ROSACEA MEDICAL MANAGEMENT GUIDELINES

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Objectives
(1) Provide an overview of the fundamental concepts of rosacea and quality of life implications
(2) Outline available pharmacologic treatments for rosacea with reference to supporting data

- The pharmacologic agents discussed are inclusive of those that are Food and Drug Administration (FDA)-approved based on phase III pivotal trials, commonly used agents based on extensive clinical experience, and less commonly used alternatives reviewed in peer-reviewed literature.

Disease State Fundamentals
- Rosacea is a common facial disorder presenting most commonly in adults; the exact incidence is unknown, estimated to affect ~16 million Americans. Proximity of the disorder to acne vulgaris (90% overlap) and presentation of similar inflammatory disease states of rosacea and quality of life implications is characteristic. Clinical signs of rosacea include facial erythema, telangiectasia, papules, pustules, and inflammatory plaques. The underlying cause of rosacea is unknown, however, several pathophysiologic abnormalities have been reviewed in the literature. Major pathologic components appear to include inflammatory, vascular, and ocular involvement.
- The most clinical presentations of rosacea include the inflammatory (palpable nodules and telangiectasia), vascular (telangiectasia and postinflammatory hyperpigmentation), and ocular (congestion and keratitis).
- The pathophysiologic associations have been reviewed in the literature.
- Rosacea worldwide, estimated to affect ~14 million Americans.1,2 The exacerbation.
- Rosacea, approximately 70% claim that their disorder has had a lower self-confidence and lower self-esteem as a result of their rosacea; clinical presentations of ocular rosacea include conjunctivitis, blepharitis, stye formation and keratitis.1-3

Quality of Life Implications
- Rosacea has been shown to exhibit a negative impact on quality of life (QoL) for the lay public, have prompted recommendations that patients with severe rosacea, approximately 70% claim that then disorder has had a negative impact on their professional relationships, and nearly 30% have missed work as a result of their condition, with 41% of patients avoiding public contact or canceling social engagements. Furthermore, among patients with severe rosacea, approximately 70% claim that then disorder has had a negative impact on their professional relationships, and nearly 30% have missed work as a result of their condition.
- Effective treatment of rosacea has been correlated with marked improvement in quality of the lives.

Pharmacologic Treatment of Rosacea: Topical Therapy
Sulfacetamide 10%–Sulfur 5%
- Found to be the most potent product that provides the effects for rosacea treatment based on drug efficacy study implementation (DESI) drug designations.
- Multiple randomized vehicle-controlled and comparative studies, two blinded and open-label have confirmed its effectiveness in patients with inflammatory rosacea measured as marked improvement in signs and symptoms.
- Multiple vehicle formulations are available, including cleanser, moisturizer, and photoprotection, including sunblock/sunscreen.
- Metronidazole
- Approved by the FDA for inflammatory rosacea based on phase III pivotal trials (double-blind, randomized, vehicle-controlled studies).
- Multiple, placebo-based open-label, and double-blinded vehicle-controlled clinical trials have confirmed the efficacy and safety of metronidazole, including in adults with severe inflammatory rosacea.
- Both oral and topical agents are indicated for patients with inflammatory rosacea; clinical presentations of oral rosacea include conjunctivitis.

Pharmacologic Treatment of Rosacea: Oral Therapy
Antibiotic/Inflammatory Agents
- Tetracycline agents, including tetracycline, doxycycline (papulopustular), and minocycline (nodular, inflammatory) are FDA-approved for treatment of rosacea.
- The use of tetracycline, isotretinoin, and doxycycline (other than the anti-inflammatory dose) are FDA-approved for treatment of rosacea, with efficacy demonstrated in some cases and little benefit observed in others.16-19
- Data supporting use of topical clindamycin or erythromycin for rosacea is very limited, and there is no convincing evidence of benefit to other antibiotics, including oral clindamycin. The clinical effects of oral clindamycin or erythromycin are not generally recommended for treatment of rosacea.
- Topical tretinoin (0.025%-0.05%)19 has been shown to be effective for inflammatory rosacea.20
- Topical antibiotics, such as metronidazole, have been shown to be effective in case reports of inflammatory rosacea that were diagnosed as demodectic folliculitis.21
- Topical retinoid therapy suggested an additional benefit for rosacea, although supporting data is very limited.22

- Pharmacologic Treatment of Rosacea: Oral Therapy
Antibiotic/Inflammatory Agents
- Doxycycline 40mg controlled-release formulation (anti-inflammatory dosing)19,20,21,22,23,24 is FDA-approved for treatment of inflammatory rosacea in adults based on phase III pivotal trials demonstrating gel, and topical efficacy.
- An oral-inflammation dose doxycycline (administered once daily) is not considered by the FDA as an antibiotic, a sequel to inflammatory activity based on microbiologic and pharmacologic studies completed up to 16 months, and is unique in its bioavailability profile as compared to other doxycycline formulations.25
- Anti-inflammatory dose doxycycline is the only systemic therapy FDA-approved for treatment of inflammatory rosacea based on phase III pivotal trials demonstrating gel, and topical efficacy.

