

Oxymetazoline Therapeutic Cheat Sheet

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TRADE NAME

- > Rhofade (1% oxymetazoline hydrochloride cream)
- > Upneeq (0.1% oxymetazoline hydrochloride ophthalmic solution)

MECHANISM OF ACTION

- > Oxymetazoline is a selective α 1A adrenoceptor agonist and partially selective α 2A adrenoceptor agonist.^{1,2}
- > In rosacea, the superficial cutaneous blood vessels are in a sustained dilated state and respond to adrenergic stimuli. This response is primarily facilitated by α 1-adrenoceptors and a subset of α 2-adrenoceptors located post-synaptically on vascular smooth muscle cells. Activation of these postsynaptic adrenoceptors results in cutaneous vasoconstriction and thereby reduced erythema.^{1,2}
- > Some evidence also suggests that oxymetazoline has anti-inflammatory effects such as reduction in pro-inflammatory cytokines and T-cell stimulation, regulation in arachidonic acid and arachidonic acid-derivative protein activity, and inhibition of respiratory burst activity. Additionally, α -adrenoceptor agonist treatments have been linked to reduced vascular endothelial growth factor expression resulting in inhibition of neovascularization.¹
- > As an ophthalmic solution, oxymetazoline activates the α -adrenergic receptors on the levator palpebrae muscle (Mueller's muscle) causing the muscle to contract and raise the upper eyelid.⁵

*** Of note, in contrast to oxymetazoline, brimonidine is a highly selective α 2-adrenoceptor agonist, which also leads to vasoconstriction; however, presence of presynaptic and endothelial cell α 2-adrenoceptors may contribute to vasodilation and subsequent rebound erythema.^{3,4}

FDA APPROVED FOR^{2,5}

- > Rhofade is approved for Persistent Facial Erythema (PFE) associated with rosacea in adults.
- > Upneeq is approved for blepharoptosis.

OFF-LABEL DERMATOLOGIC USES^{6,7}

- > Rhofade has been used off-label for post-acne erythema and erythromelalgia of the knee.

DOSING

- > Rhofade is for topical use only and patients should apply a pea-sized amount of cream to the affected area once daily, avoiding eyes and lips.¹
 - > In both the REVEAL1 and REVEAL2 Phase 3 clinical trials, significantly greater proportions of patients treated with oxymetazoline vs. vehicle achieved at least a two-grade improvement in the Clinician Erythema Assessment (CEA) and Subject Self-assessment of Erythema (SSA) scores at 3-, 6-, 9-, and 12-hours post-treatment and response was maintained on day 29.²
- > Upneeq is for ophthalmic use only and patients should instill one drop into one or both ptotic eyes once daily.⁵
 - > Studies demonstrated about 1 mm upper eyelid lift from Upneeq, with effects taking onset as early as 5 minutes post-instillation. Additionally, each dose was noted to be effective for about 6 hours, and this maintenance effect was visualized over 42 days of use.⁶

WARNINGS AND PRECAUTIONS^{2,5}

- > Potential impacts on cardiovascular disease: As α -adrenergic agonists may impact blood pressure, use with caution in patients with severe or uncontrolled cardiovascular disease, hypertension, and/or hypotension.
- > Potentiation of vascular insufficiency: Use with caution in patients with cerebral or coronary insufficiency, Raynaud's phenomenon, thromboangiitis obliterans, scleroderma, or Sjögren's syndrome.
- > There is an increased risk of angle closure glaucoma in patients with narrow angle glaucoma, and patients should seek immediate medical care if they develop signs and symptoms of acute angle closure glaucoma.

SIDE EFFECTS

- > Rhofade^{2,4,9-10}
 - > Most common side effects include application site dermatitis, pain, paresthesia, and pruritus. Less common side effects include upper respiratory infection, headache, sinusitis, hypertension, and nasopharyngitis.
 - > In the clinical trial, about 3% of patients experienced worsening inflammatory lesions of rosacea, however, rebound erythema (recurrent erythema worse than baseline post-treatment or paradoxical erythema after application of medication) was noted in less than 1% of study participants. In contrast, 6.5% of patients experienced rebound erythema with brimonidine during the clinical trial, and 20% noted worsening of baseline erythema during post-marketing surveillance.
- > Upneeq⁵
 - > Most common side effects include punctate keratitis, conjunctival hyperemia, dry eye, blurred vision, instillation site pain, eye irritation, and headache.

DRUG INTERACTIONS^{2,5}

- > No direct drug interactions are noted; however, caution is advised when using in conjunction with beta-blockers, anti-hypertensives, cardiac glycosides, α 1 adrenergic receptor antagonists, and monoamine oxidase inhibitors as oxymetazoline may affect blood pressure and amine metabolism.

CONTRAINDICATIONS^{2,5}

- > None

PREGNANCY AND BREASTFEEDING^{2,5,10}

- > There is no available data on the use of Rhofade and/or Upneeq in pregnant women and no clinical data is available during lactation.
- > Oxymetazoline 0.05% nasal spray is category C in pregnancy.

MONITORING

- > None

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