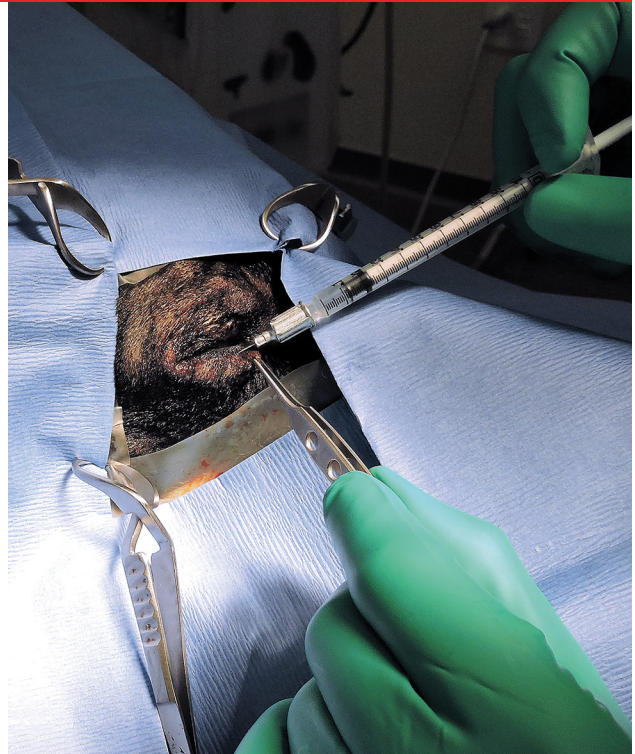


Enucleation & Pharmacologic Ciliary Body Ablation of the Eye

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Although the primary goals in ophthalmology are to preserve vision and maintain a healthy globe, salvage procedures such as enucleation or ciliary body ablation (CBA) may be necessary in some cases.

Enucleation

Enucleation is the most commonly performed orbital surgical procedure in veterinary medicine.¹ Globe enucleation is indicated in painful and irreversibly blind eyes with severe ocular pathology. Such pathologies may include intraocular neoplasia unamenable to other forms of surgical and/or medical treatment, uncontrollable endophthalmitis or panophthalmitis, unregulated glaucoma, perforating ocular trauma, and severe ocular trauma with intraocular hemor-

rhage.¹⁻³ Enucleation may also be indicated in cases in which the owner cannot provide long-term treatment to maintain comfort in a patient with a diseased eye.³

The most common immediate post-operative complications of enucleation are hemorrhage, orbital swelling, hemorrhagic discharge from the wound, and periorbital skin bruising. Cold compresses, pressure bandages, and patient sedation are usually sufficient to control hemorrhage.¹ Long-term complications can include draining fistulas that may result from incomplete removal of secretory tissue (eg, conjunctiva with its goblet cells, nictitating membrane gland) and/or the lacrimal caruncle at the medial canthus.¹

Enucleation is the most commonly performed orbital surgical procedure in veterinary medicine.¹

CBA = ciliary body ablation

Ciliary Body Ablation

In CBA, the ciliary body is ablated via injection of a cytotoxic drug—most often gentamicin, though cidofovir use has been described in a study⁴—into the vitreous chamber to eliminate aqueous humor production and achieve low intraocular pressure (IOP) readings.

In contrast to enucleation, a pharmacologic CBA is indicated only to treat and provide comfort in end-stage blind, glaucomatous eyes in cases in which medical and other potential therapies (eg, surgery) for primary glaucoma have failed. CBA is not indicated in cats because of risk for intraocular sarcoma development.⁵ It is imperative that CBA *only* be used in dogs with uncontrolled primary glaucoma and in otherwise disease-free eyes.⁶

A recent study showed a 39.5% likelihood of post-CBA intraocular tumor formation in dogs.⁶ If tumor formation is detected, subsequent enucleation and histopathologic evaluation should be recommended. It is unclear if gentamicin causes tumor formation or if the injection augments a potential pre-existing intraocular tumor.⁶ Globe evaluation may have been incomplete in

this study (none of the globes underwent ocular ultrasonography); malignant or premalignant processes may have been present before drug injection.⁶

According to the literature, CBA has an approximate success rate of 65% to 86%.^{1,7} Cosmetic outcome is variable. All dogs will develop cataracts, the cornea often becomes fibrotic, and phthisis bulbi (ie, shrinking of the globe) will occur at varying degrees. Intraocular hemorrhage is the main immediate complication, and some dogs require long-term treatment for intraocular inflammation. Heavy sedation or short-acting general anesthesia is required.

