KEEP A CLEAR EYE
on canine ophthalmic health

for Canine Bacterial Eye Infections **Gentocin® Durafilm®**
(GENTAMICIN SULFATE AND BETAMETHASONE)
Ophthalmic Solution

A drop that ACTS like an ointment

for Chronic Canine KCS* **Optimmune®**
(0.2% Cyclosporine, USP)
Ophthalmic Ointment

Consistent, dependable quality

MERCK
Animal Health

Gentocin® Durafilm® Ophthalmic Solution

Three powerful reasons to treat canine bacterial eye infections with Gentocin Durafilm

- **GENTAMICIN SULFATE**—A broad-spectrum antibiotic with highly effective results against gram-positive bacterial and gram-negative bacterial infections of the eye
- **BETAMETHASONE ACETATE**—A rapid-acting anti-inflammatory corticosteroid that provides symptomatic relief from bacterial, allergic, or traumatic tissue responses
- **DURAFILM**—An aqueous colloidal solution that coats the conjunctiva to maintain extended contact with the active, therapeutic ingredients

A proven performer that goes on like a drop… coats like an ointment

- Prolonged contact, efficacy, and safety
- Unique formulation with a history of success
- Supports treatment and compliance

Gentocin® Durafilm®
(GENTAMICIN SULFATE AND BETAMETHASONE)
Ophthalmic Solution

Corticosteroids are contraindicated in initial treatment of corneal ulcers. The antibiotic sensitivity of the infective organism in bacterial conjunctivitis should be determined prior to the use of this preparation. Cushing's syndrome in dogs has been reported in association with prolonged or repeated steroid therapy. A transient stinging sensation, usually expressed as some form of resentment by the animal, following topical application of the drug, has been noted in a small number of cases. Usually this does not require discontinuance of therapy. See Package Insert for full safety information.

Optimmune® Ophthalmic Ointment

In cases of KCS* and Pannus, Optimmune treats the underlying immune-mediated cause[1]

- Increases natural tear production by restoring lacrimal gland production†
- Promotes and protects conjunctival and corneal health while reducing inflammation
- Offers prolonged contact time, allowing a safer and lower dose concentration
- Sterile and preservative-free formulation—reduces risk of irritation or secondary infection
- Stable shelf life of up to 24 months; refrigeration not required
- Schirmer Tear Test can rule out KCS or establish a baseline in predisposed breeds

Left untreated, canine KCS and Pannus can lead to blindness[2]—choose Optimmune for consistent quality, safety, efficacy, and dose concentration

Incidence of KCS

Chronic and/or undiagnosed KCS has been shown to affect over 8% of dogs in predisposed breeds, and over 4.5% of the general canine population.[3]

Optimmune®
(0.2% Cyclosporine, USP)
Ophthalmic Ointment

For ophthalmic use in dogs only. The safety of OPTIMMUNE® Ophthalmic Ointment has not been determined in cases of preexisting viral or fungal ocular infections, nor in puppies, pregnant bitches, or dogs used for breeding. In clinical trials, ocular and periocular inflammatory reactions, transient hyperemia, epiphora, mild discomfort of the eye, and mild alopecia were reported in a small number of treated dogs. For full prescribing information, including directions for use, precautions and adverse reactions, see accompanying package insert.

*KCS=keratoconjunctivitis sicca.

†Clinical improvement in cases of KCS is not necessarily dependent on an increase in aqueous tear production.

References: 1. Williams DL. Immunopathogenesis of keratoconjunctivitis sicca in the dog. *Vet Clin North Am Small Anim Pract.* 2008;38:251-268. **2.** Sanchez RF, Innocent G, Mould J, Billson FM. Canine keratoconjunctivitis sicca: disease trends in a review of 229 cases. *J Small Anim Pract.* 2007;48:211-217. **3.** Peirce V, Williams D. Evaluation of breed variation of Schirmer tear test values in 1000 ophthalmoscopically normal dogs. BSAVA Congress 2006. Abstract.

