INDICATIONS AND USAGE

Pilocarpine Hydrochloride Ophthalmic Solution, USP 1%, 2% and 4% is a muscarinic cholinergic agonist indicated for:

- The reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension (1.1)
- The management of acute angle-closure glaucoma (1.2)
- The prevention of postoperative elevated IOP associated with laser surgery (1.3)
- The induction of miosis (1.4)

DOSE AND ADMINISTRATION

- Instill one drop in the eye(s) up to four times daily (2).

DOSAGE FORMS AND STRENGTHS

- Solution containing 1% (10 mg/mL), 2% (20 mg/mL) or 4% (40 mg/mL) pilocarpine hydrochloride (3)

CONTRAINDICATIONS

None.

WARNINGS AND PRECAUTIONS

- Poor illumination: Exercise caution in night driving and other hazardous occupations in poor illumination (5.1).
- Pre-existing retinal disease: Rare cases of retinal detachment have been reported; a thorough examination of the retina, including fundoscopy, is advised in all patients prior to the initiation of therapy (5.2).
- Iritis: Caution is advised in patients with iritis (5.3).
- Congenital glaucoma: Caution is advised in pediatric patients with primary congenital glaucoma for control of IOP as cases of a paradoxical increase in IOP have been reported (5.4).

ADVERSE REACTIONS

Most common adverse reactions are headache/browache, accommodative change, eye irritation, eye pain, blurred vision, and/or visual impairment (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact Akorn, Inc. at 1-800-932-5676 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 4/2012
5.2 Pre-existing Retinal Disease
As with all miotics, rare cases of retinal detachment have been reported when used in certain susceptible individuals and those with pre-existing retinal disease; therefore, a thorough examination of the retina including funduscopy is advised in all patients prior to the initiation of therapy.

5.3 Iritis
Pilocarpine Hydrochloride Ophthalmic Solution is not recommended to be used when iritis is present.

5.4 Primary Congenital Glaucoma
Caution is advised when using Pilocarpine Hydrochloride Ophthalmic Solution in pediatric patients with primary congenital glaucoma for control of intraocular pressure (IOP) as cases of a paradoxical increase in IOP have been reported. In addition, the use of Pilocarpine Hydrochloride Ophthalmic Solution is not recommended in pediatric patients diagnosed with glaucoma secondary to anterior segment dysgenesis or uveitis (especially if uveitis is active).

5.5 Contact Lens Wear
Contact lens wearers should be advised to remove their lenses prior to the instillation of Pilocarpine Hydrochloride Ophthalmic Solution and to wait 10 minutes after dosing before reinserting their contact lenses.

6 ADVERSE REACTIONS
Clinical Studies Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety data described below reflect exposure in four controlled clinical trials of 90 days to 2 years duration in 317 patients diagnosed with open-angle glaucoma or ocular hypertension. In the four clinical trials, patients were treated with Pilocarpine Hydrochloride Ophthalmic Solution 2%, two to four times daily or with Pilocarpine 1%, 1.75% or 2% in fixed combination with Betaxolol 0.25%, two or three times daily. The most frequently reported adverse reactions occurring in >5% of patients in the Pilocarpine 2% populations were: headache/browache, accommodative change, blurred vision, eye irritation, visual impairment (dim, dark, or "jumping" vision), and eye pain. The adverse reaction profile reported for the use of Pilocarpine Hydrochloride Ophthalmic Solution in pediatric patients is comparable to that seen in adult patients.

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
Pregnancy. Category C. Animal reproduction studies have not been conducted with pilocarpine hydrochloride. It is also not known whether pilocarpine hydrochloride can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Pilocarpine Hydrochloride Ophthalmic Solution should be given to a pregnant woman only if clearly needed.

8.3 Nursing Mothers
It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Pilocarpine Hydrochloride Ophthalmic Solution is administered to a nursing woman.

8.4 Pediatric Use
Safety and effectiveness of Pilocarpine Hydrochloride Ophthalmic Solution in pediatric patients have been established.

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

10 OVERDOSAGE
Systemic toxicity following topical ocular administration of pilocarpine is rare, but occasionally patients who are sensitive may develop sweating and gastrointestinal overactivity following the suggested dosage and administration. Overdosage can produce sweating, salivation, nausea, tremors and slowing of the pulse and a decrease in blood pressure. In moderate overdosage, spontaneous recovery is to be expected and is aided by intravenous fluids to compensate for dehydration. For patients demonstrating severe poisoning, atropine, the pharmacologic antagonist to pilocarpine, should be used.