Evisceration

An evisceration procedure involves removal of all intraocular content through a limbal or scleral incision and replacement with an appropriately sized silicone sphere. Cosmetic results are usually acceptable. The main indication is end-stage primary glaucoma that has become unresponsive to medical or surgical therapy. Globes with intraocular infection or neoplasia are not candidates for a successful evisceration with an intraocular prosthesis procedure.

For information about in-depth surgical technique for evisceration, see *Suggested Reading*, page 42.

CBA = ciliary body ablation
IOP = intraocular pressure

STEP-BY-STEP ENUCLEATION Subconjunctival Enucleation with Intraorbital Prosthesis Placement

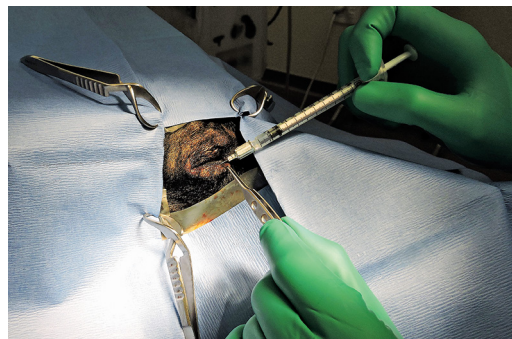
With globe enucleation, the eye, eyelid, third eyelid (including lacrimal gland), and conjunctiva are excised. The transpalpebral and lateral approaches to enucleation minimize exposure of the orbit to contaminants of the ocular surface, intraocular infections, and/or neoplasms.¹⁻³ The subconjunctival approach is the simplest, fastest, and most frequently used technique.¹⁻³

WHAT YOU WILL NEED

- ▶ Sterile drapes, gown, and gloves
- ▶ Extraocular pack with Mayo scissors, tenotomy scissors, Bishop-Harmon forceps, Brown-Adson forceps, enucleation scissors, Derf needle holder, suture scissors, and enucleation scissors (with or without an eyelid speculum)
- ▶ Sterile orbital prosthesis
- ▶ Sterile gauze
- ▶ 4-0 or 5-0 absorbable and nonabsorbable suture

STEP 1

Clip and prepare the peri-orbital skin and eyelids for aseptic surgery. Using a diluted aqueous povidone-iodine solution (5%-10%), copiously lavage the conjunctival sac and globe surface.



Author Insights

Povidone-iodine solutions are used in ophthalmologic procedures to avoid corneal and conjunctival ulcerations. In enucleation, it is important to protect the contralateral eye from surface injury.

A preoperative retrobulbar block and eyelid block with a sodium channel blocker may improve intra- and initial perioperative analgesia and decrease the need for initial postoperative rescue analgesia.⁸

STEP 2

After draping the periocular region, perform a lateral canthotomy. (A) Use Mayo scissors to facilitate increased globe exposure, and remove 3 to 5 mm of the inferior and superior eyelid margin. (B) Using Brown-Adson tissue forceps, grasp the nictitating membrane, including its lacrimal gland, then protract and dissect at the base. Blot with gauze sponges and apply digital pressure to control hemorrhage.

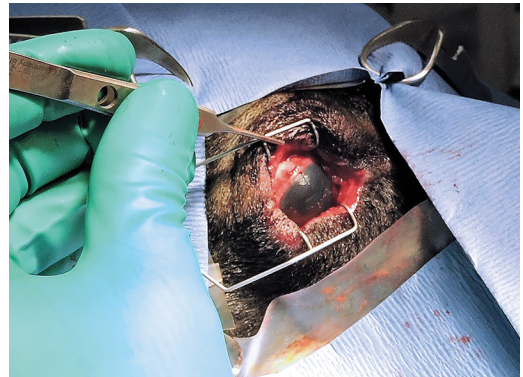


Author Insight

Removing the inferior lid before the superior lid is recommended, as doing so can prevent (sometimes moderate) hemorrhaging on the second lid incision.

STEP 3

With tenotomy scissors, incise the bulbar conjunctiva and Tenon capsule at the 12 o'clock position approximately 5 mm posterior to the limbus. Using blunt dissection, continue the dissection plane between the sclera and Tenon capsule deeper into the orbit and in the medial and lateral direction to create a 180° to 360° perilimbal incision. Identify and incise the insertions of all extraocular muscles at their tendinous insertions. Avoid incising the muscle bellies, as this can cause unnecessary hemorrhage.



STEP 4

After excising all major rectus muscles, displace the globe, which should be more mobile, in the anterior direction. Avoid excessive anterior traction on the globe, as this can cause a reduction in heart rate (ie, oculocardiac reflex), damage to the optic chiasm (particularly in cats and dolichocephalic dogs), and subsequent blindness to the contralateral eye.³

Use enucleation scissors to sever the optic nerve and retractor bulbi muscle close to their scleral attachments. Diffuse, often mild hemorrhage may occur; control this by placing 1 to 2 surgical sponges in the orbit for a short period, then carefully remove them without dislodging initial clot formation.



