

Ocurest-AH[®]

Composition:

Each ml of Ocurest AH eye drops contains:

Chlorpheniramine	0.1%w/v
Phenylephrine hydrochloride	0.12% w/v
Naphazoline hydrochloride	0.05% w/v
Menthol	0.005% w/v
Camphor	0.01% w/v

Pharmacokinetic properties:

Chlorphenamine maleate is absorbed relatively slowly from the gastrointestinal tract, peak plasma concentrations occurring about 2.5 to 6 hours after oral doses. Bioavailability is low, values of 25 to 50% having been reported. Chlorphenamine appears to undergo considerable first-pass metabolism. About 70% of chlorphenamine in the circulation is bound to plasma proteins. There is wide inter individual variation in the pharmacokinetics of chlorphenamine; values ranging from 2 to 43 hours have been reported for the half-life. Chlorphenamine is widely distributed in the body, and enters the CNS. Chlorphenamine maleate is extensively metabolised. Metabolites include desmethyl- and didesmethylchlorphenamine. Unchanged drug and metabolites are excreted primarily in the urine; excretion is dependent on urinary pH and flow rate. Only trace amounts have been found in the faeces. Duration of action of 4 to 6 hours has been reported; this is shorter than may be predicted from pharmacokinetic parameters. More rapid and extensive absorption, faster clearance, and a shorter half-life have been reported in children.

Phenylephrine has low oral bioavailability owing to irregular absorption and first-pass metabolism by monoamine oxidase in the gut and liver. When injected subcutaneously or intramuscularly it takes 10 to 15 minutes to act; subcutaneous and intramuscular injections are effective for up to about 1 hour and up to about 2 hours, respectively. Intravenous injections are effective for about 20 minutes. Systemic absorption follows topical application

Systemic absorption has been reported after topical use of solutions of naphazoline. It is not given systemically, but it is readily absorbed from the gastrointestinal tract. Naphazoline instilled into the eye causes conjunctival vasoconstriction within 10 minutes and effects can last for up to 6 hours.

Camphor is readily absorbed from all administration sites. It is hydroxylated in the liver to yield hydroxycamphor metabolites which are then conjugated with glucuronic acid and excreted in the urine. Camphor crosses the placenta.



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After absorption, menthol is excreted in the urine and bile as a glucuronide. The systemic absorption of camphor, menthol, and methyl salicylate from dermal patches containing all three ingredients has been studied. The absolute bioavailability of these compounds could not be determined from this study, but there did not appear to be any substantial systemic accumulation even after unrealistically high exposure for prolonged periods.

Mechanism of Action

In allergic reactions, an allergen interacts with and cross-links surface IgE antibodies on mast cells and basophils. Once the mast cell-antibody-antigen complex is formed, a complex series of events occurs that eventually leads to cell-degranulation and the release of histamine (and other chemical mediators) from the mast cell or basophil. Once released, histamine can react with local or widespread tissues through histamine receptors. Histamine, acting on H₁-receptors, produces pruritis, vasodilatation, hypotension, flushing, headache, tachycardia, and bronchoconstriction. Histamine also increases vascular permeability and potentiates pain. Chlorpheniramine maleate binds to the histamine H₁ receptor. This block the action of endogenous histamine, which subsequently leads to temporary relief of the negative symptoms brought on by histamine.

Phenylephrine hydrochloride is an α -1 adrenergic agonist drug that is used in ophthalmology mainly for its mydriatic effect. After topical application to the conjunctiva, phenylephrine acts directly on α -adrenergic receptors in the eye, producing contraction of the dilator muscle of the pupil and constriction of the arterioles in the conjunctiva.

Naphazoline ophthalmic solution causes constriction of blood vessels in the eyes. It also decreases itching and irritation of the eyes. Naphazoline constricts the vascular system of the conjunctiva. It is presumed that this effect is due to direct stimulation action of the drug upon the alpha adrenergic receptors in the arterioles of the conjunctiva resulting in decreased conjunctival congestion.

Menthol primarily activates the cold-sensitive TRPM8 receptors in the skin. Menthol, after topical application, causes a feeling of coolness due to stimulation of 'cold' receptors by inhibiting Ca⁺⁺ currents of neuronal membranes. It may also yield analgesic properties via kappa-opioid receptor agonism.

Camphor provides cooling and soothing effect.

