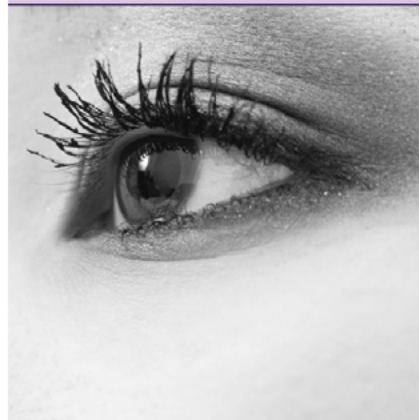


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LUMIFY® Redness Reliever Eye Drops

An Advance in Redness Reduction:
Brimonidine Tartrate 0.025%



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Agenda

- **Rationale for Development**

- **Brief History of Brimonidine**

- **Product Profile**

- **Mechanism of Action**

- **US Clinical Development Program**
 - Phase 2
 - Phase 3 (BL861)
 - Phase 3 Safety Study (BL862)

- **Summary**

Rationale for Development of LUMIFY® Redness Reliever Eye Drops

Historically, OTC vasoconstrictors are α 1- or mixed α 1-/ α 2-adrenergic receptor (α -AR) agonists

- Selective α 1-AR agonists (phenylephrine, tetrahydrozoline)
- Mixed α 1/ α 2-AR agonists (naphazoline, oxymetazoline)
- Long-term use was generally restricted by tachyphylaxis, rebound redness, mydriasis and systemic adverse events (e.g. somnolence, dizziness)¹⁻⁴

α 1-ARs predominantly expressed in arteries vs. α 2-ARs in veins^{5,6}

- Tachyphylaxis associated with internalization/downregulation of α 1-ARs
- Rebound redness associated with vasoconstrictor-induced tissue ischemia

1. Spector SL, Raizman MB. *J Allergy Clin Immunol*. 1994;94:134-6. 2. Tappeiner C et al. *Eur J Ophthalmol*. 2009;19:129-132. 3. Vaidyanathan S et al. *Am J Respir Critical Care Med*. 2008;178:1005-1010. 4. Soparkar CN et al. *Arch Ophthalmol*. 1997;115:34-8. 5. Corboz et al. *Pulm Pharmacol Ther*. 2008;21:449-54. 6. Fratelli M, De Blasi A. *FEBS Lett*. 1987;212(1):149-53.

Brief History of Brimonidine



Brimonidine Tartrate is a selective α 2-AR agonist



Used topically as Rx ophthalmic at concentrations >0.1% for lowering IOP in patients with OAG or OHT¹

- Acts on iris-ciliary body α 2-ARs to lower IOP by reducing aqueous humor production²
- Also increases uveoscleral outflow over longer-term³



Used topically as Rx dermal at 0.33% (gel) for treatment of persistent facial erythema rosacea⁴



Dose-dependent effect on conjunctival blood vessels

- High doses → associated with hyperemia⁵
- Low doses → associated with conjunctival 'whitening or blanching'⁶

1. Rahman MQ et al. *Expert Opin Drug Saf.* 2010;9:483-92. Potter DE et al. *J Ocul Pharmacol.* 1990;6:251-7. 3. Toris CB et al. *Arch Ophthalmol.* 1995;113:1514-7. 4. Fowler J Jr et al. *J Dermatol.* 2013;12:650-6. 5. Melamed S, David R. *Clin Ther* 2000;22:103-11. 6. Data on file.

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