front

back

200 mm

120 mm

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only.

℞ Nepafenac Ophthalmic Suspension 0.3% w/v

ZYNEP-OD™

Eye Drops

ज़ेनेप-ओडी

GENERIC NAME
Nepafenac Ophthalmic Suspension 0.3%w/v
QUALITATIVE AND QUANTITATIVE COMPOSITION
Nepafenac ophthalmic suspension is greenish yellow to yellowish orange colour suspension filled in opaque white colour LDPE vial.

Composition:

Nepafenac	0.3%w/v
Stabilized	
Oxychloro Complex	0.01% w/v
(As Preservative)	
Sterile Aqueous Vehicles	q.s

DOSAGE: As directed by the physician.

CLINICAL PARTICULARS
Therapeutic indication
For the treatment of pain and inflammation associated with cataract surgery.
Posology and method of administration
Posology
One drop of Nepafenac ophthalmic suspension 0.3% should be applied to the affected eye one-time-daily beginning 1 day prior to cataract surgery, continued on the day of surgery and through the first 2 weeks of the postoperative period. An additional drop should be administration 30 to 120 minutes prior to surgery.
Method of Administration: For ocular use only.
Patients should be instructed to shake the bottle well before use.
After cap is removed , if tamper evident snap collar is loose, remove before using product. If more than one topical ophthalmic medicinal product is being used, the medicinal product must be administered at least 5 minutes apart.
Eye ointments should be administered last. To prevent contamination of the dropper tip and solution, care must be taken not to touch the eyelids, surrounding areas or other surfaces with the dropper tip of the bottle. Patients should be instructed to keep the bottle tightly closed when not in use.
If a dose is missed, a single drop should be applied as soon as possible before reverting to regular routine. Do not use a double dose to make up for the 1 missed.
Contraindications
Nepafenac ophthalmic suspension 0.3% is contraindicated in:
- Patients with known hypersensitive to Nepafenac or to any of the component of this formulation.
- Patients who are hypersensitive to other non-steroidal anti-inflammatory drug (NSAIDs)
- Patients in whom attacks of asthma, urticarial or acute rhinitis are precipitated by acetylsalicylic acid or other NSAIDS.