NADA # 141-052, Approved by FDA **PRODUCT INFORMATION**

Optimmune® (0.2% Cyclosporine, USP)

Ophthalmic Ointment

For ophthalmic use in dogs only.

Sterile

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

DESCRIPTION: Each gram of OPTIMMUNE® Ophthalmic Ointment contains 2 mg of cyclosporine, USP; petrolatum, USP; corn oil, NF; petrolatum and lanolin alcohol. Cyclosporine (cyclosporin A), the active ingredient of OPTIMMUNE® Ophthalmic Ointment, is a cyclic undecapeptide metabolite of the fungus *Tolypocladium inflatum gams*.

MODE OF ACTION: When applied ophthalmically, cyclosporine is believed to act as a local immunomodulator of diseases suspected to be immune-mediated such as keratoconjunctivitis sicca (KCS) and chronic superficial keratitis (CSK). In the management of KCS, the mechanism by which cyclosporine causes an increase in lacrimation is poorly understood. Clinical improvement in cases of KCS is not necessarily dependent on an increase in aqueous tear production (as measured by the Schirmer Tear Test [STT]). See **EFFICACY**.

INDICATIONS: OPTIMMUNE® Ophthalmic Ointment is indicated for management of chronic keratoconjunctivitis sicca (KCS) and chronic superficial keratitis (CSK) in dogs.

PRECAUTIONS: The clinical effects of OPTIMMUNE® Ophthalmic Ointment have not been determined in dogs with KCS due to the following conditions: congenital alacrima, sulfonamide usage, canine distemper virus, metabolic disease, surgical removal of the third eyelid gland, and facial nerve paralysis with loss of the palpebral reflex. Some of the underlying conditions which may lead to KCS can be either transient (eg, facial nerve trauma) or correctable with appropriate treatment. Consequently, recovery from clinical signs attributed to KCS may be observed and treatment options may need reconsideration.

When switching to cyclosporine from another therapeutic agent (eg, frequent application of an artificial tear preparation) for KCS or CSK, it should be kept in mind that clinical efficacy is not necessarily apparent immediately after initiation of OPTIMMUNE® Ophthalmic Ointment therapy. Several days to a few weeks may be required before the clinical effects of OPTIMMUNE® Ophthalmic Ointment are of sufficient magnitude such that previously initiated therapy can be safely withdrawn. Abrupt cessation of a therapeutic agent immediately upon initiation of OPTIMMUNE® Ophthalmic Ointment therapy can result in rapid clinical relapse which may be erroneously interpreted as an adverse reaction to OPTIMMUNE® Ophthalmic Ointment.

The safety of OPTIMMUNE® Ophthalmic Ointment has not been determined in cases of preexisting viral or fungal ocular infections. It is recommended that in such cases, OPTIMMUNE® Ophthalmic Ointment therapy be delayed until the fungal/viral ocular infection has been successfully treated.

The safety of OPTIMMUNE® Ophthalmic Ointment in puppies, pregnant bitches, or dogs used for breeding has not been determined.

EFFICACY: *1. KCS* A well-controlled clinical field trial was conducted by veterinary ophthalmologists in 9 states and included 132 dogs afflicted with KCS of which 124 were evaluated for efficacy. Dogs were randomly assigned to BID treatment with either 0.2% (OPTIMMUNE® Ophthalmic Ointment) or 0% (placebo vehicle) cyclosporine ophthalmic ointment for 12 weeks. Treatment with OPTIMMUNE® Ophthalmic Ointment resulted in an average 8 to 9 mm increase in STT by the end of the study period (vs 3 to 4 mm for the placebo vehicle). Most of the increase in STT, approximately 6 mm, occurred in the first week of therapy. Some dogs improved clinically (ie, exhibited a decrease in conjunctival and/or corneal pathology) without an increase in STT values. This is thought to occur through suppression of inflammation by cyclosporine on the ocular surface. In this clinical field trial, OPTIMMUNE® Ophthalmic Ointment therapy was also associated with an improvement in clinical signs in comparison to the placebo. Blepharitis, blepharospasm, and "other signs of ocular discomfort" (eg, pawing at eyes), were markedly reduced. Improvement in conjunctival health as manifested by reduced conjunctival hypertrophy, reduced hyperemia, reduced conjunctival discharge volume, and improved character of discharge was evident. Improvement in corneal health as manifested by improved corneal surface contour, reduced corneal edema and corneal neovascularization was also noted. Overall improvement was noted in 81% of eyes treated with OPTIMMUNE® Ophthalmic Ointment.

