Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Benzoyl Peroxide

August 2026

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the Office of Generic Drugs.

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word should in Agency guidances means that something is suggested or recommended, but not required.

Active Ingredient: Benzoyl peroxide

Dosage Form: Cream

Route: Topical

Strength: 5%

Reference Listed Drug: NDA 214510

Recommended Studies: Comparative clinical endpoint bioequivalence study

Meeting recommendations: The benzoyl peroxide in the reference listed drug (RLD) is in a solid form that is incorporated into a microcapsule. For proposed generic products that have differences in formulation design compared to the RLD, it would be imperative to ascertain the stability of the proposed formulation prior to conducting the recommended comparative clinical endpoint bioequivalence study. Applicants intending to submit an abbreviated new drug application (ANDA) for this drug product are encouraged to seek feedback about their drug product development program by submitting a pre-ANDA product development meeting request that includes information related to the proposed formulation design and available stability data prior to initiating the comparative clinical endpoint bioequivalence study. Additionally, applicants intending to propose an alternative approach by which to demonstrate bioequivalence should also consider a pre-ANDA product development meeting. Refer to the guidance for industry *Formal Meetings Between FDA and ANDA Applicants of Complex Products Under GDUFA*[a] for additional information describing the procedures on how to clarify regulatory expectations regarding your individual drug development program.

1. Class of study: Bioequivalence
   Type of study: Comparative clinical endpoint bioequivalence study
   Design: Randomized, double blind, parallel, placebo-controlled, in vivo
   Strength: 5%
   Subjects: Males and non-pregnant, non-lactating females with rosacea

Additional study design recommendations for the comparative clinical endpoint bioequivalence study:

1. FDA recommends conducting a comparative clinical endpoint bioequivalence study in the treatment of moderate to severe rosacea. Subjects are to be randomized to receive the test product, the reference standard (RS), or placebo (vehicle) once daily for 12 weeks. The primary endpoint is to be evaluated at the end of treatment (Study Week 12).

2. Inclusion criteria (the sponsor may add additional criteria):
   a. Males or non-pregnant, non-lactating females aged ≥18 years with a clinical diagnosis of moderate to severe facial rosacea, defined as the presence of all the following criteria:
      - A total of 8 to 50 combined papules/pustules on the face, and
      - At least moderate erythema, and
      - Telangiectasia
   b. Subject willing to minimize external factors that might trigger rosacea flare-ups (e.g., spicy foods, thermally hot foods and drinks, hot environments, prolonged sun exposure, strong winds and alcoholic beverages).

3. Exclusion criteria (the sponsor may add additional criteria):
   a. Pregnant or lactating or planning to become pregnant during the study period
   b. Presence of any skin condition on the face that would interfere with the diagnosis or assessment of rosacea
   c. Excessive facial hair (e.g., beards, sideburns, moustaches, etc.) that would interfere with diagnosis or assessment of rosacea
   d. History of hypersensitivity or allergy to any component of the formulation
   e. Use within 6 months prior to baseline of oral retinoids or therapeutic vitamin A supplements of greater than 10,000 units/day (multivitamins are allowed)
   f. Use for less than 3 months prior to baseline of estrogens or oral contraceptives; use of such therapy must remain constant throughout the study
   g. Use within 1 month prior to baseline of (1) topical retinoids to the face, (2) systemic antibiotics known to have an impact on the severity of facial rosacea (e.g., containing tetracycline and its derivatives, erythromycin and its derivatives, sulfamethoxazole, or trimethoprim), or (3) systemic corticosteroids
   h. Use within 2 weeks prior to baseline of (1) topical corticosteroids, (2) topical antibiotics, or (3) topical medications for rosacea (e.g., metronidazole, azelaic acid)
   i. Subjects with moderate or severe rhinophyma, dense telangiectases, or plaque-like facial edema

j. Ocular rosacea (e.g., conjunctivitis, blepharitis, or keratitis) of sufficient severity to require topical or systemic antibiotics

4. The protocol should include a list of the prescription and over-the-counter drug products that are prohibited during the study, such as:
    a. Any other topical products applied to the target site (e.g., metronidazole, topical antibiotics, topical steroids)
    b. Oral retinoids
    c. Systemic (e.g., oral or injectable) antibiotics known to have an impact on the severity of facial rosacea (e.g., containing tetracycline, erythromycin, sulfamethoxazole, or trimethoprim or their derivatives)
    d. Systemic corticosteroid or immunosuppressive drugs
    e. Antipruritics, including antihistamines, within 24 hours of study visits

5. Subjects should not apply moisturizers, new brands of make-up, creams, lotions, powders or any topical product other than the assigned treatment to the treatment area. Occlusive dressings or wrappings should be avoided in treatment areas. Subjects should minimize exposure to sunlight, including sunlamps, while using the product. Use of sunscreen products and protective clothing over treated areas is recommended when sun exposure cannot be avoided.

6. Areas to be treated should be washed with a mild cleanser before application and patted dry with a soft towel. A thin layer of study treatment should be gently massaged into the affected areas on the face once daily for 12 weeks. Contact with the mouth, eyes and other mucous membranes should be avoided. The hands should be washed following application.

7. The recommended primary endpoint of the study is the mean percent change from baseline to Week 12 in the inflammatory (papules and pustules) lesion counts of rosacea. The protocol should clearly define papules, pustules, and nodules. When counting facial lesions, it is important that all lesions be counted, including those present on the nose. Counts of nodules should be reported separately and not included in the inflammatory lesion counts.

8. Application site reactions such as erythema, dryness, burning/stinging, erosion, edema, pain and itching are to be recorded at each visit to allow a comparison between treatment groups. A descriptive analysis comparing the application site reactions for each treatment group is recommended. It is important to ensure that the test product is not worse than the RS with regard to the expected and unexpected application site reactions.

9. Refer to the FDA product-specific guidance *Adapalene; Benzoyl Peroxide Topical Gel* (NDA 207917)[b] for a recommended approach to statistical analysis and study design for the comparative clinical endpoint bioequivalence studies.

10. Refer to the Study Data Standards Resources website https://www.fda.gov/industry/fda-resources-data-standards/study-data-standards-resources.

Document History: Recommended August 2026

[a] We update guidances periodically. For the most recent version of a guidance, refer to the FDA guidance webpage at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

[b] We update guidances periodically. For the most recent version of a product-specific guidance, refer to the FDA guidance webpage at https://www.accessdata.fda.gov/scripts/cder/psg/index.cfm.