Special warnings and precautions for use
Increase bleeding Time: With some non-steroidal anti-inflammatory drugs including Nepafenac ophthalmic suspension 0.3%, there exists the potential for increased bleeding time due to interference with thrombocyte aggregation. There have been reports that ocularly applied non-steroidal anti-inflamatory drugs may cause increased bleeding of ocular tissue (including hyphema) in conjunction with ocular surgery.
It is recommended that Nepafenac ophthalmic suspension 0.3% be used with caution in patients with known bleeding tendencies or who are receiving other medications which may prolong bleeding time.
Delayed healing: Topical non-steroidal anti-inflammatory drugs (NSAIDs) including Nepafenac opyhemic suspension 0.3% may slow or delay healing. Topical corticosteroids are also known to slow or delay healing. Concomitant use of topical NSAIDs and topical steroidal may increase the potential for healing problems.
Corneal effects: Use of topical NSAIDs may result in keratitis. In some susceptible patients, continued use of topical NSAIDs may results in epithelial breakdown, corneal thinning, corneal erosion, corneal ulceration or corneal perforation. These events may be sight threatening. Patients with evidence of corneal epithelial breakdown should immediately discontinue use of topical NSAIDs including Nepafenac ophthalmic suspension 0.3% and should be closely monitored for corneal health.
Post-marketing experience with topical NSAIDs suggest that patients with complicated ocular surgeries (e.g. dry eye syndrome), rheumatoid arthritis, or repeat ocular surgeries within a short period of time may be at increased risk for corneal adverse which may become sight threating. Topical NSAIDs should be used with caution in these patients.
Post-marketing experience with topical NSAIDs also suggests that use more than 1 day prior to surgery or use beyond 14 days post- surgery may increase patients risk and severity of corneal adverse events.
Contact lens wear: Nepafenac ophthalmic suspension 0.3% should not be administered while using contact lenses.
Stabilized Oxychloro complex: Nepafenac contains benzalkonium chloride which may cause irritation and is known to discolour soft contact lenses. If contact lenses need to be used during treatment, patients should be advised to remove contact lenses prior to application and wait at least 15 minutes before reinsertion.
Benzalkonium chloride has been reported to cause punctate keratopathy and/or toxic ulcerative keratopathy. Since Nepafenac ophthalmic suspension contains benzalkonium chloride, close monitoring is required with frequent or prolonged use.
Drugs interactions
Neither nepafenac nor amfenac inhibits any of the major human cytochrome P450 (CYP1A2, CYP2C9, CYP2C19, CYP2D6, CYP2E1, and CYP3A4) metabolic activities in vitro at concentrations up to 300 ng/mL. Therefore, drug-drug interactions involving CYP-mediated metabolism of concomitantly administered drugs are unlikely. Drug-drug interactions mediated by protein binding are also unlikely.
Drug-drug interactions: Nepafenac ophthalmic suspension, 0.3% may be administered in conjunction with other topical ophthalmic medications such as beta-blockers, carbonic anhydrase inhibitors, alpha agonists, cycloplegics, and mydriatics.
The administration of Nepafenac ophthalmic suspension in conjunction with prostaglandin analogues was not evaluated in clinical trials. Interaction between Nepafenac ophthalmic suspension and prostaglandin analogues are not anticipated following topical ocular administration.
There is a potential cross-sensitivity to acetylsalicylic acid, phenylacetic acid derivatives and other non-steroidal anti-inflammatory agents.
Concomitant use of topical NSAIDs and topical corticosteroids may increase the potential for healing complications. Concomitant use of Nepafenac with medications that prolong bleeding time may increase the risk of haemorrhage.
Drug-food Interactions: Interactions with food are not anticipated following topical ocular administration.
Drug-herb Interactions: Interactions with herbal products are not anticipated following topical ocular administration.
Drug-laboratory Interactions: Interactions with laboratory tests are not anticipated following topical ocular administration.
Use in special populations
Women of childbearing potential: Nepafenac ophthalmic suspension 0.3% should not be used by women of child bearing potential not using contraception.
Pregnancy: There is no adequate data regarding the use of nepafenac in pregnant women. Studies in animals have shown reproductive toxicity. The potential risk for humans is unknown. Since the systemic exposure in non-pregnant women is negligible after treatment with Nepafenac ophthalmic suspension, the risk during pregnancy could be considered low. Nevertheless, as inhibition of prostaglandin synthesis may negatively affect pregnancy and/or embryonal/foetal development and/or postnatal development, Nepafenac ophthalmic suspension is not recommended during pregnancy.
Breast-feeding: It is unknown whether is excreted in human milk. Animal studies have shown excretion of Nepafenac in the milk of rats. However, no effects on the suckling child are anticipated since the systemic exposure of the breast-feeding woman to Nepafenac is negligible. Nepafenac Ophthalmic suspension can be used during breast-feeding.
Fertility: There is no data on the effect of Nepafenac ophthalmic suspension 0.3% on human fertility.
Effects on ability to drive and use machines
Effects on ability to drive and use machines effects on ability to drive and use medicines
Nepafenac ophthalmic suspension has no or negligible influence on the ability to drive and use machines. Temporary blurred vision or other visual disturbances may affect the ability to drive or use machines. If blurred vision occurs at instillation, the patient must wait until the vision clears before driving or using machines.
Undesirable effects
Summary of the safety profile

