AZELASTINE (Ophthalmic)

Introduction

VA CLASSIFICATION (Primary)¾ OP801

Commonly used brand name(s):Optivar.

Note: For a listing of dosage forms and brand names by country availability, see Dosage Forms section(s).

Category

Antihistaminic (H1¾receptor), ophthalmic; antiallergic, ophthalmic.

Indications

Accepted

Conjunctivitis, allergic (treatment)¾Azelastine is indicated for the treatment of symptoms of allergic conjunctivitis. 1

Pharmacology/Pharmacokinetics

Physicochemical characteristics:

Molecular weight¾ 418.37 1

pH¾ 5 - 6.5. 1

Melting point¾225°C. 1

Mechanism of action/Effect:

Antihistaminic, ophthalmic¾Acting as a selective histamine H1-receptor antagonist, azelastine inhibits the release of histamine and reduces the associated irritation and itching. 1

Antiallergic, ophthalmic¾From human in vitro cell studies, azelastine also reduces allergic reactions by inhibiting various inflammatory cellular mediators such as leukotrienes and platelet activating factor. 1

Absorption:

After ocular administration, absorption of azelastine occurs in low concentrations. In a study involving symptomatic patients, the administered dosage of one drop per eye two to four times a day (0.06 to 0.12 mg) developed patient plasma concentrations between 0.02 and 0.25 nanograms per mL after 56 treatment days. 1

Distribution:

Volume of distribution (Vol D)¾Steady state: 14.5 L per kg. It is unknown whether azelastine is excreted into human breast milk. 1

Protein binding:

Azelastine¾High (88%) 1

N-desmethylazelastine¾Very high (97%) 1

Biotransformation:

Hepatic; resulting in one primary metabolite, N-desmethylazelastine, via oxidation by the cytochrome P450 enzyme system. 1

Half-life:

Elimination¾ 22 hours. 1

Onset of action:

Ophthalmic administration¾Within 3 minutes of administration. 1

Duration of action:

Ophthalmic administration¾Approximately 8 hours. 1

Elimination:

Fecal¾75% (less than 10% unchanged) after oral administration. 1

Precautions to Consider

Carcinogenicity/Mutagenicity

Studies in rats and mice have shown that azelastine is not carcinogenic. This conclusion was reached after 24 months of oral administration of azelastine, with doses for rats up to 30 mg per kg per day and doses for mice up to 25 mg per kg per day. Respectively, these doses represent the equivalent of approximately 25,000 and 21,000 times greater than the maximum daily recommended ocular human dose. Mutagenicity findings were negative as verified by the following genotoxic tests: Ames test; DNA repair test; mouse lymphoma forward mutation assay; mouse micronucleus test; or chromosomal aberration test in rat bone marrow. 1

Pregnancy/Reproduction

Fertility¾At oral doses of up to 25,000 times the maximum recommended ocular human dose, reproduction and fertility studies showed no effects on male or female rats. 1

Pregnancy¾No adequate and well-controlled studies in pregnant women have been done. 1

Animal studies with mice and rats showed evidence of fetotoxic and teratogenic effects when given azelastine orally at doses of 68.6 mg per kg per day (57,000 times the recommended ocular human dose). 1

FDA Pregnancy Category C. 1

Breast-feeding

It is not known whether azelastine is distributed into human breast milk. 1

Pediatrics

Appropriate studies on the relationship of age to the effects of azelastine have not been performed in children under 3 years of age. Safety and efficacy have not been established in this population. 1

Geriatrics

Appropriate studies performed to date have not demonstrated geriatrics-specific problems that would limit the usefulness of azelastine in the elderly. 1

Medical considerations/Contraindications

The medical considerations/contraindications included have been selected on the basis of their potential clinical significance (reasons given in parentheses where appropriate)¾ not necessarily inclusive (>> = major clinical significance).
Risk-benefit should be considered when the following medical problems exist

Hypersensitivity to azelastine 1

Side/Adverse Effects

The following side/adverse effects have been selected on the basis of their potential clinical significance (possible signs and symptoms in parentheses where appropriate)¾not necessarily inclusive:
Those indicating need for medical attention

Incidence less frequent (1% to 10%)

Asthma 1 (cough; difficulty breathing ; noisy breathing ; shortness of breath ; tightness in chest; wheezing); dyspnea 1 (shortness of breath; difficult or labored breathing; tightness in chest; wheezing)
Those indicating need for medical attention only if they continue or are bothersome

Incidence more frequent (greater than 10%)

Bitter taste in mouth 1; headaches 1; transient eye burning or stinging 1

Incidence less frequent (1% to 10%)

Conjunctivitis 1 (redness, pain, swelling of eye, eyelid, or inner lining of eyelid; burning, dry or itching eyes; discharge; excessive tearing); eye pain 1; fatigue 1 (unusual tiredness or weakness); influenza-like symptoms 1 (chills; cough; diarrhea; fever; general feeling of discomfort or illness; headache; joint pain; loss of appetite ; muscle aches and pains; nausea; runny nose; shivering; sore throat ; sweating; trouble sleeping; unusual tiredness or weakness; vomiting); pharyngitis 1 (body aches or pain; congestion; cough; dryness or soreness of throat; fever; hoarseness; runny nose; tender, swollen glands in neck; trouble in swallowing; voice changes); pruritus 1 (itching skin); rhinitis 1 (stuffy nose; runny nose; sneezing); temporary blurring vision 1

Patient Consultation

As an aid to patient consultation, refer to Advice for the Patient, Azelastine (Ophthalmic).
In providing consultation, consider emphasizing the following selected information (>> = major clinical significance):
Before using this medication

>> Conditions affecting use, especially:

Hypersensitivity to azelastine
Proper use of this medication

>> Importance of removing contact lenses prior to administration of medication; not using if eyes are red or irritated due to contact lenses

>> Proper administration technique for ophthalmic solution

>> Preventing contamination: Not touching applicator tip to any surface; keeping container tightly closed

>> Proper dosing
Using as soon as possible; not using if almost time for next dose; using next dose at regularly scheduled time; not doubling doses
>> Proper storage
Precautions while using this medication

>> Checking with physician if symptoms do not improve or if condition worsens

Side/adverse effects

Signs of potential side effects, especially asthma and dyspnea

General Dosing Information

Because the preservative, benzalkonium chloride, may be absorbed by contact lenses, it is recommended that they be removed prior to administration of azelastine. The lenses may be reinserted 10 minutes after administration of the medication. 1

Azelastine should not be administered if eyes are red or irritated secondary to use of contact lenses. 1

Ophthalmic Dosage Forms

AZELASTINE HYDROCHLORIDE OPHTHALMIC SOLUTION

Usual Adult and Adolescent Dose

Allergic conjunctivitis¾Topical to the conjunctiva, 1 drop in the affected eye(s) 2 times per day. 1

Usual Pediatric Dose

Allergic conjunctivitis¾Children younger than 3 years of age: Safety and efficacy have not been established. 1

Children 3 years of age and older: See Usual adult and adolescent dose.

Usual Geriatric Dose

SeeUsual adult and adolescent dose.

Strength(s) usually available
U.S.¾0.5 mg (0.457 mg base) per mL (Rx)[Optivar (Benzalkonium chloride 0.125 mg) (disodium edetate dihydrate) (hydroxypropylmethylcellulose) (sorbitol solution) (sodium hydroxide) (water)] 1

Packaging and storage:

Store upright below 40 °C (104 °F), preferably between 2 and 25 °C (36 and 77 °F). 1

Auxiliary labeling:

· For the eye.