Clinical Commentary

Equine conjunctival diseases: A commentary

D. E. Brooks

Department of Large Animal Clinical Sciences, College of Veterinary Medicine, University of Florida, USA.

Overview

Conjunctivitis is inflammation of the conjunctiva or mucous membrane, which covers the posterior aspects of the eyelids and nictitating membrane (palpebral conjunctiva), and the superficial surface of the sclera (bulbar conjunctiva). It is a nonspecific finding of ophthalmic and often systemic diseases, as the eye has limited ways to react to injury (Brooks 2005, 2008; Brooks and Matthews 2007; Plummer 2008). Infectious and noninfectious diseases of the eyelids, cornea, sclera, anterior uvea, nasolacrimal system and orbit commonly result in conjunctivitis in the horse.

Causes

Conjunctivitis is often associated with ulcerative keratitis (**Fig 1**), corneal stromal abscesses (**Fig 2**), equine recurrent uveitis (**Fig 3**) and obstructed nasolacrimal ducts in horses (Brooks 2005, 2008; Gilger 2005; Brooks and Matthews 2007; Plummer 2008). Conjunctivitis in the horse may be secondary to trauma to the globe, conjunctival foreign bodies and debris, and allergic reactions to dust, hay, sand, dirt, ammonia, pollen, ash and environmental irritants. Equine neonates may develop conjunctivitis from placentitis (**Fig 4**), septicaemia, subconjunctival or episcleral haemorrhages secondary to birth trauma, and pneumonia. Conjunctivitis caused by environmental irritants is common among neonates with recumbent foals being especially at risk (Brooks 2005, 2008; Gilger 2005; Brooks and Matthews 2007; Plummer 2008). Infectious causes of equine conjunctivitis include the parasites *Habronema megastoma*, *H. muscae*, *Draschia megastoma*, *Onchocerca cervicalis*, *Thelazia lacrimalis* and *Trypanosoma* sp. Viral causes of conjunctivitis include equine adenovirus, equine herpesvirus *types 1* and *2*, equine infectious anemia, equine viral arteritis, and equine influenza *type A2*. The bacteria *Moraxella equi*, *Streptococcus equi* ssp. *equi*, *Rhodococcus* sp., *Actinobacillus* sp. and *Leptospira* sp., and the fungi *Aspergillus* and *Fusarium* spp. can cause conjunctivitis in horses. Conjunctivitis can be seen with equine protozoal myeloencephalitis (EPM) (Brooks 2005, 2008; Gilger 2005; Brooks and Matthews 2007; Plummer 2008).

Fig 1: Traumatic corneal ulcer with severe conjunctival hyperaemia is present in this horse eye.

Equine conjunctivitis may also be found with systemic diseases such as polyneuritis equi, vestibular disease syndrome, African horse sickness, epizootic lymphangitis and neonatal maladjustment syndrome (Brooks 2005, 2008; Gilger 2005; Brooks and Matthews 2007; Plummer 2008).

Neoplastic causes of equine conjunctivitis include squamous cell carcinoma (SCC) (**Fig 5**), lymphoma (**Fig 6**), papilloma, haemangioma, haemangiosarcoma, mast cell tumours (**Fig 7**), melanomas and multiple myeloma (Brooks 2005, 2008; Gilger 2005; Brooks and Matthews 2007; Plummer 2008). The prevalence of equine ocular SCC increases with age. White, grey-white and Palomino hair colour predisposes to ocular squamous cell carcinoma (Plummer 2008). The development of SCC has been associated with cell damage caused by the UV

Corresponding author email: brooksd@vetmed.ufl.edu

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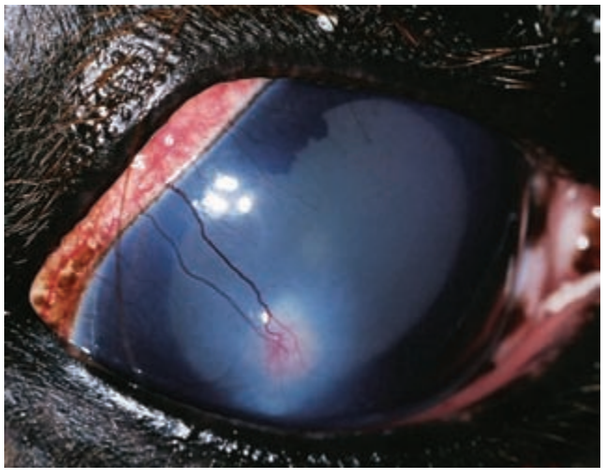

Fig 2: Conjunctival hyperaemia and chemosis is found with a deep stromal abscess.