Other pharmacodynamic properties:

Chlorpheniramine maleate is a histamine H₁ antagonist of the alkylamine class. It competes with histamine for the normal H₁-receptor sites on effector cells of the gastrointestinal tract, blood vessels and respiratory tract. It provides effective, temporary relief of sneezing, watery and itchy eyes, and runny nose due to hay fever and other upper respiratory allergies.

Phenylephrine is a powerful vasoconstrictor. It is used as a nasal decongestant and cardiostimulant agent. Phenylephrine is a postsynaptic α ₁-receptor agonist with little effect on β -receptors of the heart. Parenteral administration of phenylephrine causes a rise in systolic and diastolic pressures, a slight decrease in cardiac output, and a considerable increase in



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peripheral resistance; most vascular beds are constricted, and renal, splanchnic, cutaneous, and limb blood flows are reduced while coronary blood flow is increased. Phenylephrine also causes pulmonary vessel constriction and subsequent increase in pulmonary arterial pressure. Vasoconstriction in the mucosa of the respiratory tract leads to decreased edema and increased drainage of sinus cavities.

Naphazoline is a direct acting sympathomimetic adrenergic alpha-agonist used to induce systemic vasoconstriction, thereby decreasing nasal congestion and inducing constriction around the conjunctiva. The sympathomimetic action of Naphazoline constricts the smaller arterioles of the nasal passages, producing a decongesting effect. Naphazoline ophthalmic causes constriction of blood vessels in the eyes. It also decreases itching and irritation of the eyes. Naphazoline constricts the vascular system of the conjunctiva. It is presumed that this effect is due to direct stimulation action of the drug upon the alpha adrenergic receptors in the arterioles of the conjunctiva resulting in decreased conjunctival congestion. Naphazoline belongs to the imidazoline class of sympathomimetics.

Menthol is a covalent organic compound made synthetically or obtained from peppermint or other mint oils. Menthol's ability to chemically trigger cold-sensitive receptors in the skin is responsible for the well-known cooling sensation that it provokes when inhaled, eaten, or applied to the skin. It should be noted that menthol does not cause an actual drop in temperature.

Indication:

OCUREST AH EYE DROPS is indicated for:

- Temporary relief of discomfort and congestion occurring with minor eye irritation due to hayfever, dust, smoke, smog, colds, wind, sun, swimming.
- In allergic conjunctivitis, vernal conjunctivitis, phlyctenular conjunctivitis.
- Ocular itching, redness and tearing.

Contraindication:

The use of OCUREST AH EYE DROPS is contraindicated in patients with narrow angle glaucoma.

Drug Interaction:

Although, clinically significant drug-drug interactions between OCUREST AH EYE DROPS and systemically administered drugs are not expected but may occur when co administered with monoamine oxidase inhibitors or beta blockers.

Adverse effects:

- Prolonged use of decongestants may result in rebound congestion.
- Adverse reactions to OCUREST AH EYE DROPS are rare and may include tachycardia, hypertension, headache, blurred vision and flushed skin. Pupillary dilation with increased intra-ocular pressure and drowsiness may be experienced by some patients.



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Warnings and Precautions:

- The use of OCUREST AH EYE DROPS should be with caution in patients with heart disease, hypertension or difficulty in urination due to enlargement of the prostate gland.
- Prolonged use of decongestants is associated with rebound congestion.
- The use of OCUREST AH EYE DROPS should be discontinued If patient experiences pain, changes in vision, continued redness or irritation, or if the condition worsens, or persists for more than 72 hours.
- It is advisable not to drive, operate machinery or perform other hazardous activities when on treatment with OCUREST AH EYE DROPS.

Use in special population:

1. **Pediatric:** Safety and efficacy in children has not been established.
2. **Geriatric:** Safety and efficacy in elderly patients has not been established.
3. **Liver impairment:** There is no data available.
4. **Renal failure:** Caution to be advised in patients with severe impaired renal function.
5. **Pregnancy and lactation:** There are no well-controlled trials with OCUREST AH EYE DROPS in pregnant and lactating women. Therefore, OCUREST AH EYE DROPS should only be used if clearly indicated.

Dosage:

As directed by physician.

Presentation:

OCUREST AH EYE DROPS is available in a 10 ml lupolen vial

Storage and handling:

Store in cool and dry place.



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