

# **OCULAST eye drops ( Azelastine 0.05 % )**

## **Composition**

Each mL of OCULAST contains: Azelastine hydrochloride, BP 0.5mg ;  
Preservative: Benzalkonium chloride Solution IP 0.02% ;

## **Clinical Pharmacology**

OCULAST is a relatively selective histamine H<sub>1</sub> antagonist and an inhibitor of the release of histamine and other mediators from cells (e.g. mast cells) involved in the allergic response. Based on in-vitro studies using human cell lines, inhibition of other mediators involved in allergic reactions (e.g. leukotrienes and PAF) has been demonstrated with azelastine hydrochloride. Decreased chemotaxis and activation of eosinophils has also been demonstrated.

## **Pharmacokinetics and Metabolism**

Absorption of azelastine following ocular administration was relatively low. A study in symptomatic patients receiving one drop OCULAST in each eye two to four times a day (0.06 to 0.12 mg azelastine hydrochloride) demonstrated plasma concentrations of OCULAST to generally be between 0.02 and 0.25 ng/mL after 56 days of treatment. Three of nineteen patients had quantifiable amounts of N-desmethylazelastine that ranged from 0.25-0.87 ng/mL at Day 56.

## **Clinical Trials**

In a conjunctival antigen challenge study, OCULAST was more effective than its vehicle in preventing itching associated with allergic conjunctivitis. OCULAST had a rapid (within 3 minutes) onset of effect and duration of effect of approximately 8 hours for the prevention of itching.

In environmental studies, adult and pediatric patients with seasonal allergic conjunctivitis were treated with OCULAST for two to eight weeks. In these studies, OCULAST was more effective than its vehicle in relieving itching associated with allergic conjunctivitis.

## **INDICATIONS AND USAGE**

OCULAST is indicated for the treatment of itching of the eye associated with allergic conjunctivitis.

## **Contraindications**

OCULAST is contraindicated in persons with known or suspected hypersensitivity to any of its components.

## **Warnings**

OCULAST is for ocular use only and not for injection or oral use.

### **Carcinogenesis, Mutagenesis, Impairment of Fertility:**

OCULAST administered orally for 24 months was not carcinogenic in rats and mice at doses up to 30 mg/kg/day and 25 mg/kg/day, respectively. Based on a 30 µl drop size, these doses were approximately 25,000 and 21,000 times higher than the maximum recommended ocular human use level of 0.001 mg/kg/day for a 50 kg adult. OCULAST showed no genotoxic effects in the Ames test, DNA repair test, mouse lymphoma forward mutation assay, mouse micronucleus test, or chromosomal aberration test in rat bone marrow. Reproduction and fertility studies in rats showed no effects on male or female fertility at oral doses of up to 25,000 times the maximum recommended ocular human use level. At 68.6 mg/kg/day (57,000 times the maximum recommended ocular human use level), the duration of the estrous cycle was prolonged and copulatory activity and the number of pregnancies were decreased. The numbers of corpora lutea and implantations were decreased; however, the implantation ratio was not affected.

### **Pregnancy:**

*Teratogenic Effects: Pregnancy Category C.* OCULAST has been shown to be embryotoxic, fetotoxic, and teratogenic (external and skeletal abnormalities) in mice at an oral dose of 68.6 mg/kg/day (57,000 times the recommended ocular human use level). At an oral dose of 30 mg/kg/day (25,000 times the recommended ocular human use level), delayed ossification (undeveloped metacarpus), and the incidence of 14th rib were increased in rats. At 68.6 mg/kg/day (57,000 times the maximum recommended ocular human use level) OCULAST caused resorption and fetotoxic effects in rats. The relevance to humans of these skeletal findings noted at only high drug exposure levels is unknown. There are no adequate and well-controlled studies in pregnant women. OCULAST should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

### **Nursing Mothers:**

It is not known whether OCULAST is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when OCULAST is administered to a nursing woman.

### **Pediatric Use:**

Safety and effectiveness in pediatric patients below the age of 3 have not been established.

### **GERIATRIC USE:**

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

**ADVERSE REACTIONS:**

In controlled multiple-dose studies where patients were treated for up to 56 days, the most frequently reported adverse reactions were transient eye burning/stinging (approximately 30%), headaches (approximately 15%), and bitter taste (approximately 10%). The occurrence of these events was generally mild. The following events were reported in 1-10% of patients: asthma, conjunctivitis, dyspnea, eye pain, fatigue, influenza-like symptoms, pharyngitis, pruritus, rhinitis and temporary blurring. Some of these events were similar to the underlying disease being studied.

**DOSAGE AND ADMINISTRATION:**

The recommended dose is one drop instilled into each affected eye twice a day.

**PRESENTATION:**

5 ml Lupolen vial.