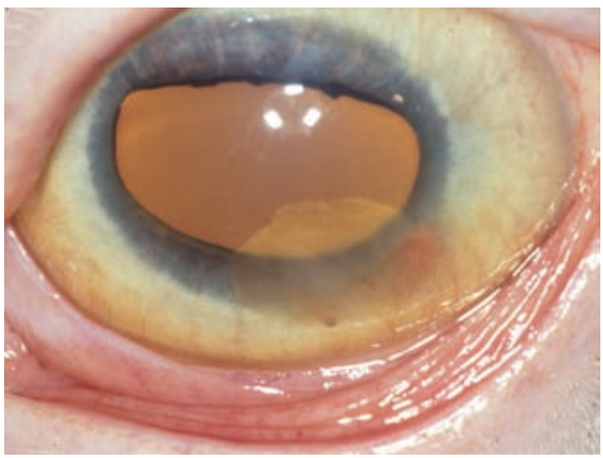

Fig 3: An eye with equine recurrent uveitis has dramatic chemosis and conjunctival vascular congestion.

component of solar radiation. Animals with higher levels of exposure to sunlight or that live in high altitudes are also more likely to develop SCC (Plummer 2008).

Signs of conjunctivitis

The horse conjunctiva has limited ways to react when inflamed (Brooks 2008; Plummer 2008). The clinical signs of conjunctivitis may be quite striking and include conjunctival hyperaemia, chemosis (oedema), and ocular discharge that is serous (viral, environmental/ allergic) to purulent (bacterial). Conjunctival thickening from cellular infiltrates may be found with parasite invasion, dermoids and conjunctival tumours. Conjunctival lymphoma can masquerade or appear as conjunctivitis (Plummer 2008). Lymphoid follicles may form in some eyes (Gilger 2005; Brooks and Matthews 2007; Plummer 2008).

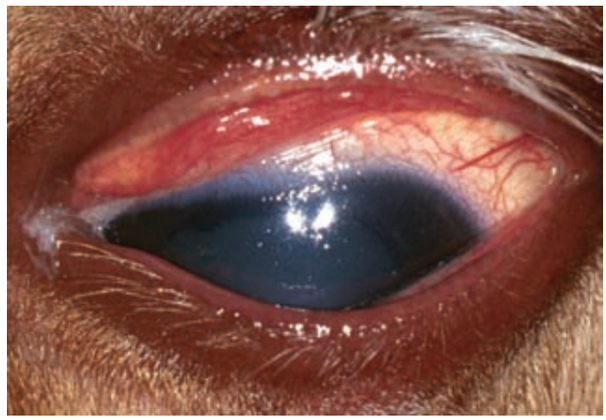

Fig 4: Limbal keratitis and severe conjunctivitis in a foal with placentitis.

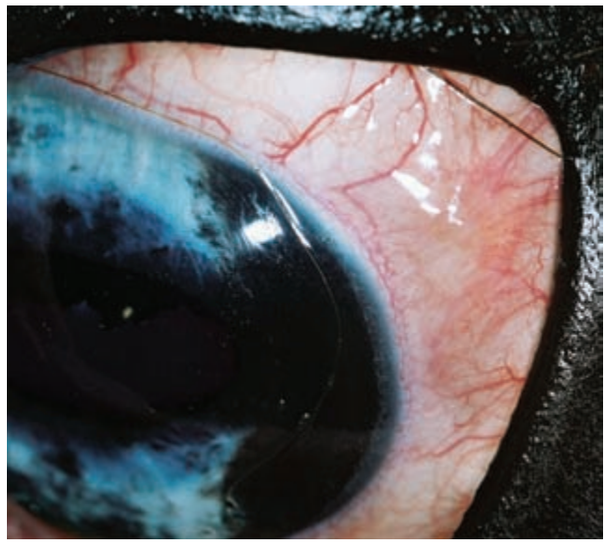

Fig 5: A conjunctival squamous cell carcinoma appears as localised conjunctivitis in this eye.

