HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Pilocarpine Hydrochloride Ophthalmic Solution safely and effectively. See full prescribing information for Pilocarpine Hydrochloride Ophthalmic Solution.

Pilocarpine Hydrochloride Ophthalmic Solution 1%, 2% and 4%

WARNINGs AND PRECAUTIONs

• Poor illumination: Exercise caution in night driving and other hazardous occupations in poor illumination.

• Pre-existing Retinal Disease: Rare cases of retinal detachment have been reported; a thorough examination of the retina including funduscopic examination is advised in 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 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 photophobia. (6)

OVERDOSAGE

To report SUSPECTED ADVERSE REACTIONS, contact Sandoz Inc. at 1-800-525-8474 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

17.4 Contact Lens Wear

Contact lenses should be removed to allow the lenses to settle in the lower fornix. Do not drive or use machinery until vision is fully recovered. (17)

17.5 Geriatric Use

No overall differences in safety or effectiveness have been observed between elderly and younger patients. (17)

6 ADVERSE REACTIONS

6.1 Reduction of Elevated Intraocular Pressure (IOP) in Patients with Open-angle Glaucoma or Ocular Hypertension

Pilocarpine Hydrochloride Ophthalmic Solution 1%, 2% or 4% (or two drops administered five minutes apart) should be applied topically to the eye in the following cases:

1. 2.5% to 5% increase in IOP

2. 5% to 10% increase in IOP

3. 10% or more increase in IOP

4. IOP > 30 mmHg

5. IOP > 35 mmHg

6. IOP > 40 mmHg

7. IOP > 45 mmHg

8. IOP > 50 mmHg

9. IOP > 55 mmHg

10. IOP > 60 mmHg

11. IOP > 65 mmHg

12. IOP > 70 mmHg

13. IOP > 75 mmHg

14. IOP > 80 mmHg

15. IOP > 85 mmHg

16. IOP > 90 mmHg

17. IOP > 95 mmHg

18. IOP > 100 mmHg

In clinical trials reported in the medical literature, pilocarpine ophthalmic solution reduced 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 IOP increase, and in the management of acute angle-closure glaucoma.

10 OVERDOSAGE

10.1 Systemic Overdosage

Systemic following topical ocular administration of pilocarpine is rare, but occasionally patients who are sensitive to medication may experience systemic symptoms. These symptoms may include:

1. Hypotension

2. Bradycardia

3. Tachycardia

4. Arrhythmia

5. Syncope

6. Seizures

7. Nausea

8. Vomiting

9. Abdominal discomfort

10. Diarrhea

11. Rash

12. Urticaria

13. Anaphylaxis

14. Hypersensitivity reactions

15. Seizures

16. Coma

17. Death

18. Hypersensitivity reactions

19. Anaphylaxis

20. Seizures

21. Death

19. Comatose

20. Respiratory arrest

21. Death

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Pilocarpine is a direct acting cholinergic agonist which acts through direct stimulation of muscarinic receptors and smooth muscles such as the iris and secretory glands.

Pilocarpine contracts the ciliary muscle, causing increased tension on the scleral spur and opening of the trabecular meshwork spaces to facilitate outflow of aqueous humor. Outflow resistance is decreased by lowering intraocular pressure (IOP). Pilocarpine also produces miosis through contraction of the iris sphincter muscle. For this reason, pilocarpine may cause an additional angle narrowing and closure, which lowers IOP in certain types of angle-closure glaucoma.

12.2 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 8 days. A comparison of Cmax values on Days 5 and 6 indicated that pilocarpine concentrations in plasma reached steady-state following topical administration of Pilocarpine Hydrochloride Ophthalmic Solution 4%. The mean (SD) Cmax and AUC0-last values on Day 5 were 3.7 (2.2) ng/mL and 7.8 (4.0) ng•h/mL, respectively. The Tmax values on Day 5 ranged from 0.1 to 0.5 hours.

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 studies, pilocarpine ophthalmic solution has been studied in patients with open-angle glaucoma. Pilocarpine solution has also been shown to be effective in the induction of miosis, in the prevention of postoperative IOP increase, and in the management of acute angle-closure glaucoma.

16.1 Storage/Stability

Pilocarpine Hydrochloride Ophthalmic Solution 1%, 2%, and 4% is supplied in sterile single use containers. Use the container within 2 months of first opening after resealing the contact lenses.

6 ADVERSE REACTIONS

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