



June 18, 2025

Dr. Eng. Pawet Wajss
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Dear Dr. Eng. Wajss,

Thank you for your letter of February 20, 2025, to the U.S. Food and Drug Administration (FDA). In your letter, you describe your view and request action regarding the public health risk associated with the use of muscarinic receptor antagonists (parasympatholytics) and the insufficient communication from manufacturers, distributors, doctors, and medical staff concerning the potential risks of their use.

You state that information about this risk is not widely disseminated among medical personnel or patients. You also state that the summaries of product characteristics and package leaflets contain only general warnings about "bright light" or "illumination" without specifically addressing the risks associated with solar radiation. You state that you consider it essential to take action to introduce detailed and explicit warnings in product documentation and to provide patients with appropriate protective measures.

Your article attached to your letter to the FDA maintains that large-scale controlled studies are required to investigate potential lesions to the retina of the dilated eye when affected by solar radiation, but notes that due to limited access to the clinical trials' proceedings and results you are unable to verify if such hazards have been already studied.

Such large trials have been conducted and reviewed by the FDA, and they have not noted lesions to the retina of the dilated eye from solar radiation. For example, atropine sulfate ophthalmic solution is approved for use in creating pupillary dilation, cycloplegia, and in the treatment of amblyopia. Atropine sulfate ophthalmic solution has been used for pupillary dilation and cycloplegia for over 65 years.

Studies have been conducted to evaluate the effect of atropine on the eyes for over 160 years and reported in the literature.¹ Studies range from evaluations of a few patients to studies of over 1500 patients. These studies include subjects from two months² through 92³ years of age, of different races and ethnicities, and with a range of eye colors. Adverse events related to the use of atropine are directly related to its anticholinergic pharmacologic properties. Atropine is an antimuscarinic. It acts directly on

¹ Hughes R. Cases illustrative of the influence of belladonna. Br Med J 1860; s4-1 (193):706-7. PMC2252955.

² Hiatt RL Comparison of Atropine and Tropicamide in Esotropia Annals Ophthalmol. 1983; 15 (4):341-343.

³ Narvaez J. Pupil dilation using a standard cataract surgery regimen alone or with atropine 1.0% pretreatment. J Cataract Refract Surg. 2010; 36:563-567.



smooth and cardiac muscle and on exocrine glands innervated by postganglionic parasympathetic nerves blocking the action of acetylcholine.

The following are the most commonly reported and clinically significant reported adverse reactions for atropine sulfate ophthalmic solution. With the exception of the allergic reactions, all are a result of the known and expected pharmacologic action.

- Allergic reactions, including contact dermatitis, usually confined to the lids and conjunctiva, characterized by itching, redness, swelling, and discharge.
- Photophobia due to the increase in pupil size.
- Decreased tearing due to inhibition of the lacrimal gland.
- Dryness of the skin, mouth, and throat due to decreased secretion from the mucous membranes.
- Restlessness, irritability, or delirium due to stimulation of the central nervous system.
- Tachycardia. Low dose atropine will initially cause a slowing of the heart rate, but increased dosing can lead to tachycardia.
- Flushed skin of the face and neck is an expected pharmacologic anticholinergic reaction.

The current FDA-approved labeling for atropine sulfate ophthalmic solution, 1%, products includes a Warning and Precaution that photophobia and blurred vision due to pupil unresponsiveness and cycloplegia may last up to 2 weeks.

We appreciate you reaching out to the FDA regarding your perception of the public health risk associated with the use of muscarinic receptor antagonists (parasympatholytics) and the potential risks of their use. FDA believes the muscarinic receptor antagonists approved for ophthalmic use are adequately labeled to describe the risk-benefit profile of the products. As with all FDA-approved products, we will continue to monitor and review available safety information related to muscarinic receptor antagonists throughout the product life cycle and will take action if we determine it is appropriate to do so.

Thank you again for contacting FDA.

Sincerely,
Jacqueline A.

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Jacqueline Corrigan-Curay, JD, MD

Acting Director

Center for Drug Evaluation and Research

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