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### Authors

Werner, Kimberly  
Kobayashi, Todd T

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**Letter**

**Dermatitis medicamentosa: severe rebound erythema secondary to topical brimonidine in rosacea**

**Kimberly A Werner MD<sup>1</sup> and Todd T Kobayashi MD<sup>2</sup>**

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**<sup>1</sup>CPT, MC, USA, SAUSHEC, San Antonio Military Medical Center**

**<sup>2</sup>COL, USAF, MC, SAUSHEC Dermatology Program Director**

**Correspondence:**

Kimberly A Werner, MD  
6418 Eckhert Rd #3206  
San Antonio, TX 78240  
(757)515-4113  
Kimberlyawerner@gmail.com  
Kimberly.werner.1@us.af.mil  
Kimberly.a.werner10.mil@mail.mil

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**Abstract**

**Background:** Rebound erythema secondary to use of topical brimonidine in the setting of rosacea is an important, possibly significantly distressing potential side effect that may be under-reported; there is little photo-documentation in the literature to date. This article documents such a case.

**Observations:** A 28-year-old woman (Fitzpatrick II) with a long-standing history of untreated rosacea presented for initiation of treatment of what was noted to be primarily erythematotelangiectatic rosacea and was offered Mirvaso for daily use. Initial improvement was followed by progressive worsening of baseline erythema several hours following treatment, only improved with subsequent applications of additional Mirvaso. The patient's symptoms were improved upon discontinuing use of Mirvaso.

**Conclusions:** There are few cases documented of rebound erythema secondary to use of Mirvaso to date. Further reporting might prompt further long term investigation for this topical medication for further delineation of its role in treatment of rosacea. What is proposed is a phenomenon similar to that of rhinitis medicamentosa with upregulation of alpha-adrenergic receptors, suggesting the name "dermatitis medicamentosa" for this phenomenon.

**Keywords:** rosacea; erythematotelangiectatic; mirvaso; brimonidine; rebound erythema; rhinitis medicamentosa; flushing

**Case synopsis**

A 28-year-old woman with a long-standing rosacea presented for initiation of treatment of primarily erythematotelangiectatic rosacea with no prior treatment to date. The patient's most significant concern was with the mildly erythematous appearance of her face at baseline, as well as frequent flushing.

The patient was prescribed Mirvaso (brimonidine 0.33% gel) for daily topical use. The patient reported significant improvement to baseline erythema and flushing initially, in the first days of treatment with Mirvaso, with associated elevation of mood and self-

confidence. However, during the second week of treatment, the patient began noticing some gradual worsening of baseline erythema several hours following treatment, only improved with subsequent application of Mirvaso. The patient contacted her provider in tears two weeks into treatment for severe facial erythema at which time the patient's use of Mirvaso was discontinued resulting in improvement of erythema and flushing thereafter.

The course of symptoms that progressed with use of Mirvaso included an initial blanching for one to four hours after application (Fig. 1), with gradual facial erythema to a point beyond baseline around 12- 13 hours following application (Figure. 2).



**Figure 1.** Rosacea. One hour following application of Mirvaso with initial blanching and improvement of baseline erythema. **Figure 2.** Rosacea. Twelve hours following application of Mirvaso with significant increase in baseline erythema

The patient was offered daily topical pimecrolimus 1% cream in the affected areas of the face, which appeared to expedite resolution of symptoms elicited by Mirvaso. The patient's symptoms improved dramatically following several treatments with use of the pulsed dye laser.

## Comment

Rosacea is a common condition characterized by facial flushing and erythema that can have a significant psychosocial impact.

The erythematotelangiectatic type of rosacea poses a challenge to the provider with a complex pathogenesis to include altered blood flow, vascular dilation and proliferation. In August 2013, the topical alpha-2 agonist brimonidine was released as the first Food and Drug Association approved topical treatment indicated specifically for rosacea-associated facial erythema by eliciting constriction of superficial cutaneous blood vessels [1-3]. The medication was assessed using short-term clinical studies as well as one long-term study (only 1 year), with the most common cutaneous adverse events reported as flushing (10%) and erythema (8%).

We report a case of a patient who had immediate effective vascular constriction with control of facial erythema and flushing initially to all areas treated, with subsequent development of significant rebound erythema beyond baseline in the days following initiation of treatment, lasting several hours after application.

A possible mechanism of action for this adverse side effect is that similar to that observed in rhinitis medicamentosa, in which treatment with alpha-adrenergic nasal sprays to include oxymetazoline and xylometazoline results in rebound congestion secondary beta-receptor stimulation and rebound increase in parasympathetic activity [4]. This vasogenic rebound phenomenon secondary to use of this alpha-adrenergic medication should be addressed with the patient at the time of prescribing. This is a significantly distressing potential side effect that may be underreported with little photo documentation in the literature to date. Further long term testing is indicated for this topical medication for further delineation of its role in treatment of this chronic disorder. Perhaps what is more suited for this medication is a role similar to that of the alpha-adrenergic nasal sprays, for temporary relief, perhaps prior to an important event, rather than for long term usage.

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