

# Consensus Recommendations From the American Acne & Rosacea Society on the Management of Rosacea, Part 5: A Guide on the Management of Rosacea

James Q. Del Rosso, DO; Diane Thiboutot, MD; Richard Gallo, MD; Guy Webster, MD; Emil Tanghetti, MD; Lawrence F. Eichenfield, MD; Linda Stein-Gold, MD; Diane Berson, MD; Andrea Zaenglein, MD

*The last article in this 5-part series provides a final overview of consensus recommendations from the American Acne & Rosacea Society (AARS) on the management of the common presentations of cutaneous rosacea. Optimal management of rosacea requires careful assessment of the patient's clinical features with integration of therapies that adequately treat the presenting signs and symptoms. The treatment consensus recommendations from the AARS are based on 2 major common clinical presentations of rosacea: (1) centrofacial erythema with papulopustular*

*lesions, and (2) centrofacial erythema without papulopustular lesions. The recommendations provided here serve to guide clinicians in their clinical practice.*

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Although recommendations on the management of rosacea have been published previously by the National Rosacea Society<sup>1</sup> and the American Acne & Rosacea Society (AARS),<sup>2</sup> these recommendations were established prior to

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Dr. Del Rosso is from Touro University College of Osteopathic Medicine, Henderson, Nevada, and Las Vegas Skin and Cancer Clinics/ West Dermatology Group, Las Vegas and Henderson. Dr. Thiboutot is from Penn State University Medical Center, Hershey. Dr. Gallo is from the University of California, San Diego. Dr. Webster is from Jefferson Medical College, Philadelphia, Pennsylvania. Dr. Tanghetti is from the Center for Dermatology and Laser Surgery, Sacramento. Dr. Eichenfield is from Rady Children's Hospital, San Diego, California, and the University of California, San Diego School of Medicine. Dr. Stein-Gold is from Henry Ford Hospital, Detroit, Michigan. Dr. Berson is from Weill Cornell Medical College and New York-Presbyterian Hospital, New York, New York. Dr. Zaenglein is from Dermatology and Pediatrics, Penn State Milton S. Hershey Medical Center, Hershey, Pennsylvania.

Dr. Del Rosso is an advisory board member and consultant for Allergan, Inc; Bayer Health Care Pharmaceuticals; Galderma Laboratories, LP; Onset Dermatologics; Promius Pharma; Ranbaxy Laboratories Limited; Unilever; Valeant Pharmaceuticals International, Inc; and Warner Chilcott. He also is a researcher for Allergan, Inc; Bayer Health Care Pharmaceuticals; Galderma Laboratories, LP; Onset Dermatologics; and Valeant Pharmaceuticals International, Inc. Dr. Del Rosso also is a speaker for Allergan, Inc; Bayer Health Care Pharmaceuticals; Galderma Laboratories, LP; Onset Dermatologics; Promius Pharma; Ranbaxy Laboratories Limited; Valeant Pharmaceuticals International, Inc; and Warner Chilcott. Dr. Thiboutot is a consultant and investigator for Allergan, Inc, and Galderma Laboratories, LP. Dr. Gallo is a consultant for and has received research grants from Allergan, Inc; Bayer Health Care Pharmaceuticals; and Galderma Laboratories, LP. Dr. Webster is a consultant for Allergan, Inc; Cutanea Life Sciences; Galderma Laboratories, LP; and Valeant Pharmaceuticals International, Inc. Dr. Tanghetti is a consultant, speaker, and investigator for Allergan, Inc; Cynosure, Inc; and Galderma Laboratories, LP. Dr. Eichenfield is a consultant and investigator for Galderma Laboratories, LP, and Stiefel, a GSK company. Dr. Stein-Gold is an advisory board member, consultant, investigator, and speaker for Galderma Laboratories, LP, and LEO Pharma; an advisory board member, consultant, and investigator for Anacor Pharmaceuticals, Inc; an advisory board member, investigator, and speaker for Stiefel, a GSK company; an advisory board member and consultant for Taro Pharmaceuticals USA, Inc; a consultant and investigator for Topica Pharmaceuticals, Inc; an investigator and speaker for Allergan, Inc, and Novartis Corporation; a speaker for Promius Pharma and Ranbaxy Laboratories Limited; and a consultant for Ferndale Laboratories, Inc. Dr. Berson is an advisory board member and consultant for Allergan, Inc; Anacor Pharmaceuticals, Inc; Galderma Laboratories, LP; La Roche-Posay Laboratoire Dermatologique; Procter & Gamble; and Rock Creek Pharmaceuticals. Dr. Zaenglein reports no conflict of interest. The American Acne & Rosacea Society and the authors did not receive any form of funding or compensation for this series of articles, including this manuscript.