References
Disease State Fundamentals

- Rosacea is a common facial disorder presenting most commonly in adults, characterized by symptoms such as persistent erythema, flushing, visible blood vessels, papules, pustules, and occasional telangiectasias.
- The underlying cause of rosacea is unknown, however, several pathophysiologic alterations have been reviewed in the literature.
- Major pathogenic components appear to be inflammatory, vascular, and neurogenic in origin. There is no irreversible evidence that rosacea is caused by a microbial pathogen, such as a bacterium, parasite, or virus.
- The most common clinical presentations of cutaneous rosacea include the inflammatory (papulopustular) and telangiectatic-vasomotor subtypes. Other presentations include phymatous rosacea (such as rhinophyma), and an inflammatory and telangiectatic form of rosacea.

Quality of Life Implications

- Rosacea has been shown to exhibit a negative impact on quality of life (QoL). Patients with rosacea have reported a decrease in self-esteem, social avoidance, and significantly decreased self-image due to rosacea.
- Studies have shown that approximately 70% of rosacea patients experience negative effects on their professional relationships, and nearly 60% of rosacea patients experience a negative effect on their social lives.
- Survey conducted by the National Rosacea Society have shown that approximately 70% of rosacea patients experience a negative effect on their professional relationships, and nearly 60% of rosacea patients experience a negative effect on their social lives.

Pharmacologic Treatment of Rosacea: Topical Therapy

- Topical benzoyl peroxide 5%-clindamycin 1% has been shown to be effective in randomized, vehicle-controlled trials.
- Azelaic Acid
  - Approved by the FDA based on phase III pivotal trial of 15% gel formulation (double-blind, randomized, vehicle-controlled study).
  - Effective treatment for rosacea has been correlated with marked improvement in quality of life indices.

Pharmacologic Treatment of Rosacea: Oral Therapy

- Antibiotic/Anti-inflammatory Agents
  - Tetracyclines, including tetracycline, doxycycline (500 mg/day), and minocycline (100 mg/day), are commonly used treatment options for rosacea.
  - The use of tetracycline, minocycline, and doxycycline (other than 500 mg/day; less than 30 mg/kg of body weight body weight) is not recommended for the treatment of rosacea, as utilization on extended clinical trials has been shown to be safe and effective.
  - Other oral antibiotic/antimicrobial agents that have been shown to be effective for the treatment of rosacea in case reports and small studies are minocycline, clindamycin, and erythromycin.

References

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Disease State Fundamentals
- Rosacea is a common facial disorder presenting most commonly in adulthood. Rosacea is characterized by intermittent episodes of erythema, telangiectasia, papules, pustules, and occasionally phymas. The disease is chronic and is characterized by intermittent periods of exacerbations and remissions.
- Clinical signs of rosacea include central facial erythema, telangiectasia, papules, pustules, and phymas.
- The underlying cause of rosacea is unknown, however, several pathophysiologic associations have been reviewed in the literature.
- Major pathologic components appear to be inflammatory, vascular, and growth factor in origin. There is no definitive evidence that rosacea is caused by a microbial pathogen, such as a bacterium, parasite, or virus.1
- The most common clinical presentations of cutaneous rosacea include the inflammatory (papulosquamous) and rhinophymatous variants. Other presentations include phymatous rosacea (such as rhinophyma), periorificial rosacea, eye-related rosacea, and others.2
- Rosacea is a chronic disease, with a minimum average duration of 14 years.3 Clinical presentation of rosacea includes clinical signs that are not limited to the face, but also includes ocular, oral, and perioral involvement.

Quality of Life Implications
- Rosacea has been shown to exhibit a negative impact on quality of life (QOL) in patients with the condition.4 Studies have shown that approximately 70% of rosacea patients experience lower self-confidence, lower self-esteem, and lower self-image as a result of their condition, with 41% of patients avoiding social interactions.5 Furthermore, among patients with severe rosacea, approximately 70% claim that the disorder has had a negative effect on their professional relationships, and nearly 30% have missed work as a result of their condition.6
- Effective treatment of rosacea has been correlated with marked improvement in quality of the index.7

Pharmacologic Treatment of Rosacea: Topical Therapy
- Sulfacetamide 10%–Sulfur 5%
  - Available as a gel, cream, liquid, and shampoo. Supports the indication for rosacea treatment based on drug efficacy study (DESIGN I) drug designations.
  - Multiple randomized vehicle-controlled and comparative studies, both blinded and open-label, have confirmed the efficacy of this formulation in patients with inflammatory rosacea measured as marked improvement based on investigator assessment and patient assessment.
  - Multiple vehicle formulations are available, including cleanser, cream, gel, lotion, and topical suspension.

