NEPAFENAC

(ne-pa-*fen*-ak)

Indications/Pharmacology

Nepafenac is a nonsteroidal anti-inflammatory and analgesic prodrug. After topical ocular dosing, nepafenac penetrates the cornea and is converted by ocular tissue hydrolases to amfenac, a nonsteroidal anti-inflammatory drug. Amfenac is thought to inhibit the action of prostaglandin H synthase (cyclooxygenase), an enzyme required for prostaglandin production. Nepafenac is indicated for the treatment of pain and inflammation associated with cataract surgery.

Suggested Dosages/Precautions/Adverse Effects

One drop three times daily. Shake well before use.

Nepafenac is contraindicated in patients who have demonstrated hypersensitivity to any of the ingredients in the formulation or to other NSAIDs. Caution should be exercised when utilizing bromfenac in patients who have previously exhibited sensitivity to other NSAID drugs as there is potential for cross-sensitivity.

There have been reports that ocularly applied NSAIDs may cause increased bleeding of ocular tissues (including hyphema) in conjunction with ocular surgery due to interference with platelet aggregation. All topical NSAIDs may slow or delay healing. Concomitant use with topical steroidal agents may increase the potential for delayed healing. Use of topical NSAIDs may result in keratitis due to epithelial breakdown, corneal thinning, corneal erosion, corneal ulceration or corneal perforation. Use of bromfenac should be discontinued immediately in patients exhibiting evidence of corneal epithelial breakdown. Post marketing experience with topical NSAIDs suggests that use more than 24 hours prior to surgery or use beyond 14 days after surgery may increase patient risk for the occurrence of corneal adverse events. Bromfenac should be used with caution in patients with known bleeding tendencies or who are receiving other medications, which may prolong bleeding time. In controlled clinical studies, the most frequently reported ocular adverse events following cataract surgery were capsular opacity, decreased visual acuity, foreign body sensation, increased intraocular pressure, and sticky sensation. These events occurred in approximately 5–10% of patients. Other ocular adverse events occurring at an incidence of approximately 1–5% included conjunctival edema, corneal edema, dry eye, lid margin crusting, ocular discomfort, ocular hyperemia, ocular pain, ocular pruritus, photophobia, tearing and vitreous detachment. Some of these events may be the consequence of the cataract surgical procedure. Non-ocular adverse events reported at an incidence of 1–4% included headache, hypertension, nausea/vomiting, and sinusitis. Nepafenac ophthalmic suspension may be administered in conjunction with other topical ophthalmic medications such as beta-blockers, carbonic anhydrase inhibitors, alpha-agonists, cycloplegics, and mydriatics.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS: None

HUMAN-LABELED PRODUCTS:

Nepafenac Ophthalmic Suspension: 0.1% in 3 mL; *Nevanac*® (Alcon); (Rx). Shake well and store at room temperature.

SUPROFEN

(su-*pro*-phen)

Indications/Pharmacology

Suprofen is a non-steroidal anti-inflammatory agent similar to flurbiprofen. Suprofen and flurbiprofen are phenylalkanoic acids that inhibit the cyclo-oxygenase enzymes responsible for conversion of arachadonic acid from cell membranes into various prostaglandins. These prostaglandins mediate certain aspects of ocular inflammation including disruption of the blood-aqueous barrier, uveal vasodilation, increases in intraocular pressure, and leakage of white blood cells and protein from uveal vessels into the aqueous humor. Prostaglandins cause iris sphincter constriction (miosis) independent of cholinergic mechanisms. Suprofen can inhibit this intraocular miosis and may also be useful in the management of uveal inflammation (usually in addition to topical steroids).

Suggested Dosages/Precautions/Adverse Effects

Prior to surgery: One drop 4 times at 20 minute intervals.

Because suprofen may be as immunosuppressive as topical corticosteroids, it should not be used in patients with bacterial corneal ulcers. By blocking prostaglandin synthesis, arachidonic acid metabolites may be shunted into leukotriene pathways and this effect may result in a transient increase in intraocular pressure commonly noted after intraocular surgery. Postoperative pressure spikes following cataract surgery have been the subject of much study in recent years and a general trend away from the use of suprofen or flurbiprofen prior to cataract surgery has resulted from these studies.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS: None

HUMAN-LABELED PRODUCTS:

Suprofen Sodium 1% Solution in 2.5 mL btls; *Profenal*® (Alcon); (Rx)

Steroidal Anti-inflammatory Agents

CORTICOSTEROIDS, TOPICAL

(OPHTHALMIC)

PREDNISOLONE ACETATE
DEXAMETHASONE
LOTEPREDNOL ETABONATE

(see also Antibiotic & Corticosteroid Combinations)

Indications/Dosages/Precautions

Topical corticosteroids are used to treat diseases of the eye involving the conjunctiva, sclera, cornea, and anterior chamber. Penetration of topically applied corticosteroids into the eyelids is poor as is penetration to the posterior segment of the eye. Corticosteroid-responsive conditions affecting these areas are usually managed with systemically administered agents (with or without adjunctive topically applied medications).

Conjunctivitis in animals is often treated symptomatically, particularly during the first occurrence of the condition for any particular patient. Antibiotic agents with hydrocortisone or dexamethasone, or antibiotic agents alone initially, are used for conjunctivitis

in the dog and the horse. Allergic and eosinophilic conjunctivitis are rare diagnoses in the cat. Topically applied corticosteroids should not be used to treat conjunctivitis in cats. Herpes virus is the most common feline conjunctival pathogen and topically applied steroids can induce prolonged disease, steroid dependency and corneal complications including ulcerative keratitis and/or corneal sequestrum formation.