Withdrawal of OPTIMMUNE® Ophthalmic Ointment therapy resulted in rapid clinical regression in all but one test eye indicating the need for long-term continual therapy for almost all cases of chronic KCS.

2. CSK The efficacy of OPTIMMUNE® Ophthalmic Ointment was determined in a historical controlled clinical field trial conducted by veterinary ophthalmologists in four countries and included 36 dogs afflicted with CSK. Dogs, primarily German shepherds, a breed disposed to CSK (German shepherd pannus), were treated twice daily with OPTIMMUNE® Ophthalmic Ointment for 6 weeks. Clinical improvement was noted by the investigators in 90.3% of eyes treated with OPTIMMUNE® Ophthalmic Ointment when compared to baseline.

SAFETY: A target animal safety study and clinical field studies with OPTIMMUNE® Ophthalmic Ointment showed a wide safety margin in adult dogs. In the 6-month target animal safety study, dogs were subjected twice daily to up to 10 times the approved concentration of OPTIMMUNE® Ophthalmic Ointment. No apparent toxicity or adverse reactions were observed. Dogs in this study were vaccinated with commercially available vaccines. No effect on antibody titer response was noted. Epiphora was noted in all groups, including the placebo group, and was not associated with any inflammatory change, nor was there any correlation to gross and histopathological changes.

ADVERSE REACTIONS: In the KCS clinical field trial, there were 20 adverse reactions reported out of 132 cases enrolled. This corresponds to an adverse reaction rate of 12.9% (13 of 101 cases) for OPTIMMUNE® Ophthalmic Ointment treated dogs and 22.6% (7 of 31) for placebo treated dogs. The reactions described were primarily ocular and periocular inflammatory reactions. These were likely a function of therapy being unable to fully control the keratoconjunctivitis, rather than a true "adverse reaction." Similarly, in the CSK trial, of 36 cases evaluated for safety, adverse reactions were noted in 2 animals (5.6%). One involved transient hyperemia, epiphora, and mild discomfort of the eye. The other involved periocular/palpebral inflammation and mild alopecia.

On rare occasion, instillation of OPTIMMUNE® Ophthalmic Ointment may be associated with local irritation as manifested by periocular redness, lid spasm, and excessive rubbing. As the eyes of dogs with KCS often demonstrate considerable inflammation, it will be difficult to determine whether this local irritation constitutes a hypersensitivity to OPTIMMUNE® Ophthalmic Ointment. If this ocular irritation persists beyond 7 days, hypersensitivity to a component of OPTIMMUNE® Ophthalmic Ointment should be suspected and therapeutic options reassessed.

DOSAGE AND ADMINISTRATION: Remove debris with suitable nonirritating solutions. Apply a 1/4 inch strip ▌←→▌ of ointment to the affected eye(s) every 12 hours. The ointment may be placed directly on the cornea or into the conjunctival sac.

It is recommended that dogs exhibiting chronic recurring conjunctivitis be tested for adequate tear production to determine if they are suffering from early stages of chronic KCS.

For best results in treating KCS, cyclosporine ophthalmic ointment should be administered early in the course of the disease before irreversible damage to the lacrimal tissue, or dense corneal scarring or pigmentation occurs.

Dogs afflicted with KCS or CSK will most likely require lifelong consistent therapy (see **EFFICACY** section above). For CSK, because environmental factors such as ultraviolet (UV) radiation are implicated in the pathogenesis, clinical signs may subside in the winter months when light intensity is reduced or if the dog is moved to a lower altitude, or indoors, and thus exposed to less UV radiation.[1]

In cases refractory to cyclosporine, the diagnosis should be reevaluated and a different course of therapy considered. Periodic reassessment of the need for OPTIMMUNE® Ophthalmic Ointment therapy is recommended.