In clinical studies involving 2314 patients receiving Nepafenac 1 mg/ml the most common adverse reactions were punctate keratitis, foreign body sensation and eyelid margin crusting which occurred in between 0.4% and 0.2% of patients.
The following adverse reactions are classified according to the following convention: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to <1/1,000), very rare (< 1/10,000), or not known (cannot be estimated from available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness. The adverse reactions were obtained from clinical trials and post-marketing reports.
Immune system disorders: Rare: hypersensitivity.
Nervous system disorders: Rare: dizziness, headache.
Eye disorders: Uncommon: keratitis, punctate keratitis, corneal epithelium defect, foreign body sensation in eyes, eyelid margin crusting.
Rare: iritis, choroidal effusion, corneal deposits, eye pain, ocular discomfort, dry eye, blepharitis, eye irritation, eye pruritus, eye discharge, allergic conjunctivitis, increased lacrimation, conjunctival hyperaemia.
Not known: corneal perforation, impaired healing (cornea), corneal opacity, corneal scar, reduced visual acuity, eye swelling, and ulcerative keratitis, corneal thinning, and blurred vision.
Vascular disorders: Not known: blood pressure increased
Gastrointestinal disorders: Rare: nausea. Not known: vomiting.
Skin and subcutaneous tissue disorders: Rare: cutis laxa (dermatochalasis), allergic dermatitis.
Diabetic patients
In the two clinical studies involving 209 patients, diabetic patients were exposed to Nepafenac ophthalmic suspension 0.3% treatment for 60 days or greater for the prevention of macular edema post cataract surgery. The most frequently reported adverse reaction was punctate keratitis which occurred in 3% of patients, resulting in a frequency category of common. The other reported adverse reactions were corneal epithelium defect and allergic dermatitis which occurred in 1% and 0.5% of patients, respectively both adverse reactions with a frequency category of uncommon.
Description of selected adverse reactions
Clinical trial experience for the long-term use of Nepafenac ophthalmic suspension for the prevention of macular edema post cataract surgery in diabetic patients is limited. Ocular adverse reactions in diabetic patients may occur at a higher frequency than observed in the general population.
Patients with evidence of corneal epithelial breakdown including corneal perforation should immediately discontinue use of Nepafenac ophthalmic suspension and should be monitored closely for corneal health.
From post-marketing experience with Nepafenac ophthalmic suspension, cases reporting corneal epithelium defect/disorder have been identified. Severity of these cases vary from non-serious effects on the epithelial integrity of the corneal epithelium to more serious events where surgical interventions and/or medical therapy are required to regain clear vision.
Post-marketing experience with topical NSAIDs suggests that patients with complicated ocular surgeries, corneal denervation, corneal epithelial defects, diabetes mellitus, ocular surface diseases (eg, dry eye syndrome), rheumatoid arthritis or repeat ocular surgeries within a short period of time may be at increased risk for corneal adverse reactions which may become sight threatening. When nepafenac is prescribed to a diabetic patient post cataract surgery to prevent macular oedema, the existence of any additional risk factor should lead to reassessment of the foreseen benefit/risk and to intensified patient monitoring.
Paediatric population
The safety and efficacy of Nepafenac ophthalmic suspension in children and adolescents have not been established.
Overdose
No toxic effects are likely to occur in case of overdose with ocular use, nor in the event of accidental oral ingestion.
PHARMACOLOGICAL PROPERTIES
Pharmacotherapeutic group: Ophthalmologicals, Anti-inflammatory agents, non-steroids
Mechanism of Action
Nepafenac is a non-steroidal anti-inflammatory drug (NSAIDs) that inhibits the action of cyclooxygenase (COX) enzymes which are responsible for biosynthesis of prostaglandins and other prostanoids. Ocular hydrolases convert Nepafenac to amfenac, also NSAIDs. Both Nepafenac and amfenac inhibit the action of COX-1 and COX-2 with more selectivity for COX-1. Nepafenac is a reversible, no-time dependent inhibitor of COX enzymes, whereas amfenac is an irreversible, time dependent inhibitor of COX. The time dependent irreversible inhibition of COX enzyme by amfenac may have important clinical implications related to efficacy and safety of Nepafenac ophthalmic suspension 0.3%.
Pharmacodynamic properties
A single topical ocular dose of 0.1% or 0.3% Nepafenac in rabbits produced significant and prolonged inhibition of PGE2 synthesis in iris-ciliary body (ICB) with near maximum inhibition between 0.5 hours and 12 hours and about 90% inhibition at 24 hour after dosing. The sustained inhibition of prostaglandin synthesis in ICB is correlated to the irreversible inhibition of COX enzymes by amfenac. Both nepafenac and amfenac have also been shown to produce effective and prolonged inhibition of paracentesis-induced breakdown of the blood-aqueous barrier in at 1.2 hour, but approximately 10% inhibition at 3 hours after a single topical ocular dose of nepafenac 0.1% Nepafenac in rabbits. Therefore, topical administration nepafenac in rabbit eye has been shown to inhibit prostaglandin formation in both the anterior and posterior segments of eye. This observed rate and duration of PGE2 inhibition in retina/choroid are significantly lower and shorter respectively, compared to those in ICB after a single topical ocular dose of 0.1% Nepafenac in the animal.
Pharmacokinetics properties
Absorption: Following 3 times daily dosing of Nepafenac ophthalmic suspension in both eyes, low but quantifiable plasma concentrations of nepafenac and amfenac were observed in the majority of subjects 2 and 3 hours post-dose, respectively. The mean steady-state plasma Cmax for nepafenac and for amfenac were 0.310 ± 0.104 ng/ml and 0.422 ± 0.121 ng/ml, respectively, following ocular administration.
Distribution: Amfenac has a high affinity toward serum albumin proteins. In vitro, the percent bound to rat albumin, human albumin and human serum was 98.4%, 95.4% and 99.1%, respectively.
Studies in rats have shown that radioactive labeled active substance-related materials distribute widely in the body following single and multiple oral doses of 14C-nepafenac.
Studies in rabbits demonstrated that the topically administered nepafenac is distributed locally from the front of the eye to the posterior segments of the eye (retina and choroid).
Biotransformation: Nepafenac undergoes relatively rapid bioactivation to amfenac via intraocular hydrolases. Subsequently, amfenac undergoes extensive metabolism to more polar metabolites involving hydroxylation of the aromatic ring leading to glucuronide conjugate formation.
Radiochromatographic analyses before and after β-glucuronidase hydrolysis indicated that all metabolites were in the form of glucuronide conjugates, with the exception of amfenac. Amfenac was the major metabolite in plasma, representing approximately 13% of total plasma radioactivity. The second most abundant plasma metabolite was identified as 5-hydroxy nepafenac, representing approximately 9% of total radioactivity at Cmax.
Interactions with other medicinal products: Neither nepafenac nor amfenac inhibit any of the major human cytochrome P450 (CYP1A2, 2C9, 2C19, 2D6, 2E1 and 3A4) metabolic activities at concentrations up to 3000 ng/ml. Therefore, interactions involving CYP-mediated metabolism of concomitantly administered medicinal products are unlikely. Interactions mediated by protein binding are also unlikely.
Elimination: After oral administration of 14C-nepafenac to healthy volunteers, urinary excretion was found to be the major route of radioactive excretions, accounting for approximately 55% while faecal excretion represented approximately 6% of the dose. Nepafenac and amfenac were not quantifiable in the urine.
Following a single dose of Nepafenac ophthalmic suspension in 25 cataract surgery patients, aqueous humour concentrations were measured at 15, 30, 45 and 60 minutes post-dose. The maximum mean aqueous humour concentrations were observed at the 1 hour time-point (nepafenac 177 ng/ml, amfenac 44.8 ng/ml). These findings indicate rapid corneal penetration.
INCOMPATIBILITIES
Not applicable.

