Contains Nonbinding Recommendations

Draft Guidance on Bexarotene

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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.

Active Ingredient: Bexarotene

Dosage Form; Route: Gel; topical

Recommended Studies: In vitro studies

In Vitro Studies: To qualify for the in vitro approach to demonstrate bioequivalence for bexarotene gel, 1% the following criteria should be met:

A. The test and reference products should be qualitatively (Q1) and quantitatively (Q2) the same as defined in the Guidance for Industry: *ANDA Submissions – Refuse-to-Receive Standards*[1].

B. The test and reference products should be physically and structurally similar based upon an acceptable comparative physicochemical characterization of a minimum of three batches of the test and three batches (as available) of the reference product. The characterization of the test and reference products should include the following comparisons of physical and structural attributes between the test and reference products:

    i. Assessment of appearance with representative microscopic images at multiple magnifications.

    ii. Analysis of the rheological behavior which may be characterized using a rheometer that is appropriate for monitoring the non-Newtonian flow behavior of semi-solid dosage forms. The following evaluations are recommended:

        - Comparative viscosity data at low, medium and high shear rates should be provided.

        - Yield stress values should be reported if the material tested exhibits plastic flow behavior.

    iii. Analysis of specific gravity, weight loss (drying rate), and any other potentially relevant physical and structural similar characterizations.

C. The test and reference products should have an equivalent rate of bexarotene release based upon an acceptable in vitro release test (IVRT) comparing a minimum of one batch each of the test and reference products using an appropriately validated IVRT method. Refer to the

[1] The current version of the referenced guidance at the time of publication of this product specific guidance is Guidance for Industry: ANDA Submissions – Refuse-to-Receive Standards, Revision 2 (December 2016). However, we update guidances periodically, and current information related to guidances is maintained at https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

Draft Guidance on Acyclovir (for acyclovir topical cream, 5%)[2] for additional information regarding the development, validation, conduct and analysis of acceptable IVRT methods/studies. The batches of test and reference products evaluated in the IVRT study should be included among those for which physical and structural similarity is characterized and compared.

Analytes to measure (in appropriate biological fluid): Not applicable

Bioequivalence based on (90% CI): Refer to the *Draft Guidance on Acyclovir* (for acyclovir topical cream, 5%)[2] for additional information regarding the analysis of in vitro studies.

Waiver request of in vivo testing: Not applicable

Dissolution test method and sampling times: Not applicable

Applicants intending to propose an alternative approach by which to demonstrate bioequivalence should refer to the guidance for industry *Controlled Correspondence Related to Generic Drug Development* and 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 your individual drug development program.

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[2] The current version of the referenced guidance at the time of publication of this product specific guidance is Draft Guidance on Acyclovir for acyclovir topical cream, 5% (recommended Dec 2014; revised Dec 2016). However, we update guidances periodically, and current information related to product specific guidances is maintained at https://www.fda.gov/drugs/guidancecomplianceregulatoryinformation/guidances/ucm075207.htm.