HOW SUPPLIED: OPTIMMUNE® Ophthalmic Ointment is available in a 3.5 g tube, carton of 6 (NDC 0061-1088-01).

STORAGE CONDITIONS: Store between 2° and 25° C (36° and 77° F).

KEEP THIS AND ALL DRUGS OUT OF THE REACH OF CHILDREN.

REFERENCE: [1]Roberts, Steven M. *Pannus.* In: Kirk's Current Veterinary Therapy XII, Small Animal Practice. Philadelphia: W.B. Saunders Co; 1995:1245-1248.

Rev. 9/12

PRODUCT INFORMATION 137435 R5
NADA #34-267, Approved by FDA.

Gentocin® Durafilm®

(GENTAMICIN SULFATE AND BETAMETHASONE)
Sterile Ophthalmic Solution
Antimicrobial and Anti-inflammatory

For Use in Dogs Only

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

DESCRIPTION GENTOCIN DURAFILM Ophthalmic Solution is a sterile preparation for topical application. Each mL of buffered solution (pH approximately 6.5) contains gentamicin sulfate equivalent to 3 mg gentamicin base, 1 mg betamethasone acetate equivalent to 0.89 mg betamethasone alcohol, polyoxyl 40 stearate, polyethoxy 35 castor oil, edetate disodium, 0.1 mg benzalkonium chloride as preservative and water for injection q.s. Gentamicin is a bactericidal antibiotic of the aminoglycoside group derived from *Micromonospora purpurea* of the *Actinomyces* group. It is a powder, white to buff in color, basic in nature, readily soluble in water and highly stable in solution.
Betamethasone, a synthetic derivative of prednisolone, is 9-alpha-fluoro-16-beta-methyl-prednisolone.

INDICATIONS GENTOCIN DURAFILM Ophthalmic Solution is indicated for the treatment of external eye infections and inflammation in dogs.
Clinical reports indicate it is useful for the management of some cases of pigmentary keratitis and pannus. Temporary remission of some of the pathological lesions of the aforementioned conditions have been noted following therapy with GENTOCIN DURAFILM Ophthalmic Solution.

DOSAGE AND ADMINISTRATION The topical application of GENTOCIN DURAFILM Ophthalmic Solution should, in each instance, be administered to meet the specific needs of the individual case. One or two drops of the solution may be instilled into the conjunctival sac three or four times a day. Thereafter, the frequency of the dosage may be reduced but care should be taken not to discontinue therapy prematurely. In chronic conditions, withdrawal of treatment should be carried out by gradually decreasing the frequency of application.

CONTRAINDICATIONS Corticosteroids are contraindicated in initial treatment of corneal ulcers.
GENTOCIN DURAFILM Ophthalmic Solution is contraindicated in ocular conditions where there is deep ulceration without vascularization and in conditions of viral origin before healing has commenced.

WARNINGS Not for human use. Keep this and all drugs out of the reach of children. Clinical and experimental data have demonstrated that corticosteroids administered orally or parenterally to animals may induce the first stage of parturition when administered during the last trimester of pregnancy and may precipitate premature parturition followed by dystocia, fetal death, retained placenta, and metritis.
Additionally, corticosteroids administered to dogs, rabbits, and rodents during pregnancy have produced cleft palate. Other congenital anomalies including deformed forelegs, phocomelia, and anasarca have been reported in offspring of dogs which received corticosteroids during pregnancy.

PRECAUTIONS The antibiotic sensitivity of the infective organism in bacterial conjunctivitis should be determined prior to the use of this preparation. The preparation is contraindicated in the case of nonsusceptible microorganisms. In deep-seated infections or when systemic infection threatens, specific systemic antibiotic or sulfonamide therapy should be employed.
Extended use of topical corticosteroids may cause increased intraocular pressure in susceptible patients. In prolonged therapy, it is advisable to measure intraocular pressure. In human medicine, in diseases that cause thinning of the cornea, perforation has been known to have occurred with the use of topical steroids. Use of corticosteroids, depending on dose, duration, and specific steroid, may result in inhibition of endogenous steroid production following drug withdrawal. In patients presently receiving or recently withdrawn from systemic corticosteroid treatments, therapy with a rapidly acting corticosteroid should be considered in especially stressful situations.