Differential diagnosis

Conjunctivitis is a nonspecific sign reflecting the eye's limited mechanisms of response to injury (Brooks 2008; Plummer 2008). It is critical to differentiate primary conjunctivitis from conjunctivitis secondary to ocular or systemic disease. Conjunctivitis may be diffuse or nodular in appearance. Causes of nodular/mass lesions of conjunctiva include habronemiasis, squamous cell carcinoma, mastocytoma, haemangioma, haemangiosarcoma, papilloma and other neoplastic infiltrates, fungal granulomas, dermoids and foreign body reactions. Diffuse conjunctivitis in horses is found in primary conjunctivitis and conjunctivitis secondary to environmental irritants, intraocular inflammation and conjunctival neoplasia.

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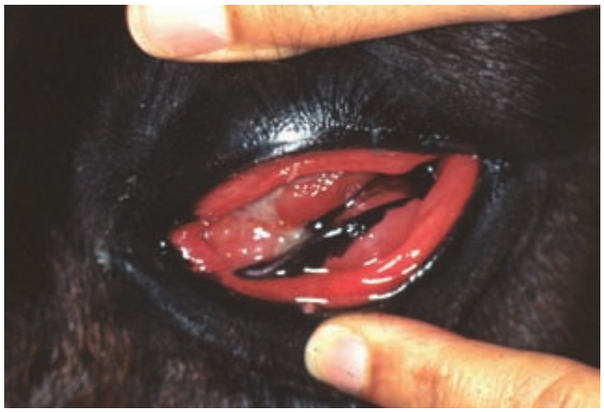

Fig 6: Severe chemosis and conjunctival hypaeremia are caused by diffuse conjunctival lymphoma in this horse.

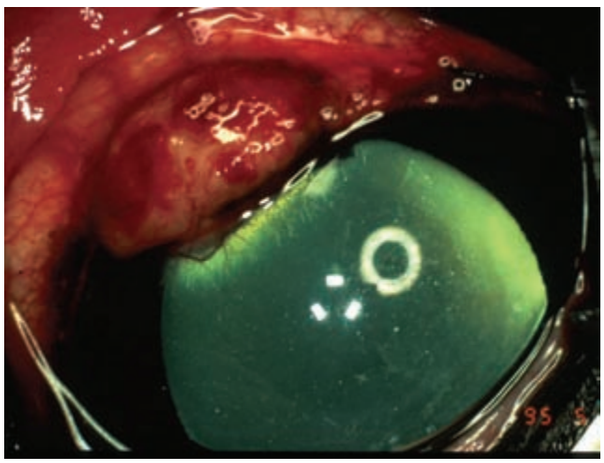

Fig 7: Nodular and diffuse conjunctivitis caused by a conjunctival mast cell tumour.

Diagnostic procedures

Complete ophthalmic examination is indicated to identify adnexal and ocular causes of conjunctivitis, including a thorough adnexal examination, fluorescein staining and examination for signs of anterior uveitis. Cytological scrapings and biopsy and histological analysis may be necessary to identify causes of equine conjunctivitis. Culture and sensitivity of mucopurulent discharge should be performed if an infectious component to the conjunctivitis is suspected. Consider cannulation and flushing of the nasolacrimal duct to rule out nasolacrimal disease for horses with conjunctivitis (Plummer 2008).

Treatment

Treatment of conjunctival neoplasia may involve local resection with adjunctive beta-irradiation, brachytherapy, cryotherapy, radiofrequency hyperthermia or intralesional chemotherapy (Plummer 2008).

Conjunctival foreign bodies and debris can usually be removed with topical anaesthesia and liberal flushing of conjunctival fornices (Plummer 2008).