- MetroSorbid
  - Approved by the FDA for inflammatory rosacea based on phase III pivotal trials (double-blind, randomized, vehicle-controlled studies).
  - Multiple, blinded, eight-week open-label vehicle-controlled studies have been conducted to support the safety and efficacy of this formulation.
  - Data collected from these studies have shown efficacy of 1% cream, gel, cream and lotion.11
  - Both 1% cream and formulations of 1% strength are available and FDA-approved for application once daily. Three formulations of the 1% strength are available including gel, lotion, and cream, FDA-approved for twice daily use.

- Azelaic Acid
  - Approved by the FDA based on phase III pivotal trials of 15% gel formulation (double-blind, randomized, vehicle-controlled studies).12
  - Safety and efficacy supported by multiple blinded and vehicle-controlled trials evaluating 15% formulation applied twice daily.13

- Miscellaneous Topical Agents
  - Other topical agents have been approved based on data from several studies.
  - Efficacy and safety supported by multiple blinded and vehicle-controlled trials.14

Pharmacologic Treatment of Rosacea: Oral Therapy
- Anti-Inflammatory Agents
  - Systemic therapy and/or oral anti-inflammatory therapies are indicated in patients with severe rosacea who have failed to respond to topical therapies or whom require more rapid improvement.15
  - Other oral antibiotic/antimicrobial agents that have been used for treatment of rosacea in case reports and small studies are metronidazole, doxycycline, minocycline, and oral isotretinoin.16
  - Anti-inflammatory dose doxycycline is the only systemic therapy approved by the FDA for treatment of rosacea.17

- Anti-Bacterial Agents
  - Systemic therapy and/or oral anti-inflammatory therapies are indicated in patients with severe rosacea who have failed to respond to topical therapies or whom require more rapid improvement.15
  - Other oral antibiotic/antimicrobial agents that have been used for treatment of rosacea in case reports and small studies are metronidazole, doxycycline, minocycline, and oral isotretinoin.16

- Other Systemic Agents
  - Other systemic agents, including isotretinoin, have been used for treatment of rosacea.18

References
Objectives

(1) Provide an overview of the fundamental Objectives of rosacea and quality of life implications

(2) Outline available pharmacologic treatments for rosacea with reference to supporting research and literature

- The pharmacologic agents discussed are inclusive of those that are Food and Drug Administration (FDA)-approved based on phase III pivotal trials, commonly used agents based on extensive clinical experience, and less commonly used alternatives reported in peer-reviewed literature.

Disease State Fundamentals

- Rosacea is a common facial disorder presenting most commonly in adulthood, characterized by episodes of redness, swelling, flushing, and increased blood flow to the skin, and can impair the quality of life.
- Clinical signs of rosacea include facial erythema, telangiectasia, papules, pustules, and ocular involvement.
- The underlying cause of rosacea is unknown; however, several pathophysiologic characteristics have been reviewed in the literature.
- Major pathologic components appear to be inflammatory, vascular, and ocular in origin; there is no definitive evidence that rosacea is caused by a microbial pathogen, such as a bacterium, parasite, or virus.
- The most common clinical presentations of ocular rosacea include the inflammatory (papular) and erythematotelangiectatic subtypes. Other presentations include pyriformis rosacea, rosacea with secondary glaucoma, and rosacea with ocular involvement.
- Clinical presentations of ocular rosacea include the inflammatory (papular), erythematotelangiectatic, and pyriformis subtypes.

Quality of Life Implications

- Rosacea has been shown to exhibit a negative impact on quality of life (QOL) of affected patients. For example, it has been shown that approximately 70% of rosacea patients experience lower self-confidence and lower self-esteem as a result of their condition, with 41% of patients avoiding public contact or canceling social engagements.
- Data supporting use of topical clindamycin or erythromycin for acne rosacea, approximately 70% claim that their disorder has had a negative impact on their professional relationships, and nearly 30% have missed work as a result of their condition.
- The inflammatory (papulopustular) and erythematotelangiectatic presentations are most common in rosacea patients, and are significant adjuncts to pharmacologic therapy.

Pharmacologic Treatment of Rosacea: Topical Therapy

Sulfacetamide 10%-Sulfur 5%

- A topical agent that has been shown to effective in case reports of refractory rosacea that were diagnosed as demodicidic folliculitis.
- Topical retinoic acid is recommended for rosacea, although supporting data is very limited.

Pharmacologic Treatment of Rosacea: Oral Therapy

Antibiotic/Inflammatory Agents

- Doxycycline 40mg controlled-release formulation (anti-inflammatory drug) is FDA-approved for treatment of rosacea. 
- The use of tetracycline, minocycline, and doxycycline is supported by FDA-approved studies evaluating 15% formulation applied twice daily. 
- Accurate dose doxycycline is not exert antibiotic resistance among government agencies, such as the FDA and Centers for Disease Control (CDC) for treatment of rosacea. 
- Patients with rosacea characteristically exhibit sensitive skin; therefore, the use of anti-inflammatory therapies may exacerbate or worsen the condition.

References