ADVERSE REACTIONS SAP and SGPT (ALT) enzyme elevations, polydipsia, and polyuria have occurred following parenteral or systemic use of synthetic corticosteroids in dogs. Vomiting and diarrhea (occasionally bloody) have been observed in dogs.
Cushing's syndrome in dogs has been reported in association with prolonged or repeated steroid therapy.
A transient stinging sensation, usually expressed as some form of resentment by the animal, following topical application of the drug, has been noted in a small number of cases. Usually this does not require discontinuance of therapy.
To report an adverse reaction, product-related problem, or human exposure, please call Merck Animal Health Technical Services at 1-800-224-5318.
To obtain a copy of the Material Safety Data Sheet (MSDS), call 1-800-770-8878.
For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or http://www.fda.gov/AnimalVeterinary/SafetyHealth/default.htm

CLINICAL PHARMACOLOGY GENTOCIN DURAFILM Ophthalmic Solution incorporates polyoxyl 40 stearate and polyethoxy 35 castor oil which provide a colloidal dispersion of active ingredients. This aqueous colloidal solution offers specific advantages in treating eye conditions. DURAFILM covers the conjunctiva with a thin, clear, quickly spreading film which carries therapeutic components to accessible structures and maintains prolonged contact.

GENTOCIN DURAFILM Ophthalmic Solution provides the antibacterial properties of gentamicin sulfate plus the anti-inflammatory action of betamethasone acetate.
Gentamicin sulfate, a wide-spectrum antibiotic, is a highly effective topical treatment in primary and secondary bacterial infections of the eye and surrounding tissues. Gentamicin is bactericidal *in vitro* against a wide variety of gram-positive and gram-negative bacteria. Concentrations of gentamicin sulfate required to inhibit growth of gram positive and gram-negative clinical and laboratory strains of bacteria tested were less than those of neomycin in most instances.[1] Gentamicin is active against most gram-negative bacteria including *Pseudomonas aeruginosa*, indole positive and negative *Proteus species, Escherichia coli, Klebsiella pneumoniae, Aerobacter aerogenes,* and *Neisseria.* Gentamicin is also active against strains of gram-positive bacteria including *Staphylococcus* species and *Group A Beta-Hemolytic Streptococci.*
Betamethasone produces hormonal and metabolic effects common to all adrenocortical steroids, and in low dosage affords anti-inflammatory, anti-allergic, and anti-rheumatic effects. Studies in man show the glucocorticoid activity of betamethasone to be 10 to 15 times greater than prednisone. Betamethasone helps control excessive tissue reaction to infections, allergens, and trauma. The corticoids control the inflammatory and exudate phases of eye conditions, particularly those affecting the anterior chamber and external structure of the eye. However, they do not curtail the growth of the causative organisms. Betamethasone therapy may reduce the damaging sequelae in certain eye diseases and injuries as well as scarring and vascularization, and appears to alter the usual tissue response to injury. In initial acute phases of inflammation, local application of betamethasone provides prompt, symptomatic relief, accomplishing temporary control of the exudative phase, whether of bacterial, allergic, or traumatic origin.
Betamethasone also inhibits fibroblast formation during tissue repair.

