Drugs for Rosacea

This common, chronic inflammatory facial eruption of unknown cause is more prevalent in women than in men. Rosacea is characterized by erythema and telangiectasia, and sometimes by recurrent, progressive crops of acneiform papules and pustules, usually on the central part of the face. Some patients develop granulomas and tissue hypertrophy, which may lead to rhinophyma (a bulbous nose), particularly in men. Blepharitis and conjunctivitis are common. Keratitis and corneal scarring occur rarely.

TOPICAL THERAPY — After starting treatment with topical drugs, it may take 4-6 weeks for improvement to become visible. Metronidazole (Metrogel, and others) and azelaic acid (Finacea for rosacea; Azelex for acne) are the standard topical antimicrobials used to treat the papules and pustules of rosacea; they appear to be about equally effective, but few well-controlled comparative trials have been published. Benzoyl peroxide, erythromycin, clindamycin, and sulfaacetamide/sulfur have also been used.1 The topical

Table 1. Some Topical Drugs for Rosacea

<table>
<thead>
<tr>
<th>Drug</th>
<th>Some Available Formulations</th>
<th>Usual Dosage1</th>
<th>Cost/Size2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azelaic acid – Finacea (Bayer)</td>
<td>15% gel</td>
<td>bid</td>
<td>$275.40/50 g</td>
</tr>
<tr>
<td>Brimonidine – Mirvaso (Galderma)</td>
<td>0.33% gel</td>
<td>once/d</td>
<td>360.00/30 g</td>
</tr>
<tr>
<td>Ivermectin – Soolantra (Galderma)</td>
<td>1% cream</td>
<td>once/d</td>
<td>275.00/30 g</td>
</tr>
<tr>
<td>Metronidazole – generic</td>
<td>0.75% gel, cream; 1% gel</td>
<td>once/d</td>
<td>157.40/45 g²</td>
</tr>
<tr>
<td>Metrocream (Galderma)</td>
<td>0.75% cream</td>
<td></td>
<td>569.10/45 g</td>
</tr>
<tr>
<td>Metrogel</td>
<td>1% gel</td>
<td></td>
<td>342.60/55 g</td>
</tr>
<tr>
<td>Metrocream 0.75% lotion</td>
<td>654.20/59 mL</td>
<td></td>
<td></td>
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</tbody>
</table>

1. A pea-sized amount should be applied in a thin layer to each affected area of the face.
2. Approximate WAC for the size listed. WAC = wholesaler acquisition cost, or manufacturer’s published price to wholesalers; WAC represents a published catalogue or list price and may not represent actual transactional prices. Source: AnalySource® Monthly, January 5, 2016. Reprinted with permission by First Databank, Inc. All rights reserved. ©2015. www.fdbhealth.com/policies/drug-pricing-policy.
3. Cost of a 45-g tube of 0.75% cream.

Recommendations for Treatment of Rosacea

- Topical antimicrobials such as metronidazole and azelaic acid are generally tried first for treatment of rosacea, sometimes in combination with oral antimicrobials.
- Oral antibiotics such as low-dose doxycycline are effective for treatment of papules, pustules, and erythema, but prolonged courses of treatment are needed.
- Ivermectin cream appears to be more effective than metronidazole cream for treatment of papulopustular rosacea.
- Topical retinoids are sometimes used for patients who do not respond to topical antimicrobials.
- Isotretinoin is generally reserved for patients with severe inflammatory disease who have not responded to other treatments.

retinoids used to treat acne are also sometimes used (off-label) to treat rosacea.

Brimonidine tartrate 0.33% (Mirvaso), an alpha-adrenergic receptor agonist, is approved for topical treatment of persistent facial erythema of rosacea in adults.2 It is not indicated for treatment of inflammatory lesions (papules and pustules). Brimonidine constricts dilated facial blood vessels to reduce the redness of rosacea. It has a rapid onset of action, with effects occurring as soon as 30 minutes after application and lasting for up to 12 hours. Rebound erythema worse than baseline and skin burning sensation occurring several hours after application have been reported.3,4

Demodex mites have been implicated in the pathogenesis of the inflammatory facial eruptions of rosacea. Ivermectin 1% cream (Soolantra) was recently approved for once-daily treatment of inflammatory lesions of rosacea.5 Ivermectin has both anti-inflammatory and antiparasitic activity. In a 16-week trial in patients with moderate to severe papulopustular rosacea, ivermectin cream was more effective and better tolerated than metronidazole cream.6

SYSTEMIC THERAPY — Oral Antimicrobials — Systemic antibiotic therapy is effective for treatment of papules, pustules, and erythema, but not for telangiectasia, rhinophyma, or the flushing that nearly always accompanies rosacea. It is generally used for symptoms that are moderate to severe or have not responded to topical therapy. Effective
treatment often requires a prolonged course (months or sometimes years) of an oral antibiotic such as doxycycline. A once-daily subantimicrobial-dose (40 mg) formulation of doxycycline (Oracea, and generics) is FDA-approved for treatment of papulopustular rosacea. Use of generic immediate-release doxycycline 20 mg twice a day is a cheaper alternative. Oral metronidazole (Flagyl, and generics) is also effective for rosacea, but it has some unpleasant side effects such as metallic taste. Oral ivermectin (Stromectol, and generics), often in combination with topical permethrin, has been used in patients with facial proliferation of Demodex mites.

Isotretinoin Patients with severe papulopustular rosacea can be treated (off-label) with low doses of isotretinoin (0.1–0.5 mg/kg/day) for 6–8 months. Isotretinoin is a potent human teratogen (pregnancy category X); careful monitoring is necessary in women of childbearing age. Significant reductions in erythema, papules, and telangiectasia occur after about 2 months of treatment. No other pharmacologic treatment has been reported to reduce telangiectasia.

LIGHT-BASED THERAPY In small clinical trials, light and laser therapies have decreased the severity of telangiectasia and erythema in patients with rosacea, but long-term studies are lacking. Adverse effects have included purpura and hyperpigmentation.

3. ET Routt and JO Levitt. Rebound erythema and burning sensation from a new topical brimonidine tartrate gel 0.33%. J Am Acad Dermatol 2014; 70:e37.