11 DESCRIPTION
Pilocarpine Hydrochloride Ophthalmic Solution, USP is a cholinergic agonist prepared as a sterile topical ophthalmic solution. The active ingredient is represented by the chemical structure:

![Chemical Structure](image)

Established name: Pilocarpine hydrochloride
Chemical name: 2(3H)-furanone, 3-ethyldihydro-4-[(1-methyl-1H-imidazo[5-yl]-methyl)monohydrochloride, (3S-cis)-
Molecular Formula: C_{14}H_{24}N_{2}O_{4} + HCl
Molecular Weight: 244.72

Each mL of Pilocarpine Hydrochloride Ophthalmic Solution, USP contains:

**Active:** Pilocarpine Hydrochloride 1% (10 mg/mL), 2% (20 mg/mL), or 4% (40 mg/mL).

**Preservative:** Benzalkonium Chloride 0.01%.

**Inactives:** Hydroxymethylcellulose (2910) 5 mg (0.5%), Boric Acid, Sodium Citrate, Sodium Chloride (present in 1% only); Hydrochloric Acid and/or Sodium Hydroxide (to adjust pH); Water for Injection.

Pilocarpine Hydrochloride Ophthalmic Solution, USP has a pH of 3.5 to 5.5 and an osmolality of 270 to 350 mOsm/kg (1% product), 290 to 350 mOsm/kg (2% product) and 500 to 600 mOsm/kg (4% product).

12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
Pilocarpine Hydrochloride is a direct acting cholinergic parasympathomimetic agent which acts through direct stimulation of muscarinic receptors and smooth muscle such as the iris and secretory glands. Pilocarpine contracts the iris muscle, causing increased tension on the scleral spur and opening of the trabecular meshwork spaces to facilitate outflow of aqueous humor. Outflow resistance is reduced, lowering intraocular pressure (IOP). Pilocarpine also produces miosis through contraction of the iris sphincter muscle. Miosis relieves appositional angle narrowing and closure, which lowers IOP in certain types of angle-closure glaucoma.

12.3 Pharmacokinetics
Systemic exposure to Pilocarpine was evaluated in 14 healthy subjects administered 2 drops of Pilocarpine Hydrochloride Ophthalmic Solution 4% to both eyes four times daily for eight days. A comparison of C_{max} values on Days 5 and 8 indicated that pilocarpine concentrations in plasma reached steady-state following topical administration of Pilocarpine Hydrochloride Ophthalmic Solution 4%. The mean (SD) C_{max} and AUC values on Day 8 were 3.7 (3.2) ng/mL and 7.7 (8.4) ng×hour/mL, respectively. The T_{max} values on Day 8 ranged from 0.5 to 1 hour.

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
There have been no long-term studies done using Pilocarpine Hydrochloride in animals to evaluate carcinogenic potential.

14 CLINICAL STUDIES
In clinical trials reported in the medical literature, Pilocarpine ophthalmic solution reduced intraocular pressure (IOP) by 3-7 mmHg in patients with open-angle glaucoma. Pilocarpine ophthalmic solution has also been shown to be effective in the induction of miosis, in the prevention of postoperative elevated IOP, and in the management of acute angle-closure glaucoma.

16 HOW SUPPLIED/STORAGE AND HANDLING
Pilocarpine Hydrochloride Ophthalmic Solution, USP 1%, 2% and 4% is supplied sterile in white low density polyethylene plastic ophthalmic bottles and natural low density polyethylene tips with green polypropylene caps.

15 mL in 15 mL bottles
1% - NDC 17478-223-12
2% - NDC 17478-224-12
4% - NDC 17478-226-12

STORAGE: Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature]. Protect from freezing. Keep tightly closed.

17 PATIENT COUNSELING INFORMATION
17.1 Avoiding Contamination of the Product
Do not touch dropper tip to any surface, as this may contaminate the contents.

17.2 Night Driving
Caution is advised with night driving and hazardous activities are undertaken in poor illumination.

17.3 Accommodative Spasm
Pilocarpine Hydrochloride Ophthalmic Solution may cause problems when changing focus between near objects and distant objects. Do not drive or use machinery if vision is not clear.

17.4 Contact Lens Wear
Contact lens should be removed prior to the instillation of Pilocarpine Hydrochloride Ophthalmic Solution. Wait 10 minutes after dosing before reinserting contact lenses.

17.5 Concomitant Topical Ocular Therapy
If more than one topical ophthalmic medication is being used, the medicines must be administered at least 5 minutes apart.

17.6 Systemic Exposure
To limit exposure to Pilocarpine to the eye alone, close eyes gently and apply pressure with finger to the corner of eye by the nose for 2 minutes after instillation of Pilocarpine Hydrochloride Ophthalmic Solution.

Rx Only