CENTENE PHARMACY AND THERAPEUTICS
DRUG REVIEW
2Q17 April – May

BRAND NAME
Rhofade™

GENERIC NAME
Oxymetazoline

MANUFACTURER
Allergan

DATE OF APPROVAL
January 18, 2017

PRODUCT LAUNCH DATE
TBD

REVIEW TYPE

☐ Review type 1 (RT1): New Drug Review
Full review of new chemical or biologic agents

☒ Review type 2 (RT2): New Indication Review
Abbreviated review of new dosage forms of existing agents that are approved for a new indication or use

☐ Review type 3 (RT3): Expedited CMS Protected Class Drug Review
Expedited abbreviated review of Centers for Medicare & Medicaid Services protected class drugs (anticonvulsants, antidepressants, antineoplastics, antipsychotics, antiretrovirals, and immunosuppressants)

FDA APPROVED INDICATION
Rhofade is indicated for the topical treatment of persistent facial erythema associated with rosacea in adults.

OFF-LABEL USES
Not applicable

CLINICAL EFFICACY[1]
Rhofade was evaluated for the treatment of persistent erythema associated with rosacea in two identical, randomized, double-blind, vehicle-controlled, parallel-group clinical trials. The trials enrolled 885 subjects aged 18 years and older. Subjects applied either Rhofade or vehicle once daily for 29 days.

Disease severity was graded by the clinician using a clinician erythema assessment (CEA) scale and by the subject on a similar subject self-assessment (SSA) scale, on which subjects scored either "moderate" or "severe" on both scales. On the 5-point CEA scale, 0=clear skin with no signs of erythema; 1=almost clear of erythema, slight redness; 2=mild erythema, definite redness; 3=moderate erythema, marked redness and 4=severe erythema, fiery redness. On the 5-point SSA scale, 0=clear of unwanted redness; 1=nearly clear of unwanted redness; 2=somewhat more redness than I prefer; 3=more redness than I prefer and 4=completely unacceptable redness.

CEA and SSA were measured over a 12-hour period at equally-spaced timepoints (hours 3, 6, 9, and 12) post-dose on Days 1, 15, and 29. The primary efficacy endpoint was defined as the proportion of subjects with at least a 2-grade reduction in erythema (improvement) from baseline (pre-dose on Day 1) on both the CEA and SSA measured at hours 3, 6, 9, and 12 on Day 29. The results from both trials on this composite primary endpoint for Day 29 are presented in the table below.

Proportion of Subjects Achieving Composite Success* on Day 29

Time-point (Hour)	Trial 1		Trial 2	
	Rhofade Cream (N=222)	**Vehicle Cream (N=218)**	**Rhofade Cream (N = 224)**	**Vehicle Cream (N=221)**
3	12%	6%	14%	7%
6	16%	8%	13%	5%
9	18%	6%	16%	9%
12	15%	6%	12%	6%

*Composite success is defined as the proportion of subjects achieving at least a 2-grade improvement on both CEA and SSA.

CONTRAINDICATIONS
Not applicable

BLACK BOX WARNINGS
Not applicable

DRUG INTERACTIONS
Rhofade has potential drug interactions with:

- Anti-hypertensive agents and cardiac glycosides – additional impact on blood pressure; caution is advised
- Alpha$_1$ adrenergic receptor antagonists – mechanism of action directly conflicts with that of Rhofade (an alpha$_1$ adrenergic receptor agonist); caution is advised
- Monoamine oxidase inhibitors – can affect metabolism and uptake of circulating amines; caution is advised

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ADVERSE REACTIONS

Adverse reactions that occurred in at least 1% of subjects treated with Rhofade, and more frequently than placebo, through 4 weeks of treatment included: application site dermatitis (2%), worsening inflammatory lesions of rosacea (1%), application site erythema (1%) and application site pain (1%).

Adverse reactions observed in an open label trial over a one-year treatment period were as follows: worsening inflammatory lesions of rosacea (3%), application site dermatitis (3%), application site pruritis (2%), application site pain (2%), and application site erythema (2%). Subjects with persistent erythema along with inflammatory lesions were allowed to use additional therapy for the inflammatory lesions of rosacea.

DOSAGE AND ADMINISTRATION

Rhofade is applied as a pea-sized amount once daily in a thin layer to cover the entire face (forehead, nose, each cheek, and chin) avoiding the eyes and lips.

PRODUCT AVAILABILITY

Cream: 1%

THERAPEUTIC ALTERNATIVES[2,3,4]

DRUG NAME	USAGE REGIMEN (route of admin/frequency of use)	COMMENTS
Mirvaso® (brimonidine)	Apply a pea-sized amount topically QD	N/A
metronidazole 0.75% (Metrolotion®, Metrocream®)	Apply topically BID	First-line therapy for papules and pustules of rosacea
metronidazole 1% (Metrogel®)	Apply topically QD	First-line therapy for papules and pustules of rosacea
Finacea® (azelaic acid)	Apply topically BID	First-line therapy for papules and pustules of rosacea
doxycycline	40 mg or 50 mg PO QD	50 mg/day

Boldface indicates generic availability

Utilization Management Recommendation
• There is not significant potential for inappropriate use. • If papules or pustules are present, it would be clinically appropriate to require a trial of or concomitant treatment with any of the following agents: topical metronidazole *(preferred)*, oral doxycycline *(preferred)* or Finacea *(non-preferred)*

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Product Comparison
• Equal therapeutic outcomes are anticipated for Rhofade and Mirvaso; therefore, it would be appropriate to provide equal access to both or to require a trial of one before the other.

REFERENCES

[1] Rhofade Prescribing Information. Irvine, CA: Allergan; January 2017. Available at: www.rhofade.com. Accessed February 2017.
[2] Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed February 2017.
[3] National Rosacea Society. Rosacea treatment algorithms. Available at: https://www.rosacea.org/physicians/treatmentalgorithms. Accessed February 2017.
[4] Scaller M, et al. Rosacea treatment update: Recommendations from the global ROSacea COnsensus (ROSCO) panel. *Br J Dermatol* 2016. Epub ahead of print. doi: 10.1111/bjd.15173.