fixed dose combination was mild transient burning 1.5% (1/66) eye irritation 1.5% (1/66) and stinging 1.5% (1/66). The most frequently reported adverse event with Olopatadine was mild transient burning 4.5% (3/63).

Olopatadine hydrochloride
The most frequently reported adverse events with olopatadine hydrochloride 0.1% ophthalmic solution are headache, blurred vision, burning or stinging, cold syndrome, dry eye, foreign body sensation, hyperaemia, nausea, pruritis, rhinitis, sinusitis and taste prevention.

Ketorolac tromethamine
The most frequently reported adverse events with ketorolac tromethamine 0.4% are transient stinging and burning on instillation, conjunctival hyperaemia, corneal infiltrates headache, ocular edema, and ocular pain. Other adverse events occurring with ketorolac tromethamine includes allergic reactions, corneal edema, iritis, ocular inflammation, ocular pain, superficial keratitis, and superficial ocular infections.

DOSAGE AND ADMINISTRATION
One drop in each affected eye, two times per day.

Storage
Store below 25°C. Do not freeze. Protect from light.

PRESENTATION
Available in 5ml, white opaque LDPE FFS vials.

Marketed by:
ALLERGAN INDIA PRIVATE LIMITED

Manufactured in India by :
Piramal Enterprises Limited
Plot No. 67-70, Sector 2,
Pithampur-454 775
Dist. Dhar, Madhya Pradesh

Printer's logo as shown

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

OLOPATADINE HYDROCHLORIDE PLUS KETOROLAC OPHTHALMIC SOLUTION

acupat®

Allergan.

DESCRIPTION
Each mL contains :

Olopatadine Hydrochloride IP equivalent to Olopatadine	1.0 mg
Ketorolac tromethamine IP	4.0 mg
Benzalkonium chloride IP	0.05 mg
Purified Water IP	q.s.

CLINICAL PHARMACOLOGY
Description: Olopatadine hydrochloride plus ketorolac tromethamine is a fixed dose combination eye drop, which contains olopatadine hydrochloride, a dual acting mast cell stabilizer with antihistaminic activity and Ketorolac tromethamine a nonsteroidal anti-inflammatory agent.

Olopatadine Hydrochloride
Olopatadine is an inhibitor of the release of histamine from the mast cell and a relatively selective histamine H1-antagonist that inhibits the in vivo and in vitro type 1 immediate hypersensitivity reaction including inhibition of histamine induced effects on human conjunctival epithelial cells.

Ketorolac Tromethamine
Ketorolac tromethamine is a nonsteroidal anti-inflammatory drug which, when administered systemically, has demonstrated analgesic, anti-inflammatory, and anti-pyretic activity. The mechanism of its action is thought to be due to its ability to inhibit prostaglandin biosynthesis. Ketorolac tromethamine given systemically does not cause pupil constriction.

CLINICAL STUDIES
In a randomized, open label, multicenter clinical trial, efficacy of a fixed dose combination of olopatadine hydrochloride 0.1% plus ketorolac tromethamine 0.4% was compared with olopatadine hydrochloride 0.1% in patients with seasonal allergic conjunctivitis for 21 days. Fifty patients in each arm were considered for efficacy analysis. The olopatadine plus ketorolac combination was found to be significantly more effective than olopatadine in treating the signs and symptoms of seasonal allergic conjunctivitis like itching, conjunctival hyperaemia, episcleral hyperaemia and chemosis. Both the study drugs were equally effective in controlling mucous discharge. Patients in both the treatment groups showed excellent tolerance and good acceptability.

INDICATIONS AND USAGE
Olopatadine hydrochloride plus ketorolac tromethamine ophthalmic solution is indicated for the treatment of signs and symptoms of seasonal allergic conjunctivitis.

CONTRAINDICATIONS
Olopatadine hydrochloride with ketorolac is contraindicated in individuals with known or suspected hypersensitivity to any of the active ingredients or excipients of the formulation.

