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

Nepafenac Ophthalmic Suspension 0.1 % w/v

SENSONAC™

For the use of Registered Medical Practitioner only

Composition:

Nepafenac ..... 0.1% w/v
Benzalkonium Chloride Solution USP ..... 0.01% v/v
(as preservative)
Water for Injection USP ..... q.s

Chemical Name
2-(2-amino-3-benzoylphenyl) acetamide
Category
Pharmacotherapeutic group: Ophthalmologicals, anti-inflammatory agents, non-steroids
ATC code: S01BC10
Description
Ophthalmic Suspension.
Greenish Yellow Colour Suspension filled in 5mL Sterile Gamma-irradiated white opaque LDPE bottle sealed with Sterile Gamma-irradiated natural transparent LDPE open nozzle and Sterile Gamma-irradiated white HDPE tamp safe cap in printed carton along with leaflet.
Pharmacology
Nepafenac is a non-steroidal 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 inhibits the action of prostaglandin H synthase (cyclooxygenase), an enzyme required for prostaglandin production. Other information
Secondary pharmacology: In rabbits, nepafenac has been shown to inhibit blood-retinalbarrier breakdown, concomitant with suppression of PGE2 synthesis. Ex vivo, a single topical ocular dose of nepafenac was shown to inhibit prostaglandin synthesis in the iris/ciliary body (85%-95%) and the retina/choroid (55%) for up to 6 hours and 4 hours, respectively.
Pharmacodynamic effects: The majority of hydrolytic conversion is in the retina/choroid followed by the iris/ciliary body and cornea, consistent with the degree of vascularised tissue. Results from clinical studies indicate that nepafenac eye drops have no significant effect on intraocular pressure.
Pharmacokinetic:
Absorption: Following 3 times daily dosing of nepafenac eye drops 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 labelled active substancerelated 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).
Metabolism: 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. Radio chromatographic analyses before and after β-glucuronidase hydrolysis indicated that all metabolites were in the form of glucuronide conjugates, with the exception ofamfenac. 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 activitiesin vitro at concentrations up to 3000 ng/ml. Therefore, interactions involving CYPmediated metabolism of concomitantly administered medicinal products are

unlikely. Interactions mediated by protein binding are also unlikely.

Excretion: After oral administration of 14C-nepafenac to healthy volunteers, urinary excretion was found to be the major route of radioactive excretions, accounting for approximately 85% while faecal excretion represented approximately 6% of the dose. Nepafenac and amfenac were not quantifiable in the urine.

Following a single dose of Nepafenac in 25 cataract surgery patients, aqueous humour concentrations were measured at 15, 30, 45 and 60 minutes post-dose. The maximum mean aqueoushumour concentrations were observed at the 1 hour time-point (nepafenac 177 ng/ml, amfenac 44.8 ng/ml). These findings indicate rapid corneal penetration.

Indications

Nepafenac Ophthalmic Suspension is indicated in adults for:

- Prevention and treatment of postoperative pain and inflammation associated with cataract surgery
- Reduction in the risk of postoperative macular oedema associated with cataract surgery in diabetic patients

Dosage & Administration

Adults, including the elderly

For the prevention and treatment of pain and inflammation, the dose is 1 drop of Nepafenac Ophthalmic Suspension in the conjunctival sac of the affected eye(s) 3 times daily beginning 1 day prior to cataract surgery, continued on the day of surgery and for the first 2 weeks of the postoperative period. Treatment can be extended to the first 3 weeks of the postoperative period as directed by the clinician. An additional drop should be administered 30 to 120 minutes prior to surgery. For the reduction in the risk of postoperative macular oedema associated with cataract surgery in diabetic patients, the dose is 1 drop of Nepafenac Ophthalmic Suspension in the conjunctival sac of the affected eye(s) 3 times daily beginning 1 day prior to cataract surgery, continued on the day of surgery and up to 60 days of the postoperative period as directed by the clinician. An additional drop should be administered 30 to 120 minutes prior to surgery.

Special populations

Patients with renal or hepatic impairment: Nepafenac Ophthalmic Suspension has not been studied in patients with hepatic disease or renal impairment. Nepafenac is eliminated primarily through biotransformation and the systemic exposure is very low following topicalocular administration. No dose adjustment is warranted in these patients.

Paediatric population: The safety and efficacy of Nepafenac Ophthalmic Suspension in children and adolescents have not been established. No data are available. Its use is not recommended in these patients until further data become available.

Geriatric population: No overall differences in safety and effectiveness have been observed between elderly and younger patients.

Method of Administration:

For ocular use only. Not for injection.

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. Indication of the most favorable time to administer the drug: 1 drop of Nepafenac Ophthalmic Suspension in the conjunctival sac of the affected eye(s) 3 times daily beginning 1 day prior to cataract surgery, continued on the day of surgery and for the first 2 weeks of the postoperative period.

Measures to be taken in case of omission of one or more doses: 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 one missed. If one dose of the medicine is forgotten, continue with the next dose as planned. If more medicine is used than recommended dose, rinse it all out with warm water. Don't put in any more drops until it's time for next regular dose.