Parasitic conjunctivitis caused by habronemiasis and onchocerciasis can be treated with debridement of nodular lesions, and topical echothiophate iodide, an ophthalmic antibiotic/corticosteroid medication if no corneal ulcers are present, and oral ivermectin or moxidectin (Plummer 2008).

Bacterial and fungal conjunctivitis can be treated with topical broad-spectrum antimicrobials initially with changes in therapy made after culture and sensitivity testing. Several antiviral medications are appropriate for treatment of horses with viral conjunctivitis. Conjunctivitis due to environmental irritants is treated with topical corticosteroids and a reduction in exposure to the inciting cause if possible (Plummer 2008).

Expected course and prognosis of equine conjunctivitis

Infectious conjunctivitis usually responds to appropriate treatment (Plummer 2008). Primary conjunctival infections respond well to topical therapy, usually within 5–7 days. Failure to respond or recurrence suggests an unidentified underlying cause (i.e. recurrent bacterial conjunctivitis associated with an unrecognised foreign body). Course and prognosis of conjunctival neoplasia depends on the specific type of neoplasia and the extent of invasion of surrounding tissues. Viral conjunctivitis may be recurrent. Environmental conjunctivitis is often difficult to eliminate completely due to the nature of the horse's environment. The prognosis associated with conjunctivitis secondary to systemic or ocular disease varies with the specific disease. Many systemic diseases that have conjunctivitis as a clinical sign can have serious and life-threatening consequences (Plummer 2008).

Eosinophilic conjunctivitis and eosinophilic keratoconjunctivitis

Eosinophilic keratoconjunctivitis (EKC) has an unknown aetiology, but may be an immune-mediated disease (Brooks 2005, 2008; Plummer 2008; Brooks and Matthews 2007; Gilger 2005). Eosinophil invasion of the ocular surface can involve the cornea alone to form eosinophilic keratitis (EK), the conjunctival alone to form eosinophilic conjunctivitis (EC) (**Fig 8**) as in the Wolfe *et al*. (2010) paper, or both the cornea and conjunctiva to cause EKC (**Fig 9**). All ages and breeds of horses can be affected, with many EKC cases reported in the spring. Clinical signs of EKC include corneal granulation tissue, blepharospasm, chemosis, conjunctival hyperaemia, mucoid discharge and corneal ulcers covered by raised, white, necrotic

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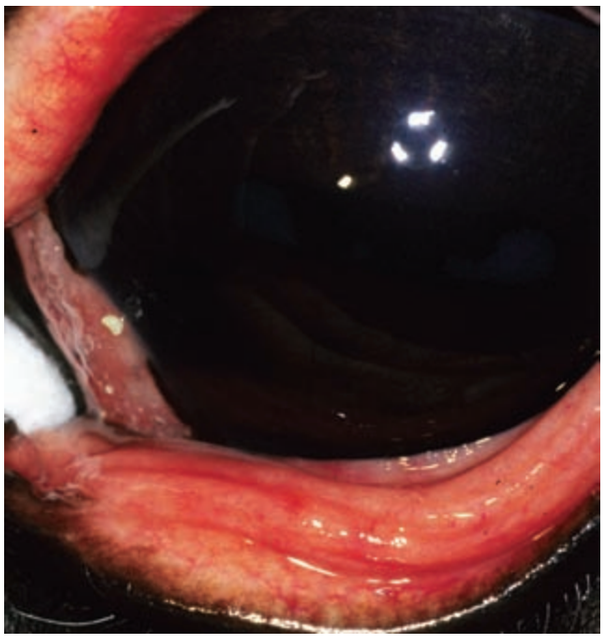

Fig 8: Eosinophilic conjunctivitis presents behind the third eyelid in a horse from Florida.