Author Insights

Ligation of the canine optic nerve is not necessary before globe removal. The nerve does not contain a central retinal vein as described in the human literature.

If hemorrhage continues after a few minutes of digital pressure, a hemostatic agent (eg, gelatin sponges) can be placed in the orbit.

STEP 5

Remove the remaining conjunctiva and lacrimal caruncle. (A and B) Inspect the orbit for remaining conjunctival tissue and abnormalities. Close the wound with or without intraorbital prosthesis placement. (C) If needed, use silicone or methyl methacrylate spheres to prevent postoperative skin depression into the orbit. Sphere diameters vary from 12 to 28 mm, depending on orbit size. (D) After placement, the sphere should fit into the orbit without causing excessive pressure on the remaining orbital content.



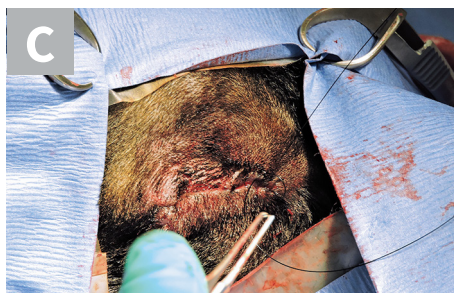
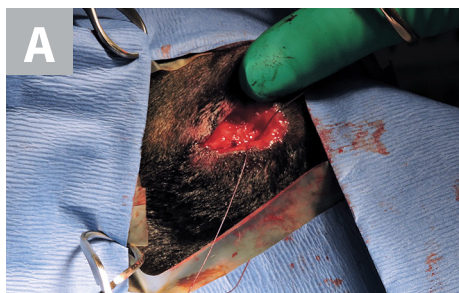
Author Insight

Contraindications for intraorbital prosthesis placement are bacterial infections and neoplasms in the orbit.¹⁻³



STEP 6

(A, B, and C) Close the wound using 4-0 or 5-0 absorbable suture material and a combination of simple interrupted and simple continuous suture patterns. Close the lid incision in a routine fashion using 4-0 to 5-0 nonabsorbable suture. Postoperative analgesia is advised.



WHAT YOU WILL NEED

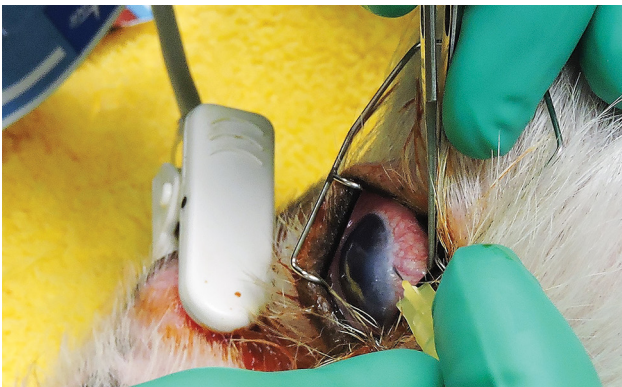
- ▶ Sterile gloves
- ▶ Eyelid speculum
- ▶ Bishop-Harmon forceps
- ▶ 25-g and 30-g needles
- ▶ 1-mL syringe
- ▶ Tonometer

STEP 1

Using a diluted aqueous povidone-iodine solution, aseptically prepare the conjunctival surface and periocular surface.

STEP 2

Place an eyelid speculum, and use small forceps to stabilize the globe. Using a 30-g needle, perform an anterior chamber aqueocentesis at the dorsal limbus to decrease preinjection IOP and to allow aqueous humor to exit during the injection.



Author Insight

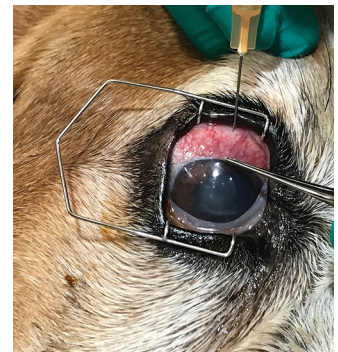
Care should be taken not to lacerate the iris during needle insertion, as this will likely cause unsightly intraocular hemorrhage. The needle should be inserted in a bevel-up fashion, pointing slightly toward the central cornea.

STEP-BY-STEP CILINARY BODY ABLATION

CBA is performed by injecting a cytotoxic drug into the posterior segment of the globe. The ciliary body (ie, the structure responsible for aqueous humor production) will be destroyed.