WARNINGS

NOT FOR INJECTION.

As per the data available on the Ketorolac tromethamine, there is the potential for cross-sensitivity to acetylsalicylic acid, phenyl acetic 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 non steroidal anti-inflammatory drugs there exists the potential for increased bleeding time due to interference with thrombocyte aggregation. There have been reports that ocular applied non steroidal anti-inflammatory drugs may cause increased bleeding of ocular tissues in conjunction with ocular surgery.

PRECAUTIONS

General
To prevent contaminating the dropper tip and solution, care should be taken not to touch the eyelids or surroundings areas with the dropper tip bottle. Keep bottle tightly closed when not in use.

Patients should be advised not to wear contact lens if the eye is red. Patients who wear soft contact lenses and whose eyes are not red should be instructed to wait at least ten minutes after instilling ACUPAT™ before they insert their contact lenses

Concomitant use of topical NSAIDS and topical steroids may increase the potential for healing problems.

Use of topical NSAIDs may result in keratitis. 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 and should be closely monitored for corneal health.

Use of topical NSAIDs more than 24 hours prior surgery or use beyond 14 days post-surgery may increase patient risk for the occurrence and severity of corneal adverse events.

Ophthalmic solution containing Ketorolac has no or negligible influence on the ability to drive and use of machinery. However transient blurring of vision may occur on instillation of eye drop. Do not drive or use hazardous machinery unless vision is cleared.

Ocular toxicity study
Ocular toxicity study of olopatadine hydrochloride and ketorolac tromethamine ophthalmic solution was carried out in rabbit species for 28 days with repeated dosing every day. Olopatadine hydrochloride and ketorolac tromethamine ophthalmic solution was administered to groups of 2 rabbits of each sex in to both eye of each rabbit daily. The drugs were administered 4 times with the one hour interval for 28 consecutive days and then sacrificed and subjected to a complete necropsy. The untreated groups and the high dose groups were further observed for a post-treatment period of 14 days to permit evaluation of the persistence, reversibility or delayed occurrence of toxic effects. Olopatadine plus ketorolac ophthalmic solution did not cause any treatment related ocular toxicity, significant toxicological effect on hematological, biochemical and urinanalysis parameters or treatment related gross pathological and histopathological alterations in the tissues of male and female rabbits.

Pregnancy

Olopatadine Hydrochloride
Olopatadine hydrochloride is reported to be non-teratogenic in rats and rabbits. There are, however, no adequate and well controlled studies in pregnant women. Because animal studies are not always predictive of human responses, this drug should be used in pregnant women only if the potential benefit to the mother justifies the potential risk to the embryo or fetus.

Ketorolac tromethamine
Ketorolac tromethamine is reported to be non-teratogenic when administered during organogenesis, in rabbits or rats. There are no adequate and well-controlled studies in pregnant women. Ketorolac tromethamine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Non-teratogenic Effects
Because of known effects of prostaglandin –inhibiting drugs on the fetal cardio-vascular system (closure of the ductus arteriosus) the use of ketorolac tromethamine during late pregnancy should be avoided.

Nursing Mothers
Caution should be exercised when Olopatadine hydrochloride plus Ketorolac is administered to a nursing woman.

Pediatric Use
Use of Ketorolac 0.4% and olopatadine hydrochloride 0.1% as individual ophthalmic solutions for above the age of 3 years have been established. However the safety and efficacy of combined olopatidine plus ketorolac ophthalmic solution in pediatric patient have not been established.

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

ADVERSE EFFECTS

Olopatadine hydrochloride and Ketorolac tromethamine
In a randomized open label, multicenter trial, safety of a fixed dose combination of olopatadine hydrochloride 0.1% plus ketorolac tromethamine 0.4% was compared with olopatadine hydrochloride 0.1% ophthalmic solution in 129 patients (olopatadine plus ketorolac, n=66) olopatadine, n=63) with seasonal allergic conjunctivitis. The adverse events reported with the