STORAGE: Store in a dry, well-ventilated place at a temperature not exceeding 25°C.

KEEP OUT OF REACH OF CHILDREN.
SHAKE WELL BEFORE USE.
PATIENT COUNSELLING INFORMATION
Slow or Delayed Healing: Patients should be informed of the possibility that slow or delayed healing may occur while using nonsteroidal anti-inflammatory drugs (NSAIDs).
Avoiding Contamination of the Product: Patients should be instructed to avoid allowing the tip of the dispensing container to contact the eye or surrounding structures because this could cause the tip to become contaminated by common bacteria known to cause ocular infections. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions. Use of the same bottle for both eyes is not recommended with topical eye drops that are used in association with surgery.
Contact Lens Wear: Nepafenac ophthalmic suspension 0.3% should not be administered while wearing contact lens.
Intercurrent Ocular Conditions: Patients should be advised that if they develop an intercurrent ocular condition (e.g., trauma, or infection) or have ocular surgery, they should immediately seek the physician's advice concerning the continued use of the multi-dose container.
Concomitant Topical Ocular Therapy: If more than one topical ophthalmic medication is being used, the medicine must be administered at least 5 minutes apart.
The Patients should be instructed to shake well before each use.
PRESENTATION
ZYNEP-OD eye drops is available in nilspell.

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