

Combination Topical Products for the Treatment of Acne Vulgaris

Dermatologists at times seek to maximize efficacy for the treatment of acne in the clinical setting by using a combination of drug substances separately in the same patient. Fixed combination topical drug products have been approved previously for use in the treatment of acne vulgaris.

Combination drug policy is articulated in 21 CFR 300.50, Fixed-combination prescription drugs for humans. The primary statement is:

“Two or more drugs may be combined in a single dosage form when each component makes a contribution to the claimed effects and the dosage of each component (amount, frequency, duration) is such that the combination is safe and effective for a significant patient population requiring such concurrent therapy as defined in the labeling for the drug.”

Combination topical products for the treatment of acne vulgaris are considered under 21 CFR 300.50 and require evidence for the contribution of each active component or components that are purported to provide for added efficacy. The patient population requiring such concurrent therapy must also be defined in the labeling for the drug product.

Applying the combination drug policy for 2 drugs, component substances A and B having the same endpoint, in a three or four arm clinical trial, success is demonstrated by:

$$(A + B) > A, B > \text{placebo}$$

When a drug product for acne has multiple drug substances, the Agency has required that each of the substances demonstrate a contribution to the overall effect of the drug on lesion counts and in the Physicians' Global Assessment by showing superiority. In this manner, a contribution to overall efficacy is demonstrated.

Currently marketed combination drug products for acne have combined a topical antibiotic (erythromycin or clindamycin) [= A] with benzoyl peroxide [= B]. Studies to address the combination policy for these drugs have shown that the most difficult superiority to demonstrate is the contribution of the antibiotic to the efficacy already achievable with benzoyl peroxide alone ((A + B) > B).