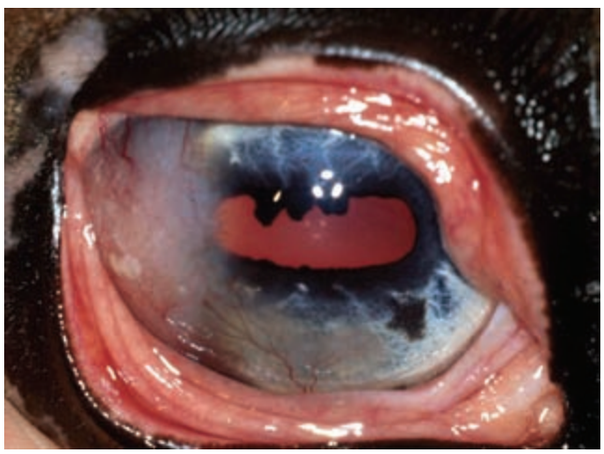

Fig 9: Eosinophilic keratoconjunctivitis was severe and bilateral in this horse.

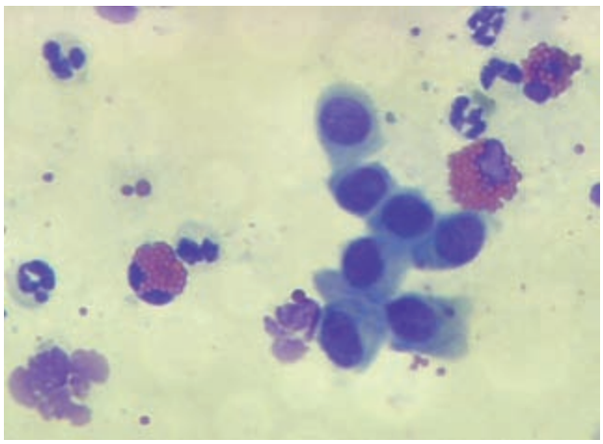

Fig 10: Eosinophils and epithelial cells are characteristic findings in eosinophilic ocular surface disease of the horse.

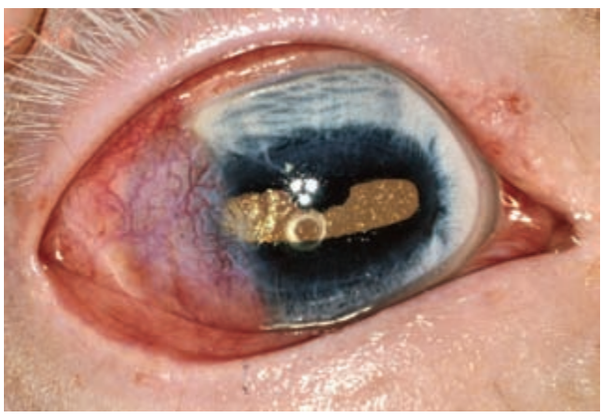

Fig 11: Squamous cell carcinoma of the horse ocular surface can be similar in appearance to eosinophilic keratoconjunctivitis.

plaques (Plummer 2008). Corneal and conjunctival cytology typically contains numerous eosinophils (**Fig 10**) and a few mast cells. EKC resembles corneal or conjunctival tumours in appearance (**Fig 11**). The paper by Wolfe *et al*. (2010) documents equine EC without corneal involvement. It also identifies another form of conjunctivitis in the horse, and further characterises equine EKC.

Treatment for EK, EC and EKC can last months, as was found by Wolfe *et al*. (2010). Medical therapy in conjunction with superficial lamellar keratectomy for EK and EKC, or conjunctivalectomy for EC to remove the plaques significantly speeds healing. Topical corticosteroids and NSAIDs are beneficial in the early stages, but corticosteroids must be used cautiously if corneal ulcers are present (Brooks 2005, 2008; Gilger 2005; Brooks and Matthews 2007; Plummer 2008). Topical antibiotics, atropine (1%), and phospholine iodide (0.03% BID), in combination with systemic dexamethasone and NSAIDs are also effective for EK. Standard ivermectin antiparasite treatments 10 days apart can also be beneficial. Topical antibiotics, uveitis therapy and the mast cell stabilisers cromolyn sodium (Crolom 4%)[1], and iodoxamide (Alomide 0.1%)[2] and the histamine H-1 receptor antagonists olopatadine HCl (Patanol 0.1%)[2] and azelastine HCl (Optivar 0.05%)[3] are used topically in recalcitrant EK cases (Plummer 2008). Caution should always be exercised with topical corticosteroid use in equine corneal disease. The confirmation of the diagnosis cytologically is critical to differentiate EK from other keratopathies such as squamous cell carcinoma, superficial fungal plaque, or stromal abscesses.

