



# **APPROVED DRUG PRODUCTS**

**WITH**

**THERAPEUTIC  
EQUIVALENCE  
EVALUATIONS**

**40<sup>th</sup> EDITION**

**THE PRODUCTS IN THIS LIST HAVE BEEN APPROVED UNDER  
SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT.**

**U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION  
OFFICE OF MEDICAL PRODUCTS AND TOBACCO  
CENTER FOR DRUG EVALUATION AND RESEARCH  
OFFICE OF GENERIC DRUGS  
OFFICE OF GENERIC DRUG POLICY**

**2020**

# **APPROVED DRUG PRODUCTS with THERAPEUTIC EQUIVALENCE EVALUATIONS**

The products in this list have been approved under section 505 of the Federal Food, Drug, and Cosmetic Act. This volume is current through December 31, 2019.

## **40<sup>th</sup> EDITION**



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## 1.2 Therapeutic Equivalence-Related Terms

**Pharmaceutical Equivalents.** Pharmaceutical equivalents are drug products in identical dosage forms and route(s) of administration that contain identical amounts of the identical active drug ingredient, i.e., the same salt or ester of the same therapeutic moiety, or, in the case of modified-release dosage forms that require a reservoir or overage or such forms as prefilled syringes where the residual volume may vary, that deliver identical amounts of the active drug ingredient over the identical dosing period; do not necessarily contain the same inactive ingredients; and meet the identical compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times, and/or dissolution rates.<sup>2</sup> They may differ in characteristics such as shape, scoring configuration, release mechanisms, packaging, excipients (including colors, flavors, preservatives), expiration date/time, and, within certain limits, labeling.

**Pharmaceutical Alternatives.** Pharmaceutical alternatives are drug products that contain the identical therapeutic moiety, or its precursor, but not necessarily in the same amount or dosage form, or the same salt or ester (e.g., tetracycline hydrochloride, 250mg capsules vs. tetracycline phosphate complex, 250mg capsules; quinidine sulfate, 200mg tablets vs. quinidine sulfate, 200mg capsules).<sup>3</sup> Each such drug product individually meets either the identical or its own respective compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times, and/or dissolution rates.<sup>4</sup> Different dosage forms and strengths within a product line by a single manufacturer are pharmaceutical alternatives, as are extended-release products when compared with immediate-release or standard-release formulations of the same active ingredient.

**Therapeutic Equivalents.** Approved drug products are considered to be therapeutic equivalents if they are pharmaceutical equivalents for which bioequivalence has been demonstrated, and they can be expected to have the same clinical effect and safety profile when administered to patients under the conditions specified in the labeling.<sup>5</sup>

FDA classifies as therapeutically equivalent those drug products that meet the following general criteria: (1) they are approved as safe and effective; (2) they are pharmaceutical equivalents in that they (a) contain identical amounts of the identical active drug ingredient in the identical dosage form and route of administration, and (b) meet compendial or other applicable standards of strength, quality, purity, and identity; (3) they are bioequivalent in that (a) they do not present a known or potential bioequivalence problem, and they meet an acceptable *in vitro* standard, or (b) if they do present such a known or potential problem, they are shown to meet an appropriate bioequivalence standard; (4) they are adequately labeled; and (5) they are manufactured in compliance with Current Good Manufacturing Practice regulations. The concept of therapeutic equivalence applies only to drug products containing the identical active ingredient(s) and does not encompass a comparison of different therapeutic agents used for the same condition (e.g., meperidine hydrochloride vs. morphine sulfate for the treatment of pain). Any drug product in the Orange Book repackaged and/or distributed by other than the applicant is considered to be therapeutically equivalent to the applicant's drug product even if the applicant's drug

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<sup>2</sup> 21 CFR 314.3(b).

<sup>3</sup> See 21 CFR 314.3(b).

<sup>4</sup> 21 CFR 314.3(b).

<sup>5</sup> 21 CFR 314.3(b).

product is single source or coded as non-equivalent (e.g., **BN**). Distributors or repackagers of an applicant's drug product are not identified in the Orange Book.

FDA considers drug products to be therapeutically equivalent if they meet the criteria outlined above, even though they may differ in certain other characteristics such as shape, scoring configuration, release mechanisms, packaging, excipients (including colors, flavors, preservatives), expiration date/time, certain aspects of labeling (e.g., the presence of specific pharmacokinetic information), and storage conditions. When such differences are important in the care of a particular patient, it may be appropriate for the prescribing physician to require that a specific product be dispensed as a medical necessity. With this limitation, however, FDA believes that products classified as therapeutically equivalent can be substituted with the full expectation that the substituted product can be expected to have the same clinical effect and safety profile as the prescribed product when administered to patients under the conditions specified in the labeling.

**Strength.** Strength refers to the amount of drug substance contained in, delivered, or deliverable from a drug product, which includes: (1) (a) the total quantity of drug substance in mass or units of activity in a dosage unit or container closure (e.g., weight/unit dose, weight/volume or weight/weight in a container closure, or units/volume or units/weight in a container closure); and/or, as applicable, (b) the concentration of the drug substance in mass or units of activity per unit volume or mass (e.g., weight/weight, weight/volume, or units/volume); or (2) such other criteria the Agency establishes for determining the amount of drug substance contained in, delivered, or deliverable from a drug product if the weights and measures described in clause (1) (a) do not apply (e.g., certain drug-device combination products for which the amount of drug substance is emitted per use or unit time).<sup>6</sup> Note that if the criteria the Agency establishes for determining and expressing the amount of drug substance in a product evolves over time, the Agency generally does not intend to revise the expressions of strength for drug products already included in the Orange Book, but rather intends to apply the criteria prospectively to drug products added to the Orange Book.

Although the strength of drug products in the Orange Book is generally expressed in terms of the amount of drug substance (active ingredient) in the drug product, it is sometimes expressed in terms of the amount of the active moiety. For example, certain drug products included in the Orange Book include a designation of "EQ" next to their expression of strength. This "EQ" designation generally is used in connection with salt drug products to indicate that the strength of such drug product is being expressed in terms of the equivalent strength of the active moiety (e.g., "EQ 200MG BASE"), rather than in terms of the strength of the active ingredient.

**Bioavailability.** Bioavailability is the rate and extent to which the active ingredient or active moiety is absorbed from a drug product and becomes available at the site of drug action. For drug products that are not intended to be absorbed into the bloodstream, bioavailability may be assessed by scientifically valid measurements intended to reflect the rate and extent to which the active ingredient or active moiety becomes available at the site of drug action.<sup>7</sup>

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<sup>6</sup> 21 CFR 314.3(b).

<sup>7</sup> 21 CFR 314.3(b).