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Draft – Not for Implementation

Draft Guidance on Oxybutynin

February 2026

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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: Oxybutynin

Dosage Form: Film, extended release

Route: Transdermal

Strength: 3.9 mg/24 hr

Recommended Studies: One in vivo bioequivalence study with pharmacokinetic endpoints, one in vivo adhesion study, and one in vivo skin irritation study

1. Type of study: Bioequivalence study with pharmacokinetic endpoints
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 3.9 mg/24 hr
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments:
   a. In this document, this dosage form is referred to as a transdermal delivery system (TDS) and includes products that may be described elsewhere or known as *patches, systems,* or *extended release films*.
   b. Unless otherwise justified, the oxybutynin TDS should be applied to the same anatomical site on all subjects, selected from among those recommended in the approved labeling for the reference listed drug (RLD), and worn for 96 hours. Applicants should randomize subjects to receive either drug product TDS in a given study period. When possible, the TDS administered in the second study period should be applied to the same anatomical site as in the first study period, but on the contralateral side of the body.

c. Contact of the TDS with the skin is essential for the in vivo performance of the TDS, and the pharmacokinetics may be altered when a TDS loses its adherence to the skin. Therefore, the adhesion of each TDS should be monitored and recorded throughout the bioequivalence study with pharmacokinetic endpoints. The applicant should prespecify their inclusion criteria for the statistical analysis of pharmacokinetic endpoints and perform their primary pharmacokinetic analysis on the per protocol population; however, samples should be collected and analyzed from all subjects at all sampling times regardless of the adhesion scores of the TDS and regardless of the inclusion criteria for the statistical analysis of pharmacokinetic endpoints. Provisions should be included in the study protocol to ensure that deliberate actions with the intent to re-apply a detached area of the TDS, to apply pressure to the TDS, or to reinforce TDS adhesion with the skin (e.g., overlays) are avoided throughout the study.
d. The applicant should refer to the most recent version of the guidance for industry *Bioequivalence Studies with Pharmacokinetic Endpoints for Drugs Submitted Under an ANDA*[a] for the design and conduct of the bioequivalence study with pharmacokinetic endpoints.

Analyte to measure: Oxybutynin in plasma

Bioequivalence based on (90% CI): Oxybutynin

Waiver request of in vivo testing: Not applicable

In vitro drug release method and sampling times: In vitro release should be included for quality control. Provide an in vitro release method development report for the test product containing information and data that demonstrate the appropriateness of the selected in vitro release method[1] and sampling times, such as the discriminating ability to detect changes in critical quality attributes that could potentially impact drug product performance.

2. Type of study: Adhesion study
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 3.9 mg/24 hr
Subjects: Healthy males and non-pregnant, non-lactating females
Additional comments:
   a. The applicant may elect to evaluate the bioequivalence (study 1) and the adhesion (study 2) in a single study with a combined purpose, or in independent studies. In either case, the studies should be adequately powered to evaluate the bioequivalence, and independently, the comparative assessment of adhesion.
   b. The applicant should refer to the most recent version of the guidance for industry *Assessing Adhesion With Transdermal and Topical Delivery Systems for ANDAs*[a] for the design and conduct of the independent adhesion study or the combined study to evaluate both bioequivalence and adhesion.

[1] Applicant-developed, United States Pharmacopeia (USP) drug product monograph, or Dissolution Methods database, https://www.accessdata.fda.gov/scripts/cder/dissolution/index.cfm

