

## Finding a Place for Topical Anti-inflammatory Acne Therapy

Dermatologists and patients are discovering how a novel topical therapy offers a different way to target acne in certain individuals.

Several months after the market launch of topical dapsone gel 5% (Aczone, Allergan), clinicians still seem to be trying to acquaint themselves with the agent and identify its ideal place in the management of acne patients. Patients, too, may be trying to familiarize themselves with this new and as yet not readily identified prescription product. A cursory review of some Internet discussion boards for acne reveal quite a bit of dialogue about topical dapsone but few factual details. The following review highlights what we know about topical dapsone and its potential role in acne management.

### Efficacy and Safety

Use of dapsone for the management of acne is not entirely new. It had been considered a possible acute, systemic intervention for severe, nodulocystic, inflammatory acne, and its use for this indication has been advocated as recently as last year.<sup>1</sup> However, due to a lack of data to support the use of oral dapsone for severe acne and the risk of adverse effects associated with the agent, including hematologic effects, its use for acne has been limited.<sup>2</sup>

Topical dapsone expands the potential utility of the drug for acne. Several publications have presented and reviewed the efficacy of topical dapsone gel 5% in treating mild to moderately severe acne.<sup>3,4</sup> In 12-week clinical trials comparing topical dapsone to vehicle, treated patients had greater improvements in investigator's global

acne assessment and mean percentage reduction in inflammatory, non-inflammatory, and total lesion counts, compared to controls. Statistically significant improvement in lesion counts was evident by week four.<sup>3</sup>

Topical application is associated with low systemic exposure and obviates concerns about hematologic side effects, with studies showing that only two of 50 study participants with glucose-6-phosphate dehydrogenase (G6PD) deficiency experienced a drop in hemoglobin levels; those fluctuations were similar to changes observed in non-G6PD deficient subjects.<sup>5</sup> As dermatologists are aware, FDA dropped an initial requirement for screening for G6PD prior to topical dapsone therapy.

### A Context

While data support the efficacy of topical dapsone gel, there are no trials comparing the intervention to other available topical therapies. Additionally, there may be some confusion regarding the agent's method of action in acne vulgaris and, thus, its therapeutic role.

Dapsone is a sulfone and has long been used to manage leprosy, caused by bacteria *Mycobacterium leprae* and *Mycobacterium lepromatosis*. The drug has been recognized as conferring anti-inflammatory effects—beneficial in the management of leprosy—but current evidence questions the degree to which dapsone provides antimicrobial effects. One trial found that even at very high concentrations, dapsone

demonstrated no antibacterial effects against *Streptococcus pyogenes*, *Staphylococcus aureus*, or *Escherichia coli*.<sup>6</sup> No published data report antibacterial effects of dapsone against *P. acnes*. Though, as the maxim holds, absence of evidence is not evidence of absence, these facts present interesting questions. Publications describe topical dapsone gel as an antibacterial agent;<sup>7</sup> marketing materials for the new formulation do not mention antibacterial effects.

Marketing emphasizes the anti-inflammatory properties demonstrated by topical dapsone gel in trials. Among 486 patients who used topical dapsone gel twice daily for up to 12 months, there was a 58.2 percent reduction in mean inflammatory lesions at the end of the study period, compared to a 19.5 percent reduction in mean non-inflammatory lesions.<sup>8</sup> Overall reduction in mean total lesion counts was 49 percent. Investigations are reportedly underway to examine the use of topical dapsone for rosacea, a disease with a significant inflammatory component.<sup>7</sup> Precisely how dapsone confers anti-inflammatory effects is not fully understood.

Given that recent recommendations from the Global Alliance to Improve Outcomes in Acne group emphasize that acne is a chronic, inflammatory disease, similar to atopic dermatitis or psoriasis,<sup>9</sup> the availability of a topical anti-inflammatory agent may prove helpful in the clinic. Persistent concerns about developing microbial

## ■ ■ ■ Clinical Focus: Acne

### Rosacea Flare Forecast

If you notice an influx of rosacea patients during the summer months, your practice probably isn't unique. According to a recent survey of rosacea patients conducted by the National Rosacea Society (NRS), about half of respondents said their skin condition is worse in the summer months. Results of the survey of 1,190 rosacea patients, published in *Rosacea Review*, show that a majority (85 percent) said their rosacea is affected by changes in seasons; 46 percent said they have to make the most lifestyle adjustments during summer months to reduce the likelihood of a flare-up of signs and symptoms. The cold poses problems, as well. Thirty-five percent of all respondents and 46 percent of those who live in the northern US said their symptoms are at their worst during cold weather.

Advising patients on preventive skincare and sun protection as well as recommending appropriate seasonal or pre-seasonal therapeutic modifications may help minimize exacerbations.

—PD Staff

resistance associated with the use of antibiotics also support the need for alternative therapeutic agents for acne management.

#### Finding a Niche

Based on the available data, topical dapsone seems especially well-suited to the management of primarily inflammatory mild to moderate acne. Use of the product is not associated with cutaneous irritation, such as burning or peeling common with the use of topical benzoyl peroxide or retinoids. Therefore, it is a suitable option for patients with sensitive skin.

Given that the trend in acne therapy is to target as many pathogenic factors as possible, monotherapy is rarely indicated. In fact, guidelines suggest that most patients with mild to moderate acne should be managed or maintained with a topical retinoid. Topical antimicrobials, particularly benzoyl peroxide, are also emphasized in recommendations.<sup>9</sup> Taken together, these various considerations suggest that most patients prescribed topical dapsone therapy may be candidates for additional topical intervention(s).

There are no published studies on the use of topical dapsone in combination with other topical acne interven-

tions. The Prescribing Information indicates that concomitant application of benzoyl peroxide and dapsone gel produced a yellow or orange discoloration of the skin in seven of 95 subjects that lasted up to 57 days in some individuals. There is no report of the efficacy of the combination or whether either agent inactivated the other. Still, the risk of skin discoloration is sufficient to recommend against concomitant application. There are no other reports of interactions or contraindications with dapsone gel and standard topical acne therapies.

Dapsone gel is indicated for twice-daily application. However, if it is used in conjunction with other topical agents, until further evidence is available, it may be wise to reduce application of dapsone to once daily and substitute a retinoid or antimicrobial, such as benzoyl peroxide, at the other application time.

Although topical dapsone gel may not become a first-line treatment option for a majority of people with acne, it may be an important treatment option for a number of patients. It offers a unique mechanism of action and effectively targets inflammation—one of the key pathogenic features of this ubiquitous dermatitis. ■

*Dr. Anderson has served as a consultant to Allergan; She has not consulted regarding Aczone.*

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