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Correspondence: James Q. Del Rosso, DO (jqdelrosso@yahoo.com).

the emergence and/or consolidation of more recent data on the pathophysiologic mechanisms of rosacea and their correlation with clinical features.<sup>1-7</sup> The focus of the AARS consensus recommendations is to address the more common clinical presentations of cutaneous rosacea, specifically centrofacial erythema, both with and without papulopustular lesions, and to provide an update to recommendations that were previously published.<sup>1,2,8-11</sup>

An extensive, evidence-based analysis on interventions for rosacea published in 2011 found 58 randomized controlled trials (RCTs) that met the eligibility criteria for review, comprising 6633 study subjects. The conclusions of this analysis, based on strict adherence to levels of evidence criteria, indicated that there is some evidence to support the effectiveness of topical metronidazole, topical azelaic acid, and anti-inflammatory-dose doxycycline (40-mg modified-release capsule once daily) in the treatment of moderate to severe papulopustular rosacea, with a definite need for more well-designed, adequately powered RCTs in rosacea.<sup>12</sup> In fact, clinicians are forced to work with their best clinical judgment and the best information available at the time, which in some scenarios may require looking beyond US Food and Drug Administration (FDA)-approved indications and large-scale RCTs.

The AARS brings forth the following recommendations as a guide to assist clinicians in the management of patients with cutaneous rosacea based on both a thorough review of the medical literature and observations from clinical experience.

## OVERALL ASSESSMENT PRIOR TO THERAPY

Clinical management of rosacea warrants assessment of the clinical features present at baseline. The consensus management recommendations from the AARS are based on 2 major common clinical presentations of rosacea: (1) centrofacial erythema with papulopustular lesions, and (2) centrofacial erythema without papulopustular lesions. Prior to initiating therapy, it also is important to note other clinical features such as the presence and severity of telangiectases and fine facial scaling (rosacea dermatitis) as well as symptoms such as stinging and burning. Phymatous changes and/or ocular rosacea also should be addressed when present, but their management is not discussed in this article.

Prior to treatment, it is critical for clinicians to meet with patients to identify the aspects of their rosacea that are most bothersome to them and address relevant details regarding treatment options and reasonable expectations for a favorable therapeutic outcome. The recommendations and clinical

scenarios discussed in this article are based on adult patients who have not been previously treated for rosacea or have been off of any rosacea therapy for several weeks to months, have not undergone prior or recent treatments with physical modalities or devices for rosacea, do not exhibit any contraindications to therapy, and do not need to avoid any of the recommended therapies. Additionally, these recommendations assume the patient has reasonable access to therapeutic options, as in some cases access and/or financial considerations, including third-party coverage, may influence how therapies are selected or utilized by patients. Consistent with the 2008 recommendations from the AARS for management of rosacea,<sup>2</sup> the prevailing belief is that medical therapies that are anti-inflammatory in nature are best suited for the initial treatment of rosacea, especially in papulopustular rosacea, to avoid antibiotic selection pressure and production of bacterial strains that are less sensitive to antibiotics. Oral antibiotic therapy, including antibiotic-dose doxycycline (50–200 mg/d), is more applicable in cases that respond poorly to a reasonable trial of topical therapy and/or subantimicrobial-dose doxycycline (40 mg/d of modified-release formulation).

## Centrofacial Erythema With Papulopustular Lesions

Although a severity grading scale for rosacea has not been firmly established, one report assists in formulating a common system for clinical use.<sup>13</sup> In patients presenting with flares of centrofacial erythema with papulopustular lesions, it is suggested that clinicians utilize a grading system that classifies the primary clinical features of rosacea (ie, papulopustular lesions, facial erythema, symptoms) as mild (ie, <10 papules/pustules, mild erythema, with or without symptoms), moderate (ie, 10–19 papules/pustules, moderate erythema, with or without symptoms), or severe ( $\geq 20$  papules/pustules, severe erythema, with or without symptoms). Severity and frequency of facial vasodilation (flushing) as well as presence and grading of telangiectasia also can be included. Further details on severity grading of rosacea are reviewed in the literature.<sup>13</sup> Individual disease features can be assessed at follow-up visits to more accurately evaluate response to therapy.

