ADVERSE REACTIONS
Below is the summary of adverse reactions following Clinical Studies.

Eye Pain.

Postmarketing Experience.
The following additional adverse reactions have been identified during postmarketing use of **Optive Fusion™** in clinical practice. Postmarketing reporting of these reactions is voluntary and from a population of uncertain size. it is not always possible to reliably estimate the frequency of these reactions.

EYE DISORDERS
Eye discharge. Eye irritation, Eyelid edema, Foreign body sensation in eyes, increased lacrimation, Eye swelling.

IMMUNE SYSTEM DISORDERS
Hypersensitivity.

OVERDOSE
Since carboxymethylcellulose sodium is pharmacologically inert and not absorbed systemically, the likelihood of systemic intoxication from topical overdose is not expected from the administration of **Optive Fusion™**. Additionally, no toxic side effects are expected should accidental systemic overdose occur.

DOSAGE
Instill 1 or 2 drops of **Optive Fusion™** in the affected eye(s) as needed. If used for postoperative care (e.g., following LASIK surgery), It is recommended for the patient to follow their eye doctor's instructions. Concomitant ocular medications should be administered at least 5 minutes apart from the instillation of **Optive Fusion™** to avoid washout effects.

HOW SUPPLIED
Optive Fusion™ Lubricant Eye Drops are supplied in 5 mL (Physician's sample), 5 mL and 10 mL (Sales Pack) plastic dropper bottles.

NOTE
Store in a cool place. Protect from light. The bottle should be kept tightly closed when not in use.

Use the solution within one month after opening the container.

MARKETED BY:
ALLERGAN INDIA PRIVATE LIMITED

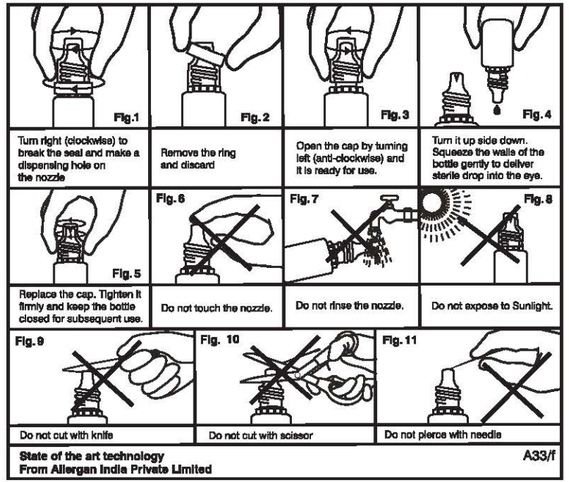
MANUFACTURED IN INDIA BY:
Piramal Enterprises Limited
Plot No. 67-70, Sector 2, Pithampur - 454 775,
Dist. Dhar, Madhya Pradesh

® & ™ marks owned by Allergan, Inc.

© 2015 Allergan. All rights reserved

Updated on Dec. 2013

A 479 □ 20715782



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

CARBOXYMETHYLCELLULOSE SODIUM EYE DROPS

optive **FUSION**™ *Lubricant Eye Drops*

ALLERGAN

Dual Action Lubricating and Moisturizing Comfort Solution

COMPOSITION
Each mL contains:

Sodium Carboxymethylcellulose IP/USP	5 mg
Stabilized Oxychloro Complex (Purite®)	0.1 mg
Purified Water IP	q.s.

(With : Sodium hyaluronate, Erythritol, Boric acid, Calcium chloride dihydrate, Magnesium chloride hexahydrate, Potassium chloride, Sodium borate decahydrate, Glycerin and Sodium citrate dihydrate)

Optive Fusion™ is unique dual-action formula provides long-lasting comfort.

Optive Fusion™ lubricates the surface of the eye and moisturizes the ocular surface cells by restoring natural osmotic balance.

Optive Fusion™ contains a unique, mild, non-sensitizing preservative PURITE® which breaks down into natural tear components on the eye.

CLINICAL PHARMACOLOGY
No clinical pharmacology studies were performed with **Optive Fusion™**. Carboxymethylcellulose sodium has no pharmacological receptor-mediated properties. The mode of action of Carboxymethylcellulose sodium is based on its physical properties which provides a lubricant effect and prolonged residence time on the eye. Carboxymethylcellulose sodium increases tear viscosity and has pseudoelastic (i.e. shear thinning) properties. Since Carboxymethylcellulose sodium is an ionic polymer containing carboxyl and hydroxyl groups, its chemical structure is similar to mucin in the tear film, and thus it has mucoadhesive properties. These properties promote prolonged residence time on the eye which alleviate the symptoms of tear deficiency. A multicenter, double-masked, randomized, 3-arm, parallel-group study was conducted to compare the safety, efficacy, and acceptability of 2 investigational eye drop formulations, **Optive Fusion™** and a formulation of **Optive Fusion™** that was similar, except it contained a higher concentration of HA with REFRESH TEARS, for 3 months in subjects with dry eye disease. A total of 286 subjects completed the study.
The primary efficacy endpoint was the change from baseline in OSDI symptom questionnaire score at day 90/ early exit. Secondary efficacy measures included symptom scale, near visual acuity, TBUT, Corneal staining and Schirmer test. Other efficacy measures included Visual Disturbance Questionnaire, Study product Usage Questionnaire, and MNREAD.