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Manufacturers' addresses

[1]Bausch and Lomb, Rochester, New York, USA.
[2]Alcon, Ft Worth, Texas, USA.
[3]Muro Pharmaceuticals, Tewksbury, Massachusetts, USA.

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Wolfe, J.E., Utter, M.E., Boyle, A.G. and Habecker, P.L. (2010) Limbal conjunctival plaques and idiopathic eosinophilic conjunctivitis. *Equine vet. Educ.* **22**, 375-381.

NADA 141-186, Approved by FDA
Veterinary Package Insert

Surpass®

(1% diclofenac sodium)
Topical Anti-Inflammatory Cream
For Use in Horses

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

Description: Surpass® topical cream contains 1% diclofenac sodium. Diclofenac is a non-steroidal anti-inflammatory drug (NSAID) of the phenylacetic acid class. The chemical name for diclofenac is sodium [o- (2,6-dichloroanilino)phenyl] acetate. The empirical formula is $C_{14}H_{10}Cl_2NNaO_2$ and the molecular weight is 318.13. Surpass topical cream contains 1% diclofenac sodium in a base composed of Phospholipon 90H, propylene glycol, alcohol (5.94%), vitamin E acetate, benzethonium chloride and purified water in the Wisdom® liposomal formulation.

Indications: Surpass topical cream is indicated for the control of pain and inflammation associated with osteoarthritis (OA) in tarsal, carpal, metacarpophalangeal, metatarsophalangeal and proximal interphalangeal (hock, knee, fetlock and pastern) joints in horses.

Dosage and Administration: Always provide the Client Information Sheet with the prescription.

Dosage: Apply a five-inch (5") ribbon of Surpass topical cream twice daily over the affected joint for up to ten days.

Administration: Wear rubber gloves to prevent absorption into the hands. Rub the cream thoroughly into the hair covering the joint until it disappears.

Contraindications: Surpass topical cream is contraindicated in animals with known hypersensitivity to diclofenac.

Warnings: Not for horses intended for human consumption.

User Safety: Keep out of reach of children. Not for human use. Consult a physician in case of accidental ingestion by humans.

Wear gloves to prevent absorption into the hands. Direct contact with the skin should be avoided. If contact occurs, the skin should be washed immediately with soap and water.

Animal Safety: **For topical use in horses only.** Owners should be advised to observe for signs of potential drug toxicity (see Information for Owner or Person Treating Animal and Adverse Reactions).

Precautions: Exceeding the recommended dosage or treating multiple joints may increase plasma concentrations of diclofenac (see Animal Safety). The systemic effects of excess diclofenac doses that exceed the recommended label amount and duration have not been evaluated.

Horses should undergo a thorough history and physical examination before initiation of NSAID therapy. Appropriate laboratory tests should be conducted to establish hematological and serum biochemical baseline data before and periodically during administration of any NSAID. Owners should be advised to observe for signs of potential drug toxicity (see Information for Owner or Person Treating Animal).

Treatment with Surpass cream should be terminated if signs such as inappetence, colic, fecal abnormalities, anemia or depression are observed.

As a class, NSAIDs may be associated with gastrointestinal and renal toxicity. When NSAIDs inhibit prostaglandins that cause inflammation, they may also inhibit prostaglandins that maintain normal homeostatic function. These anti-prostaglandin effects may result in clinically significant disease in patients with underlying or preexisting disease more often than in healthy patients. Patients at greatest risk for renal toxicity are those that are dehydrated, on concomitant diuretic therapy, or those with renal, cardiovascular and/or hepatic dysfunction.

Studies to determine the effect of Surpass topical cream when administered concomitantly with other drugs have not been conducted. Since many NSAIDs possess the potential to induce gastric ulceration, concomitant use of Surpass cream with any other anti-inflammatory drugs, such as other NSAIDs and corticosteroids, should be avoided. Drug compatibility should be monitored closely in patients receiving adjunctive therapy.