Inflammatory conditions of the canine sclera and episclera include episcleritis, scleritis, nodular granulomatous episclerokeratitis, Collie granuloma and others. Potency and penetration of corticosteroid agents is important in the management of these conditions. Dexamethasone sodium phosphate ointment is often employed and the relatively reduced penetration of the fibrous ocular tunics of this medication compared with that of 1% prednisolone acetate ophthalmic suspension is made up for by increased contact time of the ointment form of this drug and by the increased potency of dexamethasone (30X cortisone) relative to prednisolone (4–5X cortisone). Dexamethasone products alone (without antibiotics) are becoming increasingly scarce in the marketplace and because of this, dexamethasone is often used in combination with an antibiotic for availability reasons only. Four times daily treatment is often the initial frequency with tapering paralleled to clinical response. Topical treatment is often used following subconjunctival injection of corticosteroid agents into or adjacent to the lesion (if focal). Systemic steroid treatment is usually not necessary.

Non-ulcerative inflammatory conditions of the cornea of animals include chronic superficial keratitis (pannus) of the German Shepherd and other breeds, eosinophilic keratitis of the cat and certain, often poorly understood, keratopathies of the equine, including Onchocerca related keratitis. German Shepherd pannus may be better managed using cyclosporine ophthalmic solution or ointment with or without concurrent topical steroids initially followed by long term management with cyclosporine ophthalmic alone (see cyclosporine ophthalmic). Eosinophilic keratitis is often treated with subconjunctival corticosteroids in addition to topical 0.1% dexamethasone ophthalmic ointment or solution or 1% prednisolone acetate ophthalmic suspension 4 times daily, tapering the dosage frequency based on clinical response. Recent research reveals that eosinophilic keratitis may be an unusual immune response to latent feline herpes virus in the corneal stroma, calling into question the value of topical steroids in the management of a disease with an infectious etiology. Despite new information pertaining to possible causes of eosinophilic keratitis in the cat, the condition continues to be well managed in most cases with infrequent topical corticosteroid treatment. Non-ulcerative, immune mediated and/or parasitic equine keratopathies are treated with 0.1% dexamethasone ointment 4 times daily with tapering of the treatment frequency based on the clinical response.

Corticosteroids are also used to manage anterior uveal inflammatory disease of companion animals. In small animals, 1% prednisolone acetate ophthalmic suspension is generally used for this purpose because of superior penetration into the anterior segment of the eye in comparison with dexamethasone products. The frequency of treatment depends on the severity of the condition. Severe anterior uveitis can be treated with subconjunctival corticosteroids given in combination with hourly topical corticosteroids with reevaluation performed again 24 hours after beginning treatment. Moderate to mild uveitis and that found following surgery of the anterior segment is often treated initially at the QID level with tapering based on clinical response. Anterior uveitis in animals can often be associated with an underlying systemic infectious or neoplastic condition in animals. Clinicians are advised to evaluate the patient for generalized infectious or neoplastic conditions prior to or concurrent with a course of corticosteroid antiinflammatory therapy, particularly if the condition dictates systemic treatment with these agents in combination with subconjunctival and topical treatment. Uveitis has also been successfully treated utilizing subconjunctival injections of triamcinolone acetonide. As commercially available triamcinolone injections are preserved with benzyl alcohol, veterinary ophthalmologists centrifuge triamcinolone injections and remove the alcohol-containing supernatant vehicle. An equal volume of non-preserved sodium chloride injection is then utilized to reconstitute the remaining triamcinolone to provide for an acceptable subconjunctival injection. Uveitis in the equine species is often treated with either 1% prednisolone acetate ophthalmic suspension or with 0.1% dexamethasone ointment. Many clinicians prefer to use the ointment because of increased contact time and potency and the logistics of frequent treatment of this species. 1% prednisolone acetate can be passed through a subpalpebral lavage catheter very frequently to treat equine patients with anterior uveitis when necessary.

Pred Forte®, *Econopred Plus®* or generic 1% prednisolone acetate ophthalmic suspension are the prednisolone products most used by veterinary ophthalmologists. There are few indications for *Econopred®* or *Pred Mild®* in veterinary ophthalmology.

Inflammatory conditions of the posterior segment require systemic treatment because of poor penetration of topically applied agents.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS: None

HUMAN-LABELED PRODUCTS:

Prednisolone Acetate Drops: 0.12% Suspension: *Pred Mild®* (Allergan); 0.125% Suspension: *Econopred®* (Alcon); 1% Suspension: *Econopred Plus®* (Alcon); *Pred Forte®* (Allergan), generic; (Rx)

Prednisolone Sodium Phosphate Drops: 0.125 & 1% Solution; (various); (Rx)

Prednisolone (0.25%) and Atropine (1%) Drops in 5 mL btls; *Mydrapred®* (Alcon); (Rx)

Loteprednol Etabonate Ophthalmic Suspension: 0.2% in 5 mL, 10 mL; *Alrex®* (Bausch and Lomb); (Rx). Shake well and store at room temperature. Do not freeze.

Also available: Fluorometholone or Medrysone drops

Other routes of administration: Systemically administered corticosteroids (usually orally) may be indicated for non-infectious inflammatory ocular conditions and following intraocular surgery. Subconjunctival steroids are useful in anterior segment inflammatory disease and following cataract surgery and intraocular glaucoma surgery. Subconjunctival steroids may be absorbed systemically and should be used with caution in patients with endocrinopathies (*e.g.,* diabetes mellitus) or infectious diseases. Even frequent topical steroid application in small animal patients under 20 kg can cause difficulties with diabetes mellitus regulation and after the peak inflammatory response has been suppressed, nonsteroidal antiinflammatory drugs should be considered for ongoing maintenance treatment.