.

The primary efficacy endpoint was met. The **Optive Fusion™** formulations were non-inferior to the REFRESH TEARS formulation in reducing the severity of symptoms of dry eye based on the Non-inferiority margin of 7.3 as measured by the change from baseline in OSDI score. At day 90, no statistically significant differences were observed in the between-group comparisons of mean change from baseline in OSDI score for **Optive Fusion™**, a formulation of **Optive Fusion™** that was similar, except it contained a higher concentration of HA, versus REFRESH TEARS group in the ITT population.

PHARMACOKINETIC PROPERTIES
No pharmacokinetic studies have been performed. Since carmellose sodium is pharmacologically inert and not absorbed systemically it is not expected that safety issues will arise from the topical administration of **Optive Fusion™**

PRECLINICAL SAFETY DATA
Ocular Toxicology Studies
A 3-month ocular toxicity study was conducted in rabbits with a formulation of **Optive Fusion™** that was similar, except it contained a higher concentration of HA. Thus, testing of this formulation, which provides higher doses of HA, can be used to assess the nonclinical safety of **Optive Fusion™**. One drop was instilled topically in the left eye of rabbits 6 times daily at 1-hour intervals for 28 or 91 consecutive days. Based on gross ocular irritation observations, ophthalmic examinations (slit lamp biomicroscopy with fluorescein staining, indirect ophthalmoscopy), and macroscopic and microscopic ocular pathology, this formulation with 6 times per day ocular instillation for 3 months, was well tolerated in rabbits, and there were no adverse findings for any parameter.
A 3-week ocular toxicity study of **Optive Fusion™** with contact lens wear was conducted in rabbits. One drops was instilled topically in the left eye, 4 times (2 hour intervals) daily for 3 consecutive weeks with daily contact lenses wear in both eyes, Acuvue® 2 soft hydrophillic, PureVision™ silicone hydrogel, and Boston® EO® rigid gas permeable contact lenses were used. One drop of formulation **Optive Fusion™** was added to the inside, concave surface of the lens before insertion into the left eye. Based on gross ocular irritation examinations, ophthalmic examinations (including slit lamp biomicroscopy, pupillary reflex, and indirect ophthalmoscopy), macroscopic observations of eyes and extraocular tissues, and microscopic pathology of ocular tissue, topical ocular administration of **Optive Fusion™** was well-tolerated by rabbits with daily contact lens wear.

CARCINOGENICITY AND MUTAGENICITY STUDIES
No evidence of carcinogenicity was observed in oral studies in rats and mice receiving doses of CMC ranging from approximately 1000 mg/kg/day to 10,000 mg/kg/day. No mutagenic effects were observed with CMC in the Ames test "without activation"

INDICATION
For the temporary relief of burning, irritation, and discomfort due to dryness of the eye or due to exposure to wind or sun. May be used as a protectant against further irritation.

CONTRAINDICATIONS
Optive Fusion™ is contraindicated in patients with hypersensitivity to any ingredients in this product.

WARNINGS AND PRECAUTIONS
To avoid contamination or possible eye injury, do not touch tip of the bottle or vial to any surface and avoid contact with the eye.
Replace the cap after use.
Do not use if **Optive Fusion™** packaging shows evidence of tampering. Do not use if solution changes color or becomes cloudy. Discontinue use of **Optive Fusion™** and consult a doctor if you experience eye pain, changes in vision, continued redness or irritation of the eye, or if the condition worsens.
Use before the expiration date marked on the container.

DRUG INTERACTIONS
No known drug interactions.

USE IN PREGNANCY AND LACTATION
There are no specific study data on the use of **Optive Fusion™** during pregnancy and lactation in humans; however, animal studies with CMC have not demonstrated any harmful effects in pregnancy. Animal studies using glycerin have shown no evidence of teratogenicity. **Optive Fusion™** has not been studied in breast-feeding women; however **Optive Fusion™** is not expected to have significant systemic absorption; therefore, it would not be excreted in human breast milk.

PEDIATRIC USE
Safety and effectiveness have not been demonstrated with **Optive Fusion™** in pediatric patients.

GERIATRIC USE
No overall differences in safety or effectiveness have been observed between elderly and other adult patients.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES
Optive Fusion™ may cause transient blurring of vision which may impair the ability to drive or operate machines.
The patient should wait until their vision has cleared before driving or using machinery.