*Baseline Visit*—At baseline, a gentle skin care and photoprotection regimen should be recommended for patients with mild, moderate, and severe centrofacial erythema with papulopustular lesions. It is recommended that topical therapies be administered for at least 6 to 8 weeks for accurate assessment of therapeutic response. Metronidazole and azelaic acid are the primary choices for topical treatment in these

patients for reduction of papulopustular lesions and perilesional erythema.<sup>12,14,15</sup>

In patients who may be more likely to adhere to an oral regimen versus topical therapy, subantimicrobial-dose doxycycline may be a viable treatment option for all severity grades.<sup>10</sup> It is preferred over antibiotic therapy due to avoidance of antibiotic selection pressure; however, antibiotic agents (ie, tetracyclines, azithromycin) may be warranted based on the judgment of the clinician in individual cases.<sup>12,14,16,17</sup> Anti-inflammatory-dose doxycycline offers the advantages of once-daily dosing, avoidance of antibiotic resistance, and being the only oral agent with approval by the FDA for the treatment of papulopustular rosacea.

In moderate and severe cases, concurrent use of oral and topical therapies may be an optimal approach based on the magnitude of severity perceived by the clinician and patient, the degree of symptoms, and the patient's desire for more rapid results. The combination of topical therapy with either metronidazole or azelaic acid gel 15% and anti-inflammatory-dose doxycycline has been shown to be effective, with azelaic acid demonstrating slightly more rapid improvement overall by global assessment.<sup>18,19</sup>

If centropacial erythema is diffuse or is known to persist between flares (ie, background erythema) and is a concern expressed by the patient, a topical  $\alpha$ -adrenergic receptor agonist also may be incorporated once daily in the morning. At the present time, only brimonidine gel 0.33% (brimonidine tartrate gel 0.5%) gel is commercially available and FDA approved for the topical treatment of persistent (non-transient) facial erythema associated with rosacea in adults 18 years or older.<sup>9,20,21</sup> Any persistent areas of telangiectasia can then be addressed on follow-up with the use of appropriate device therapy if any such areas are bothersome to the patient.<sup>11</sup>

**Follow-up**—Generally within 6 to 8 weeks, patients with mild to severe rosacea should return for follow-up assessment of treatment response. If the patient is pleased with the results, the current therapy may be continued. If the patient is markedly improved with adequate reduction in papulopustular lesions and perilesional erythema, the clinician should address continuation of therapy and a follow-up approach. Long-term therapy to sustain control of papulopustular rosacea, often referred to as maintenance therapy, has been evaluated with topical agents (eg, metronidazole, azelaic acid) for up to 6 months.<sup>22,23</sup> In selected cases, such as patients who prefer oral therapy over topical therapy, anti-inflammatory-dose doxycycline may be considered for more prolonged use, with some support from 9-month safety data included in FDA-approved product labeling.<sup>24,25</sup> This approach warrants discussion with the patient. Prolonged oral antibiotic

therapy is best avoided, if possible, due to induction of antibiotic-resistant bacterial strains.<sup>2,16,17,26,27</sup>

If reduction of papulopustular lesions and perilesional erythema is not adequate, the clinician may choose to recommend a full 12-week trial on the current regimen or switch to another treatment option that had not been used initially. If by 12 weeks the reduction in papulopustular lesions and perilesional erythema are poor and the patient was utilizing subantimicrobial-dose doxycycline, it may be necessary to increase the daily dose, as the patient may be a low doxycycline absorber, or to switch to an alternative oral therapy (ie, azithromycin).<sup>1,2,10,14,15</sup> It also is important to ensure that the patient is not ingesting any sources of metal ions concurrently with an oral tetracycline agent, which can reduce systemic bioavailability by decreasing gastrointestinal tract absorption due to chelation of the tetracycline agent.<sup>28,29</sup> As previously mentioned, an  $\alpha$ -adrenergic receptor agonist may be incorporated once daily in the morning for persistent nontransient facial erythema (background erythema) at follow-up if not already initiated, and appropriate device therapy may be incorporated to treat individual telangiectases and/or mats if any such areas are bothersome to the patient.