Contraindications

Hypersensitivity to the active substance or to any of the excipients.

Hypersensitivity to other nonsteroidal anti-inflammatory drugs (NSAIDs). Patients in whom attacks of asthma, urticaria, or acute rhinitis are precipitated by acetylsalicylic acid or other NSAIDs.

Warning and Precaution

The product should not be injected. Patients should be instructed not to swallow

Nepafenac Ophthalmic Suspension.
Patients should be instructed to avoid sunlight during treatment with Nepafenac Ophthalmic Suspension.

Ocular effects

Use of topical NSAIDs may result in keratitis. In some susceptible patients, continued use of topical NSAIDs may result 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 Nepafenac Ophthalmic Suspension and should be monitored closely for corneal health. Topical NSAIDs may slow or delay healing. Topical corticosteroids are also known to slow or delay healing. Concomitant use of topical NSAIDs and topical steroids may increase the potential for healing problems. Therefore, it is recommended that caution should be exercised if Nepafenac Ophthalmic Suspension is administered concomitantly with corticosteroids, particularly in patients at high risk for corneal adverse reactions described below. Post-marketing experience with topical NSAIDs suggests that patients with complicated ocular surgeries, corneal denervation, corneal epithelial defects, diabetes mellitus, ocular surface diseases (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 reactions which may become sight threatening. Topical NSAIDs should be used with caution in these patients. Prolonged use of topical NSAIDs may increase patient risk for occurrence and severity of corneal adverse reactions. There have been reports that ophthalmic NSAIDs may cause increased bleeding of ocular tissues (including hyphaemas) in conjunction with ocular surgery. Nepafenac Ophthalmic Suspension should be used with caution in patients with known bleeding tendencies or who are receiving other medicinal products which may prolong bleeding time.

An acute ocular infection may be masked by the topical use of anti-inflammatory medicines. NSAIDs do not have any antimicrobial properties. In case of ocular infection, their use with anti-infectives should be undertaken with care.

Contact lenses: Contact lens wear is not recommended during the postoperative period following cataract surgery. Therefore, patients should be advised not to wear contact lenses unless clearly indicated by their doctor.

Benzalkonium chloride: Nepafenac Ophthalmic Suspension 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

ulcerativekeratopathy. Since Nepafenac Ophthalmic Suspension contains benzalkonium chloride, close monitoring is required with frequent or prolonged use.

Cross-sensitivity: There is a potential for cross-sensitivity of nepafenac to acetylsalicylic acid, phenylacetic acid derivatives, and other NSAIDs.

The safety and efficacy of Nepafenac Ophthalmic Suspension in children and adolescents have not been established. No data are available. Its use is not recommended in these patients. 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.

Interactions

In vitro studies have demonstrated a very low potential for interaction with other medicinal products and protein binding interactions. Prostaglandin analogues There are very limited data on the concomitant use of prostaglandin analogues and Nepafenac Ophthalmic Suspension. Considering their mechanism of action, the concomitant use of these medicinal products is not recommended.

Concomitant use of topical NSAIDs and topical steroids may increase the potential for healing problems. Concomitant use of Nepafenac Ophthalmic Suspension with medications that prolong bleeding time may increase the risk of haemorrhage.

Pregnancy & Lactation

Pregnancy

There are 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 parturition

and/or postnatal development. Nepafenac Ophthalmic Suspension is not recommended during pregnancy.
Nepafenac Ophthalmic Suspension should not be used by women of child bearing potential not using contraception.
There are no data on the effect of Nepafenac Ophthalmic Suspension on human fertility.

Lactation

It is unknown whether nepafenac 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 breastfeeding woman to nepafenac is negligible. Nepafenac Ophthalmic Suspension can be used during breastfeeding.

Adverse reaction

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 notknown(cannot be estimated from available data).

System organ:classification:Adverse reactions

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, conjunctivalhyperaemia
Not known: corneal perforation, impaired healing (cornea), corneal opacity, corneal scar, reduced visual acuity, eye swelling, ulcerative keratitis, corneal thinning, 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

Overdosage

No toxic effects are likely to occur in case of overdose with ocular use, nor in the event of accidental oral ingestion.

Storage

Store between 15°C - 30 °C. Protect from light. Keep out of reach of children.

Shelf life

24 Months from the date of manufacture.

Presentation

Greenish Yellow Colour Suspension filled in 5mL Sterile Gamma-irradiated white opaque LDPE bottle sealed with Sterile Gamma-irradiated natural transparent LDPE open nozzle and Sterile Gamma-irradiated white HDPE tamp safe cap in printed carton along with leaflet.

Directions for use :

Turn the tamper proof cap anti-clockwise to break the seal.

Remove the cap, dispense drops with gentle pressure.

Replace the cap immediately after every use.

Manufactured in INDIA by :

Senses Pharmaceuticals Pvt. Ltd.,

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Bommasandra 4th Phase, Bengaluru - 560 099.
Email: info@sensespharma.com

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