ANIMAL SAFETY In a target animal safety study, GENTOCIN DURAFILM Ophthalmic Solution was administered for 14 consecutive days to healthy Beagle dogs at a dose of 2 drops/eye 4 times daily (1X maximum daily dose; 8 dogs), 4 drops/eye 4 times daily (2X maximum daily dose; 8 dogs), and 6 drops/eye (3X maximum daily dose; 8 dogs). Eight dogs received 6 drops of sterile saline/eye 4 times daily (Control 0X). A mild serous ocular discharge was observed in GENTOCIN DURAFILM treated dogs in a dose-related manner; which resolved within a few hours of dosing. Mild bilateral scleral redness was seen in the 2X and 3X groups between Days 4-8 which spontaneously resolved. Polyuria was evident in 1 of 8 dogs in the 3X group on Day 2, and was evident in a dose proportional manner in all three treatment groups after 14 days of dosing- 1X group (3 of 8 dogs), 2X group (7 of 8 dogs) and 3X group (8 of 8 dogs). In dogs from each GENTOCIN DURAFILM treated group, changes in hematological parameters included neutrophilia, lymphopenia, eosinopenia and decreased reticulocytes, and changes in blood chemistries included increased ALT, SAP, GGT, triglycerides, albumin, globulin and total protein levels and decreased CK levels. Urine specific gravity was decreased in each GENTOCIN DURAFILM treated group. Dogs in the GENTOCIN DURAFILM treated groups also had increased food consumption compared to dogs in the control group.

HOW SUPPLIED GENTOCIN DURAFILM Ophthalmic Solution, is supplied in 10 mL squeeze dropper bottles with a 5 mL fill, in banded units of 10, NDC 0061-0100-01.

Store between 2° and 25°C (36° and 77°F).

Protect from light.

REFERENCE

1. Weinstein MJ, Luedemann GM, oden eM, Wagman GH. Gentamicin, a new broad-spectrum antibiotic complex. Antimicrob Agents and Chemother. 1963:1—7.

Made in Germany
Rev. 09/13

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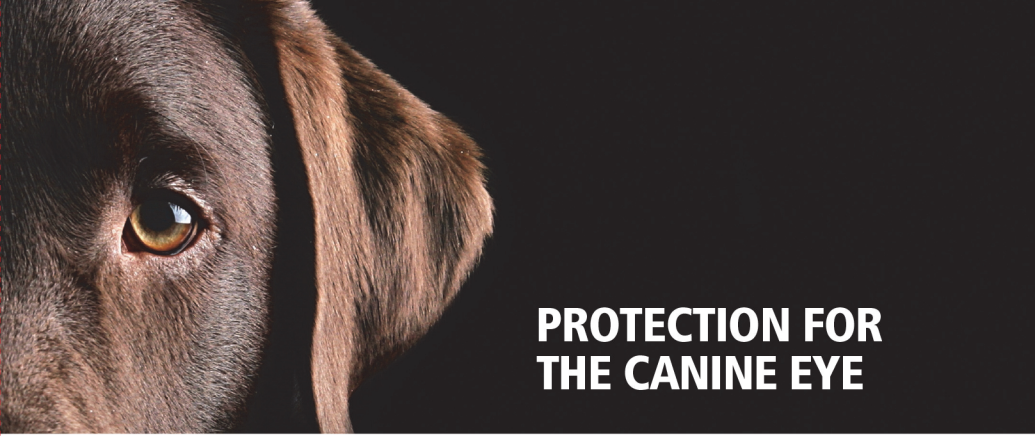
MERCK Animal Health



PROTECTION FOR THE CANINE EYE

for Canine Bacterial Eye Infections Gentocin® Durafilm®

(GENTAMICIN SULFATE AND BETAMETHASONE)
Ophthalmic Solution

A drop that ACTS like an ointment

- **GENTAMICIN SULFATE**—Efficacious, broad-spectrum antibiotic
- **BETAMETHASONE ACETATE**—Rapid anti-inflammatory corticosteroid
- **DURAFILM**—Surfactant extends medicinal contact time to cornea and conjunctiva

for Chronic Canine KCS or Pannus Optimmune®

(0.2% Cyclosporine, USP)
Ophthalmic Ointment

Effective management of both chronic keratoconjunctivitis sicca (KCS) and Pannus

- Promotes conjunctival and corneal health while reducing inflammation
- Increases tear production
- Sterile formulation that reduces risk of irritation or secondary infection

MERCK Animal Health

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