3. Type of study: Skin irritation study
Design: Randomized, evaluator-blinded, within-subject repeat design in vivo
Strength: 3.9 mg/24 hr (administered as one-half of the test articles)
Subjects: Healthy males and non-pregnant, non-lactating females
Additional comments:

a. All test articles (i.e., one-half of the 3.9 mg/24 hr strength of both drug product TDS[2], optional vehicle TDS[3], and optional negative control[4]) should be applied simultaneously to each subject at different positions on the same anatomical site recommended in the approved labeling for the RLD.
b. Sequential TDS applications of each test article should be made to the same position every 72 to 96 hours, for a total of 21 consecutive days.
c. When evaluating the irritation potential only, applicants should compare the test articles in a minimum of 40 evaluable subjects, or a sufficient number of subjects to power the study at a level of 0.80 or higher, whichever is greater.
d. If the test product contains an inactive ingredient that is not present in the RLD and is known to be sensitizing, or at a higher amount/concentration than previously used in an FDA-approved drug product with a similar context of use, FDA recommends conducting a combined irritation and sensitization study. FDA encourages applicants who have questions related to the need for a sensitization study for a proposed product (with a proposed formulation composition) to seek feedback through a controlled correspondence or product development meeting.[5]
e. There is insufficient information to determine whether it is safe to simultaneously apply two whole, active, 3.9 mg/24 hr oxybutynin TDS on the same subject during a 21-day skin irritation (and sensitization) study. Since the RLD has a matrix design that can be safely cut, the test product is anticipated to have a design that can also be safely cut to a smaller size. If the test product also has a design that can be safely cut to a smaller size, it should also be cut in half. It would not be acceptable to manufacture a separate batch of the test product in order to use a smaller TDS in this study.
f. The applicant should refer to the most recent version of the guidance for industry *Assessing the Irritation and Sensitization Potential of Transdermal and Topical Delivery Systems for ANDAs*[a] for the design and conduct of the skin irritation (and sensitization) study.

[2] The test product evaluated should be the actual TDS to be marketed.
[3] The optional vehicle TDS should contain all of the inactive ingredients in the test product and be identical to the test product in every manner except for the absence of the active ingredient.
[4] An example of the optional negative control treatment is an occlusive cover or device with normal saline applied on a polyester pad under the cover or within the device chamber.
[5] Applicants should refer to the most recent version of the guidance for industry *Controlled Correspondence Related to Generic Drug Development* and the most recent version of the guidance for industry *Formal Meetings Between FDA and ANDA Applicants of Complex Products Under GDUFA* for additional information describing the procedures on how to clarify regulatory expectations regarding the applicants' individual drug development program.

Additional comments relating to all studies:

In addition to the recommendations in the general guidances referenced above, and the product specific recommendations related to the individual studies, the following product specific recommendations should be considered.

1. Exclusion criteria (the applicant may add additional criteria):
    a. Medical history of urinary retention, gastric retention, or uncontrolled narrow-angle glaucoma; or being at risk for these conditions

2. Provide a listing of the prescription and over-the-counter drug products that are contraindicated during the study, such as:
    a. Anticholinergic drugs other than the drug product TDS

3. Subjects should be informed that heat prostration (fever and heat stroke due to decreased sweating) can occur when anticholinergic agents such as oxybutynin are used in a hot environment.

4. Subjects should be advised that anticholinergic agents such as oxybutynin may produce drowsiness (somnolence) or blurred vision, and to exercise caution in decisions to engage in potentially dangerous activities until they have determined its effects. Subjects should be informed that alcohol may enhance the drowsiness caused by anticholinergic agents such as oxybutynin.

5. Subjects should be informed of the possible adverse events that may occur with the use of oxybutynin TDS (i.e., application site pruritis, dry mouth, constipation, application site erythema, diarrhea, dysuria, application site vesicles).

Additional information:

Device:
The RLD is presented as a TDS. The TDS is the drug-device combination product.

FDA recommends that prospective applicants examine the critical design attributes of the RLD device when designing the test device.

User interface assessment:
An abbreviated new drug application for this product should include complete comparative analyses so FDA can determine whether any differences in design for the user interface of the proposed generic product, as compared to the RLD, are acceptable and whether the product can be expected to have the same clinical effect and safety profile as the RLD when administered to patients under the conditions specified in the labeling. For additional information, refer to the most recent version of the guidance for industry *Comparative Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA*.[a]

Document History: Recommended December 2009; Revised October 2018, December 2019, February 2026

Unique Agency Identifier: PSG_021351

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