ 6 on Glasgow Composite Measure Pain Scale (Licensed from New Metrics)

[†]Failures carried forward from each previous interval

CONCLUSION

- Percent of treatment success for the NOCITA-treated group was statistically significantly greater than the placebo-treated group over 0-24 hours
- Greater percent successes through 48 and 72 hours support effective use of NOCITA for up to 72 hours of analgesia



SAFETY RESULTS FROM FIELD STUDY IN DOGS

NOCITA® (bupivacaine liposome injectable suspension): Demonstrated safety and was well-tolerated in dogs following cranial cruciate ligament surgery³

Adverse Reaction	NOCITA® N = 123	Saline N = 59
Discharge from the Incision	4 (3.3%)	0 (0.0%)
Incisional Inflammation (erythema and/or edema)	3 (2.4%)	0 (0.0%)
Vomiting	3 (2.4%)	0 (0.0%)
Abnormalities on Urinalysis (isosthenuria ±proteinuria)	2 (1.6%)	0 (0.0%)
Increased ALP	2 (1.6%)	0 (0.0%)
Surgical Limb Edema ±Erythema	1 (0.8%)	3 (5.1%)
Soft Stool/Diarrhea	1 (0.8%)	1 (1.7%)
Inappetence	1 (0.8%)	1 (1.7%)
Fever	1 (0.8%)	0 (0.0%)



NOCITA DOSING FOR DOGS

- Administer at a dose of 5.3 mg/kg (0.4 ml/kg)
- Can be given by tissue infiltration injection during surgery for post-operative analgesia following cranial cruciate ligament surgery
- NOCITA is for single-dose administration only
- Avoid concurrent use with bupivacaine HCl, lidocaine or other amide local anesthetics



ADMINISTRATION IN DOGS

A. Incision

Medial view of the hind limb

Moving Needle Injection Technique

Introduce tip of the needle into the tissue

Gradually withdraw needle while injecting

B. Fascia Layer Infiltration (post joint capsule closure)

C. Deep Subcutaneous Tissue Infiltration (post retinacular fascia closure)

D. Superficial Subcutaneous Tissue Infiltration (prior to subcuticular closure)

Administer approximately 75% of total dose volume in the surgical area (joint capsule, fascia, hardware attachment sites, osteotomies, subcutaneous layer, etc.)

Administer approximately 25% of total dose volume to ensure continuous deposition around entire incision

INDICATION: For single-dose infiltration into the surgical site to provide local postoperative analgesia for cranial cruciate ligament surgery in dogs.

IMPORTANT SAFETY INFORMATION FOR DOGS: NOCITA® (bupivacaine liposome injectable suspension) is for local infiltration injection in dogs only. Do not use in dogs younger than 5 months of age, dogs that are pregnant, lactating or intended for breeding. Do not administer by intravenous or intra-arterial injection. Adverse reactions in dogs may include discharge from incision, incisional inflammation and vomiting. Avoid concurrent use with bupivacaine HCl, lidocaine or other amide local anesthetics. Please see the full Prescribing Information for more detail.

LONG-ACTING, POST-OPERATIVE PAIN CONTROL IN A SINGLE DOSE

NOCITA® (bupivacaine liposome injectable suspension) is the only long-acting, local anesthetic that's approved for use as a peripheral nerve block to provide up to 72 hours of regional post-operative pain control with just one dose for cats undergoing onychectomy.



CAT INDICATION: For use as a peripheral nerve block to provide regional postoperative analgesia following onychectomy in cats.

IMPORTANT SAFETY INFORMATION FOR CATS: NOCITA® (bupivacaine liposome injectable suspension) is for use as a peripheral nerve block in cats only. Do not use in cats younger than 5 months of age, that are pregnant, lactating, or intended for breeding. Do not administer by intravenous or intra arterial injection. Adverse reactions in cats may include elevated body temperature, infection or chewing/licking at the surgical site. Avoid concurrent use with bupivacaine HCl, lidocaine or other amide local anesthetics. Please see the full Prescribing Information for more detail.

CLINICAL EFFICACY IN CATS

NOCITA® (bupivacaine liposome injectable suspension): Provides up to 72 hours of regional post-operative analgesia following feline onychectomy

Clinical effectiveness study design⁴

- 241 client-owned cats undergoing owner-elective onychectomy
- Randomized, prospective, blinded, placebo-controlled, multicenter study
- 5.3 mg/kg/forelimb administered once prior to surgery as a 4-point nerve block, as described in the Product Insert
- Time intervals for evaluating treatment success were 0-24 hours, 0-48 hours and 0-72 hours
- Success ($P < 0.05$) was defined as no pain intervention*

EFFECTIVENESS RESULTS IN CATS

	NOCITA®	Saline	p-value
Primary endpoint 0-24 hours	75.2%	40.3%	0.0252
Secondary endpoint 0-48 hours	68.7%	34.7%	0.0395
Secondary endpoint 0-72 hours	68.4%	35.3%	0.0452

*Pain intervention = rescue analgesia or score of ≥ 6 on Modified UNESP-Botucatu Multidimensional Composite Pain (Brondani) Scale



TREATMENT SUCCESS

- Percent of treatment success for the NOCITA-treated group was statistically significantly greater than the placebo-treated group over 0-24 hours
- Greater percent successes through 48 and 72 hours support effective use of NOCITA for up to 72 hours of analgesia

SAFETY RESULTS FROM FIELD STUDY IN CATS

NOCITA® (bupivacaine liposome injectable suspension): Demonstrated safety as a peripheral nerve block in cats undergoing onychectomy⁴