STEP 3

Use a 1-mL syringe with a 25-g needle to inject a combination of 30 to 40 mg of gentamicin and a long-acting steroid (eg, dexamethasone ≤ 1 mg, triamcinolone ≤ 2 mg) into the posterior segment (vitreous). Do not exceed the maximum dose (based on the individual patient) of either medication. Alternatively, inject a long-acting steroid subconjunctivally. Insert the needle approximately 6 mm posterior to the limbus and direct it caudally to avoid the lens and the vascular ciliary body.



STEP 4

Assess IOP immediately postinjection (target, <15 mm Hg). Remove any additional aqueous humor if IOP is >30 mm Hg. Quickly taper topical antiglaucoma medications.

FOLLOW-UP

Discontinue topical antiglaucoma medications within 2 weeks of the procedure. Use oral anti-inflammatory drugs, additional pain medication, and a topical antibiotic for 1 to 2 weeks postinjection. Measure IOP 2 to 4 weeks postprocedure, once topical antiglaucoma medications have been discontinued. ■

See page 42 for references.

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Suggested Reading

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NexGard® (afoxolaner) Chewables

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

Description:

NexGard® (afoxolaner) is available in four sizes of beef-flavored, soft chewables for oral administration to dogs and puppies according to their weight. Each chewable is formulated to provide a minimum afoxolaner dosage of 1.14 mg/lb (2.5 mg/kg). Afoxolaner has the chemical composition 1-Naphthalenecarboxamide, 4-[5-[3-chloro-5-(trifluoromethyl)-phenyl]-4,5-dihydro-5-(trifluoromethyl)-3-isoxazolyl]-N-[2,2,2-trifluoroethyl]amino]ethyl.

Indications:

NexGard kills adult fleas and is indicated for the treatment and prevention of flea infestations (*Ctenocephalides felis*), and the treatment and control of Black-legged tick (*Ixodes scapularis*), American Dog tick (*Dermacentor variabilis*), Lone Star tick (*Amblyomma americanum*), and Brown dog tick (*Rhipicephalus sanguineus*) infestations in dogs and puppies 8 weeks of age and older, weighing 4 pounds of body weight or greater, for one month.

Dosage and Administration:

NexGard is given orally once a month, at the minimum dosage of 1.14 mg/lb (2.5 mg/kg).

Dosing Schedule:

Body Weight	Afoxolaner Per Chewable (mg)	Chewables Administered
4.0 to 10.0 lbs.	11.3	One
10.1 to 24.0 lbs.	28.3	One
24.1 to 60.0 lbs.	68	One
60.1 to 121.0 lbs.	136	One
Over 121.0 lbs.	Administer the appropriate combination of chewables	

NexGard can be administered with or without food. Care should be taken that the dog consumes the complete dose, and treated animals should be observed for a few minutes to ensure that part of the dose is not lost or refused. If it is suspected that any of the dose has been lost or if vomiting occurs within two hours of administration, redose with another full dose. If a dose is missed, administer NexGard and resume a monthly dosing schedule.

Flea Treatment and Prevention:

Treatment with NexGard may begin at any time of the year. In areas where fleas are common year-round, monthly treatment with NexGard should continue the entire year without interruption.

To minimize the likelihood of flea reinfestation, it is important to treat all animals within a household with an approved flea control product.

Tick Treatment and Control:

Treatment with NexGard may begin at any time of the year (see **Effectiveness**).

Contraindications:

There are no known contraindications for the use of NexGard.

Warnings:

Not for use in humans. Keep this and all drugs out of the reach of children. In case of accidental ingestion, contact a physician immediately.

Precautions:

The safe use of NexGard in breeding, pregnant or lactating dogs has not been evaluated. Use with caution in dogs with a history of seizures (see **Adverse Reactions**).

Adverse Reactions:

In a well-controlled US field study, which included a total of 333 households and 615 treated dogs (415 administered afoxolaner; 200 administered active control), no serious adverse reactions were observed with NexGard.

Over the 90-day study period, all observations of potential adverse reactions were recorded. The most frequent reactions reported at an incidence of >1% within any of the three months of observations are presented in the following table. The most frequently reported adverse reaction was vomiting. The occurrence of vomiting was generally self-limiting and of short duration and tended to decrease with subsequent doses in both groups. Five treated dogs experienced anorexia during the study, and two of those dogs experienced anorexia with the first dose but not subsequent doses.

Table 1. Dogs With Adverse Reactions.