A follow-up plan is designed based on the needs of the individual patient, with visit frequency arranged to assess additional progress, evaluate maintenance therapy if utilized, or assess response to device therapies and/or arrange additional treatment sessions. In refractory cases of papulopustular rosacea in which poor adherence has been excluded, oral isotretinoin may be a viable option in carefully selected cases.<sup>10,15</sup>

### Centropacial Erythema Without Papulopustular Lesions

In rosacea patients presenting with flares of centropacial erythema without papulopustular lesions, utilization of a grading system that evaluates individual important clinical features as mild, moderate, or severe is prudent. The suggested clinical features are facial erythema, symptom severity and frequency of facial vasodilation (flushing), and presence and grading of telangiectasia. Further details on severity grading are reviewed in the literature.<sup>13</sup> Individual features can be assessed at follow-up visits to more accurately evaluate response to therapy.

The recommendations provided here apply to all severity grades, as treatment selection for facial erythema and telangiectasia is primarily dictated by how much the visible signs and associated symptoms bother the patient, especially the impact on quality of life.

**Baseline Visit**—At baseline, a gentle skin care and photoprotection regimen should be recommended.

If the centrofacial erythema is diffuse or known to persist between flares (background erythema) and is a concern expressed by the patient, a topical  $\alpha$ -agonist may be used once daily in the morning, which often will result in a visible effect of reduced facial erythema within 30 to 60 minutes, with a peak effect evident after approximately 3 to 4 hours.<sup>7,20,21</sup> Any persistent areas of telangiectasia can then be addressed with the use of appropriate device therapy if they are bothersome to the patient. Based on the clinical presentation and judgment of the clinician and the extent of his/her experience with physical modalities, intense pulsed light or laser therapy may be incorporated as initial treatment. Repeated courses of device treatment may be needed to achieve the desired level of response or sustain therapeutic benefit over time.<sup>11</sup>

*Follow-up*—The follow-up plan may be individualized based on the needs of the specific patient and the treatment used. In patients treated with a topical  $\alpha$ -agonist, it may be prudent to have them follow up in 2 to 4 weeks to assess their response, review their utilization pattern with the therapy, and confirm that no problems have arisen related to tolerability or aggravation of facial erythema. If a physical modality has been used, follow-up is arranged based on the schedule outlined to assess response depending on the device(s) that have been used and/or for additional treatment sessions.

## GENERAL MANAGEMENT CONSIDERATIONS

In individual cases in which rosacea is refractory to a reasonable course of therapy or are intolerant to a specific treatment, the clinician will be required to adjust the therapeutic approach. It is important to explain to the patient the anticipated time course of response with any therapy used, which assumes good adherence to all treatment recommendations. Parts 1 through 4 of this series reviewed a variety of alternative treatment options that the clinician may wish to initiate in specific cases.<sup>8-11</sup> Clinicians who are not familiar with a particular treatment are advised to refer to the literature in more detail.

Long-term approaches for sustaining control of rosacea are not adequately addressed in the published literature on the management of rosacea, with only a few studies evaluating topical maintenance therapy over a duration of 6 months.<sup>22,23</sup> The natural progression of different presentations of rosacea also are not well understood; however, it appears that persistent diffuse centrofacial erythema (background erythema) may be a progressive process, as fixed changes in superficial vasculature develop secondary to repeated inflammatory signals that occur during rosacea flares.<sup>4,7</sup> It is not currently known if

available therapies such as oral doxycycline and/or topical azelaic acid that have been shown to interfere with production of cathelicidin LL-37 via 2 separate mechanisms can interfere with the progressive fixed vascular changes that contribute to background facial erythema.<sup>30,31</sup> As a result, the information we have to date based on clinical trials and case reports mostly contribute to how to manage flares of rosacea. Long-term management requires the clinical judgment of the clinician and the motivation and willingness of the patient to adhere to recommended therapies.

## CONCLUSION

Optimal management of rosacea requires careful assessment of the clinical features present in the individual patient with integration of therapies that adequately treat the presenting signs and symptoms. Proper skin care and photoprotection are important components of the management plan. Many currently available therapies address the inflammatory components of rosacea, with their predominant effects being reduction in papulopustular lesions and perilesional erythema. Topical  $\alpha$ -agonists induce vasoconstriction of superficial cutaneous vessels, which reduces background erythema over several hours after daily application. When utilized properly, devices such as intense pulsed light and the pulsed dye laser can be helpful in treating telangiectasia and vascular erythema to some extent and also may reduce associated symptoms. The recommendations provided here address the more common presentations of rosacea and offer clinicians a guide that will help them integrate individual therapies when managing patients with rosacea in their clinical practice.

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