This English version is intended to be a reference material for the convenience of users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

Summary of Investigation Results

Preparations containing brimonidine tartrate

June 11, 2024

Non-proprietary name

a. Brimonidine tartrate
b. Brimonidine tartrate/timolol maleate
c. Brimonidine tartrate/brinzolamide
d. Ripasudil hydrochloride hydrate/brimonidine tartrate

Brand name (marketing authorization holder)

a. Aiphagan Ophthalmic Solution 0.1% (Senju Pharmaceutical Co., Ltd.), and the others
b. Aibeta Combination Ophthalmic Solution (Senju Pharmaceutical Co., Ltd.)
c. Ailamide Combination Ophthalmic Suspension (Senju Pharmaceutical Co., Ltd.)
d. Gla-alpha combination ophthalmic solution (Kowa Company, Ltd.)

Japanese market launch

a. May 2012
b. December 2019
c. June 2020
d. December 2022

Indications

a.

Glaucoma and ocular hypertension when other glaucoma drugs are not sufficiently effective or cannot be used

b., c., d.

Glaucoma and ocular hypertension in patients who have not responded sufficiently to other anti-glaucoma drugs

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Summary of revisions

a., c., d.

1. A cautionary statement regarding corneal opacity should be added to the 8. IMPORTANT PRECAUTIONS section.
2. The 11.1 Clinically Significant Adverse Reactions section should be newly added to the 11. ADVERSE REACTIONS section, and “corneal opacity” should be added.

b.

1. A cautionary statement regarding corneal opacity should be added to the 8. IMPORTANT PRECAUTIONS section.
2. “Corneal opacity” should be added to the 11.1 Clinically Significant Adverse Reactions section in 11. ADVERSE REACTIONS.

Investigation results and background of the revision

Cases involving corneal opacity were evaluated. Cases for which a causal relationship between corneal opacity and preparations containing brimonidine tartrate was reasonably possible have been reported. As a result of consultation with expert advisors regarding the causality assessment of the cases and the necessity of revision of PRECAUTIONS, the MHLW/PMDA concluded that revision of PRECAUTIONS was necessary.

Reference: Number of cases*† and patient mortalities involving corneal opacity reported in Japan

a. A total of 15 cases have been reported to date. (A causal relationship between the drug and event was reasonably possible for 9 cases, including 2 cases in which the drug was administered outside the approved indication or dosage and administration.)
   No patient mortalities have been reported to date.
b. No cases have been reported to date.
c. A total of 5 cases have been reported to date (including 3 cases for which a causal relationship between the drug and event was reasonably possible).
   No patient mortalities have been reported to date.
d. No cases have been reported to date.

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* Cases collected in the PMDA's database for adverse drug reactions, etc. reports

† Among the cases which fell under MedDRA v26.1 PT “Corneal opacity” or “Corneal infiltrates” submitted by the marketing authorization holder, cases with a best-corrected visual acuity of lower than 0.5, cases with lesions (e. g., opacity, interstitial keratitis, neovascularisation, and steatosis) in the pupillary area, or cases in which corneal transplant surgery, etc. had been performed were retrieved.

The expert advisors present at the Expert Discussion regarding the current investigation were nominated based on their conflict of interest declarations concerning the relevant products, pursuant to the “Rules for Convening Expert Discussions, etc., by the Pharmaceuticals and Medical Devices Agency” (PMDA Administrative Rule No. 20-8, dated December 25, 2008).

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