	Treatment Group			
	Afoxolaner		Oral active control	
	N ¹	% (n=415)	N ²	% (n=200)
Vomiting (with and without blood)	17	4.1	25	12.5
Dry/Flaky Skin	13	3.1	2	1.0
Diarrhea (with and without blood)	13	3.1	7	3.5
Lethargy	7	1.7	4	2.0
Anorexia	5	1.2	9	4.5

¹Number of dogs in the afoxolaner treatment group with the identified abnormality.

²Number of dogs in the control group with the identified abnormality.

In the US field study, one dog with a history of seizures experienced a seizure on the same day after receiving the first dose and on the same day after receiving the second dose of NexGard. This dog experienced a third seizure one week after receiving the third dose. The dog remained enrolled and completed the study. Another dog with a history of seizures had a seizure 19 days after the third dose of NexGard. The dog remained enrolled and completed the study. A third dog with a history of seizures received NexGard and experienced no seizures throughout the study.

To report suspected adverse events, for technical assistance or to obtain a copy of the MSDS, contact Merial at 1-888-637-4251 or www.merial.com/NexGard. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at <http://www.fda.gov/AnimalVeterinary/SafetyHealth>.

Mode of Action:

Afoxolaner is a member of the isoxazoline family, shown to bind at a binding site to inhibit insect and acarine ligand-gated chloride channels, in particular those gated by the neurotransmitter gamma-aminobutyric acid (GABA), thereby blocking and post-synaptic transfer of chloride ions across cell membranes. Prolonged afoxolaner-induced hyperexcitability results in uncontrolled activity of the central nervous system and death of insects and acarines. The selective toxicity of afoxolaner between insects and acarines and mammals may be inferred by the differential sensitivity of the insects and acarines GABA receptors versus mammalian GABA receptors.

Effectiveness:

In a well-controlled laboratory study, NexGard began to kill fleas four hours after initial administration and demonstrated >99% effectiveness at eight hours. In a separate well-controlled laboratory study, NexGard demonstrated 100% effectiveness against adult fleas 24 hours post-infestation for 35 days, and was ≥ 93% effective at 12 hours post-infestation through Day 21, and on Day 35. On Day 28, NexGard was 81.1% effective 12 hours post-infestation. Dogs in both the treated and control groups that were infested with fleas on Day -1 generated flea eggs at 12- and 24-hours post-treatment (0-11 eggs and 1-17 eggs in the NexGard treated dogs, and 4-90 eggs and 0-118 eggs in the control dogs, at 12- and 24-hours, respectively). At subsequent evaluations post-infestation, fleas from dogs in the treated group were essentially unable to produce any eggs (0-1 eggs) while fleas from dogs in the control group continued to produce eggs (1-141 eggs).

In a 90-day US field study conducted in households with existing flea infestations of varying severity, the effectiveness of NexGard against fleas on the Day 30, 60 and 90 visits compared with baseline was 98.0%, 99.7%, and 99.9%, respectively. Collectively, the data from the three studies (two laboratory and one field) demonstrate that NexGard kills fleas before they can lay eggs, thus preventing subsequent flea infestations after the start of treatment of existing flea infestations.

In well-controlled laboratory studies, NexGard demonstrated >97% effectiveness against *Dermacentor variabilis*, >94% effectiveness against *Ixodes scapularis*, and >93% effectiveness against *Rhipicephalus sanguineus*. 48 hours post-infestation for 30 days. At 72 hours post-infestation, NexGard demonstrated >97% effectiveness against *Amblyomma americanum* for 30 days.

Animal Safety:

In a margin of safety study, NexGard was administered orally to 8 to 9-week-old Beagle puppies at 1, 3, and 5 times the maximum exposure dose (6.3 mg/kg) for three treatments over 28 days, followed by three treatments every 14 days for a total of six treatments. Dogs in the control group were sham-dosed. There were no clinically-relevant effects related to treatment on physical examination, body weight, food consumption, clinical pathology (hematology, clinical chemistries, or coagulation tests), gross pathology, histopathology or organ weights. Vomiting occurred throughout the study, with a similar incidence in the treated and control groups, including one dog in the 5x group that vomited four hours after treatment.

In a well-controlled field study, NexGard was used concomitantly with other medications, such as vaccines, anthelmintics, antibiotics (including topicals), steroids, NSAIDs, anesthetics, and antihistamines. No adverse reactions were observed from the concomitant use of NexGard with other medications.

Storage Information:

Store at or below 30°C (86°F) with excursions permitted up to 40°C (104°F).

How Supplied:

NexGard is available in four sizes of beef-flavored soft chewables: 11.3, 28.3, 68 or 136 mg afoxolaner. Each chewable size is available in color-coded packages of 1, 3 or 6 beef-flavored chewables.

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