Adverse Reaction	NOCITA® N = 120	Saline N = 121
Elevated body temperature	8 (6.7%)	5 (4.1%)
Surgical site infection	4 (3.3%)	1 (0.8%)
Chewing/licking of surgical site	3 (2.5%)	2 (1.7%)
Diarrhea	2 (1.7%)	1 (0.8%)
Injection site erythema	1 (0.8%)	0 (0.0%)
Swelling of paw; erythematous digits	1 (0.8%)	0 (0.0%)

NOTE: Surgical site is NOT Injection site



NOCITA DOSING FOR CATS

FDA-approved for use as a peripheral nerve block prior to onychectomy in cats

- Administer 5.3 mg/kg/forelimb once prior to surgery as a 4-point nerve block, as described in the Product Insert
- NOCITA is for administration only once prior to surgery
- Do not dilute NOCITA prior to use as a nerve block in cats
- Avoid concurrent use with bupivacaine HCl, lidocaine or other amide local anesthetics

ADMINISTRATION IN CATS



Legend

Needle insertion point

Drug injection point

SpU - Styloid process of the ulna

ACb - Accessory carpal bone

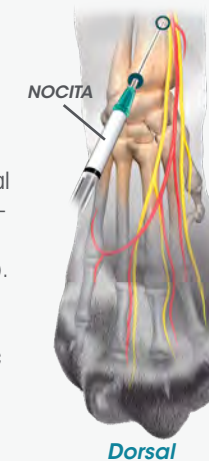
Needle withdrawal + drug injection

Needle redirection to a 90° angle to the palmar plane

A.

0.14 mL/kg (35%) Superficial Branch of the Radial Nerve

At the center of the limb, on the dorsal aspect at the level of the antebrachio-carpal joint, insert the needle subcutaneously with the bevel up (●). Advance the needle subcutaneously and inject (°) adjacent to the confluence of the accessory cephalic and cephalic veins.



B.

0.08 mL/kg (20%) Dorsal Branch of the Ulnar Nerve

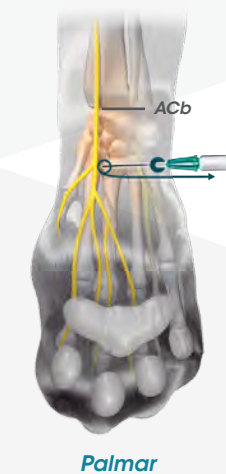
Palpate a groove between the accessory carpal bone (ACb, in the base of the carpal pad) and the styloid process of the ulna (SpU). Distal to this groove, insert the needle subcutaneously with the bevel up and advance the needle proximally. Inject once the tip reaches the midpoint of the groove.



C.

0.16 mL/kg (40%) Median Nerve and Superficial Branch of the Palmar Branch of the Ulnar Nerve

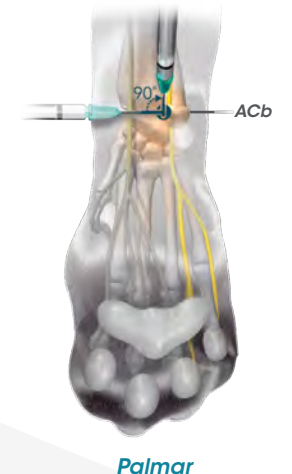
Insert the needle subcutaneously with the bevel up lateral to the distal tip of the accessory carpal pad and advance the needle medially 2/3 the width of the limb, until the tip is located near the base of the first digit. Inject 2/3 of the volume at this point and the remaining volume while withdrawing the needle (solid teal arrow). Gently massage for 5 seconds.



D.

0.02 mL/kg (5%) Deep Branch of the Palmar Branch of the Ulnar Nerve

Orient the needle perpendicular to the long axis of the limb at the level of the ACb. Insert the needle subcutaneously and advance the needle laterally until it contacts the medial aspect of the ACb. Redirect the needle dorsally by rotating the needle 90°, advance it along the medial side of the ACb 2-3 mm until it penetrates the flexor retinaculum, and inject.



INDICATION: For use as a peripheral nerve block to provide regional postoperative analgesia following onychectomy in cats.

IMPORTANT SAFETY INFORMATION FOR CATS: NOCITA® (bupivacaine liposome injectable suspension) is for use as a peripheral nerve block in cats only. Do not use in cats younger than 5 months of age, that are pregnant, lactating, or intended for breeding. Do not administer by intravenous or intra-arterial injection. Adverse reactions in cats may include elevated body temperature, infection or chewing/licking at the surgical site. Avoid concurrent use with bupivacaine HCl, lidocaine or other amide local anesthetics. Please see the full Prescribing Information for more detail.

EXTENDED, POST-OPERATIVE PAIN CONTROL WITH JUST ONE DOSE

Recovery care begins with NOCITA® (bupivacaine liposome injectable suspension)

- All surgical procedures result in some degree of tissue trauma and associated pain¹
- Local anesthetics are one of the most effective means of preventing pain, however, previous options have limitations
- NOCITA is the only long-acting local anesthetic that **controls post-op pain with one dose for up to 72 hours** following canine CCL surgery or feline onychectomy



AVAILABLE IN TWO SIZES

NOCITA is available in convenient 10 mL and 20 mL vials.

To learn more, visit nocita.aratana.com
or call Aratana Customer Care at
1-844-ARATANA (272-8262).

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References:

1. Epstein ME, Rodanm I, Griffenhagen G, et al. 2015 AAHA/AAFP pain management guidelines for dogs and cats. *J Feline Med Surg.* 2015;17(3):251-272.
2. Mathews K, Kronen PW, Lascelles D, et al. Guidelines for recognition, assessment and treatment of pain. *J Small Ani.* 2014;55(6):E10-E68.
3. NOCITA Freedom of Information Summary, NADA 141-461, 12 AUG 2016.
4. NOCITA Freedom on Information Summary, Supplemental NADA 141-461, 03 AUG 2018.