The safety of Surpass cream has not been investigated in breeding, pregnant or lactating horses, or in horses under one year of age.

Adverse Reactions: During the field study, one diclofenac-treated horse developed colic on day four of the study and responded to symptomatic treatment. One placebo-treated horse exhibited mildly jaundiced mucous membranes on day five. Adverse reactions during the safety study included a gastric ulcer in one horse that received 5.6X the recommended dosage, diarrhea and uterine discharge in one horse that received 2.8X the recommended dosage, and weight loss in four of the six horses in the 5.6X dosage group.

To report suspected adverse reactions, to obtain a Material Safety Data Sheet or for technical assistance, call 1-866-638-2226.

Information for Owner or Person Treating Animal: Owners should be advised of the potential for adverse reactions and be informed of the clinical signs associated with NSAID intolerance. Adverse reactions may include: weight loss, colic, diarrhea, or icterus. Serious adverse reactions associated with this drug class can occur without warning and, in rare situations, result in death. Owners should be advised to discontinue NSAID therapy and contact their veterinarian immediately if signs of intolerance are observed. The majority of patients with drug-related adverse reactions recover when the signs are recognized, drug administration is stopped, and veterinary care is initiated.

Clinical Pharmacology: Diclofenac is a non-steroidal anti-inflammatory drug (NSAID) with analgesic properties. The mechanism of action of diclofenac, like other NSAIDs, is believed to be associated with the inhibition of cyclooxygenase activity.

Effectiveness: In a controlled field study, 82 horses with osteoarthritis were treated with Surpass topical cream (42 horses) or placebo (40 horses). Lameness examinations were performed in horses with osteoarthritis associated with the tarsal, carpal, metacarpophalangeal, metatarsophalangeal and proximal interphalangeal joints. Investigators were masked to treatment. Investigators and owners were instructed to apply the test article over the affected joint twice daily (BID) for five days. Actual doses received by individual horses were calculated using tube weight measurements. The mean dose applied during the study was 73 mg per application. Average lameness scores showed statistically significant improvement following treatment with Surpass topical cream.

One diclofenac-treated horse developed colic and responded to symptomatic treatment on day four of the study. Day five bloodwork for the horse that colicked showed decreases in RBC, Hb and HCT, with an increase in PMNs, compared to pretreatment values. One placebo-treated horse exhibited mildly jaundiced mucous membranes on day five. No other adverse reactions were noted during the study.

Animal Safety: A controlled safety study was conducted with Surpass topical cream. Four groups of six healthy adult horses received 0, 0.6, 1.7 or 2.8X the recommended daily dose for twenty-eight days. The daily dose was divided into two applications on day one of the study. For the remainder of the study, the entire daily dose was given at one time on 0, 1, 3 or 5 joints (tarsal, carpal, metacarpophalangeal, metatarsophalangeal, and proximal interphalangeal joints), depending on the dosage group. The control group of six horses was sham-dosed by rubbing the joints daily for twenty-eight days. An additional study group evaluated six horses that received 5.6X the recommended daily dose of Surpass topical cream distributed over five joints on a single day. This dose group was observed for fourteen days without additional treatment.

Clinical examinations, hematology, serum chemistry, synovial fluid analyses, gross necropsy and histopathology were performed. At necropsy, one horse in the 5.6X group had a glandular gastric ulcer. A horse in the 2.8X group had diarrhea and uterine discharge throughout the study. Four of the six horses in the 5.6X group lost weight during the study.

Dose-dependent increases in diclofenac plasma concentrations were detected in horses in the 1.7X and 2.8X treatment groups.

Storage Information: Store at up to 25°C (77°F). Protect from freezing.

How Supplied: Surpass topical cream is white to pinkish-white and is packaged in 124-gram trilaminate tubes.

Surpass and Wisdom are registered trademarks of Boehringer Ingelheim Vetmedica, Inc.

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Manufactured under U.S. Patent Nos. 4,937,078 and 6,936,273.

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