The first potent ophthalmic NSAID prodrug

**Sensonac**
(Nepafenac 0.1% w/v) Ophthalmic Suspension

- Onset of action is within 15 minutes and persist for more than 8 hours
- Corneal permeability Co-efficient of Nepafenac is 4, 19 and 28 times greater than Diclofenac, Bromfenac and Ketorolac respectively
- Effective in treating pain and inflammation associated with cataract surgery
- Effective in treatment of cystoid macular edema
SENSONAC ™
(Nepafenac Ophthalmic Suspension) Eye Drops

Composition:
Nepafenac ...........................................0.1% w/v
Benzalkonium chloride Solution IP........0.01% w/v
(As preservative)
Sterile aqueous vehicle ......................q.s.

Pharmacological Action
SENSONAC Eye Drops contains Nepafenac (0.1%), a nonsteroidal anti-inflammatory and analgesic prodrug. After topical ocular dosing, nepafenac penetrates the cornea and is converted by ocular tissue hydrolyses to amfenac, a potent nonsteroidal anti-inflammatory drug. Amfenac is thought to inhibit the action of prostaglandin H synthase (cyclooxygenase), an enzyme required for prostaglandin production. In rabbits, a single topical ocular dose of nepafenac (0.1%) leads to a uniform inhibition (80% to 100%) of prostaglandin formation by the iris/ciliary body. Suppression of prostaglandin E2 synthesis is maintained for a period of greater than 6 hours and is accompanied by a nearly 8 hour suppression of trauma-induced vascular leakage of the blood aqueous barrier.

Pharmacokinetics
Drug-Drug Interaction: Nepafenac at concentrations up to 300 ng/mL did not inhibit the in vitro metabolism of 6 specific marker substrates of cytochrome P450 (CYP) isoenzymes (CYP1A2, CYP2C9, CYP2C19, CYP2D6, CYP2E1, and CYP3A4). Therefore, drug-drug interactions involving CYP-mediated metabolism of concomitantly administered drugs are unlikely. Drug-drug interactions mediated by protein binding are also unlikely.

Indications: SENSONAC 0.1% Eye Drops is indicated for the inhibition and treatment of pain and inflammation associated with cataract surgery.

Dosage and Administration: Shake well before use. One drop of SENSONAC 0.1% Eye Drops should be applied to the affected eye(s) three-times-daily beginning 1 day prior to cataract surgery, and continued on the day of surgery and through the first 2 weeks of the postoperative period.

Contraindications
SENSONAC 0.1% Eye Drops is contraindicated in patients with previously demonstrated hypersensitivity to any of the ingredients in the formulation or to other NSAIDs.

Caution should be exercised when SENSONAC 0.1% Eye Drops is administered to a nursing woman. SENSONAC Eye Drops is excreted in the milk of pregnant rats. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, Lactating women SENSONAC ™ during late pregnancy should be avoided.

Because of the known effects of prostaglandin biosynthesis inhibiting drugs on the fetal cardiovascular system (closure of the ductus arteriosus), the use of SENSONAC ™ during late pregnancy should be avoided.

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Warnings: For topical use only and not for injection or any other use.

Precautions: General: There is the potential for cross-sensitivity to acetylsalicylic acid, phenylacetic acid derivatives, and other nonsteroidal anti-inflammatory agents. Therefore, caution should be used when treating individuals who have previously exhibited sensitivities to these drugs.

With some nonsteroidal anti-inflammatory drugs including SENSONAC, there exists the potential for increased bleeding time due to interference with thrombocyte aggregation. There have been reports that ocularly applied nonsteroidal anti-inflammatory drugs may cause increased bleeding of ocular tissues (including hyphemas) in conjunction with cataract surgery.

Topical nonsteroidal anti-inflammatory drugs (NSAIDs) including SENSONAC, 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.

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 topical NSAIDs including SENSONAC and should be closely monitored for corneal health.

Postmarketing 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 events which may become sight threatening. Topical NSAIDs should be used with caution in these patients.

Postmarketing experience with topical NSAIDs also suggests that use more than 1 day prior to surgery or use beyond 14 days post surgery may increase patient risk for occurrence and severity of corneal adverse events.

It is recommended that SENSONAC 0.1% Eye Drops be used with caution in patients with known bleeding tendencies or who are receiving medications which may prolong bleeding time.

Drug Interactions:

Pregnancy: Category C
Reproduction studies performed with nepafenac in rabbits and rats at oral doses up to 10 mg/kg/day have revealed no evidence of teratogenicity due to nepafenac, despite the induction of maternal toxicity. At this dose, the animal plasma exposure to nepafenac and amfenac was approximately 260 and 2400 times human plasma exposure at the recommended human topical ocular dose for rats and 80 and 680 times human plasma exposure for rabbits, respectively. In rats, maternally toxic doses ≥ 10 mg/kg were associated with dystocia, increased postimplantation loss, reduced fetal weights and growth, and reduced fetal survival.

Nepafenac has been shown to cross the placental barrier in rats. There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, SENSONAC Eye Drops should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Because of the known effects of prostaglandin biosynthesis inhibiting drugs on the fetal cardiovascular system (closure of the ductus arteriosus), the use of SENSONAC ™ during late pregnancy should be avoided.

Lactating women SENSONAC Eye Drops is excreted in the milk of pregnant rats. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when SENSONAC 0.1% Eye Drops is administered to a nursing woman.

Pediatric Use
The safety and effectiveness of SENSONAC 0.1% Eye Drops in pediatric patients below the age of 10 years have not been established.

Geriatric Use
No overall differences in safety and effectiveness have been observed between elderly and younger patients

Adverse Reactions
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 to 10% of patients.

Other ocular adverse events occurring at an incidence of 1 to 5% included conjunctival oedema, corneal oedema, dry eye, lid margin crusting, ocular discomfort, ocular hyperemia, ocular pain, ocular pruritus, photophobia, tearing and vitreous detachment.

Some of these events were the consequence of the cataract surgical procedure.

Nonocular adverse events reported at an incidence of 1 to 4% included headache, hypertension, nausea/vomiting, and sinusitis.

Overdose: No data are available in humans regarding overdosage by accidental or deliberate ingestion. The risk of overdosage by ingestion of the suspension is minimal.

Storage Instructions
STORE BELOW 250C. PROTECT FROM LIGHT. KEEP OUT OF REACH OF CHILDREN. FOR EXTERNAL USE ONLY.

Presentation: Sensonac is a sterile solution supplied in an opaque plastic bottle with a cap containing 5ml of solution.