Mini Review
Open Access

FDA's orange book and ab ratings of pharmaceutical drug products: a guide to community pharmacist

Abstract

One of the major sources of error in filling prescription in community pharmacy is that not equivalent drug product substitution. Pharmacist often relies on orange book codes for therapeutic substitution when permitted by prescriber. In this mini review, we made sincere efforts to explain Orange book, therapeutic equivalent codes and how to interpret each code.

Keywords: orange book, therapeutic equivalence, AB ratings

Volume 1 Issue 3 - 2015

Vijay M Kale
Department of Pharmaceutical Sciences, Roseman University of Health Sciences College of Pharmacy, South Jordan, USA

Correspondence: Vijay M Kale, Assistant Professor of Pharmaceutical Sciences, Roseman University of Health Sciences, College of Pharmacy, 10920 S Riverfront Parkway, Utah 84095, South Jordan, USA, Tel 801-878-1078, Email vkale@roseman.edu

Received: December 29, 2015 | **Published:** January 04, 2016

Introduction

FDA orange book

The official name of FDA's orange book is Approved Drug Products with Therapeutic Equivalence Evaluations. Originally this book was published in October 1980 with orange cover and thus the name "orange book". The orange book is published annually and the 2015 edition is 35th edition of orange book.[1] It is freely available for download and it has search options available on website. This book contains the list of all drugs approved in the United States as safe and effective. It is also the authoritative source of information on the therapeutic equivalence of drug products. The orange book consist of five main sections: an introduction, a "how to use" section, the drug product lists, appendices and a patent and exclusivity information addendum.

Before understanding different drug ratings it is necessary to understand bioavailability and bioequivalence. Bioavailability refers to the rate and extent to which the active ingredient or therapeutic ingredient is absorbed from a drug product and becomes available at the site of drug action. Bioequivalence refers to equivalent release of the same drug substance from two or more drug products or formulations. These two definitions give three different classes of equivalent drugs.

Pharmaceutical equivalents

These are the drug products that contain the same active ingredients in the same strength and dosage form delivered by the same route of administration.

Bioequivalent drug products

These are the drug products that have shown comparable bioavailability when studied under similar conditions (e.g. the rate and extent of absorption of a test drug does not significantly differ from that of the reference drug).[2]

Therapeutic equivalent

These are the drug products that are pharmaceutical equivalents that are bioequivalent.

Therapeutic equivalence evaluations codes

There are broadly two types of therapeutic equivalent codes A-rated and B-rated drugs or codes.

a. **"A" codes:** A-rated drugs are those, which the FDA considers to be therapeutically equivalent and, therefore, substitutable where permitted by the prescriber. Various codes and their interpretations are described in table 1. The second letter (A, B, C, D, E, N, O, P, R, S, T or X) provides information about the dosage form, and in some cases, about the results of the FDA's evaluation of actual or potential bioequivalence problems.

b. **AA:** ingredients and dosage forms presenting neither actual nor potential bioequivalence problems (e.g., oral solutions).

c. **AB:** actual or potential bioequivalence problems have been resolved through adequate in vivo and/or in vitro testing. Often some therapeutic codes are followed by a number, such as AB1, AB2, AB3 etc. This is particularly when there are two or more drug products, containing the same ingredient, with the same strength and dosage form, which are not bioequivalent to each other. For example, a generic rated AB1 can be substituted for a brand rated AB1, but cannot be substituted for a brand rated AB2.

d. **"B" codes:** B-rated drugs are those, which the FDA considers not to be therapeutically equivalent due to actual or potential bioequivalence problems, which have not been resolved. This section is often related to pharmacokinetic differences, which arises due to product dissolution, disintegration, and absorption or metabolism and linked to specific delivery forms rather to safety and efficacy. For example the calcium channel blocker verapamil is AB-rated but its extended release formulation Covera-HS is BC-rated and thus not substitutable.[3]

Table 1 Summary of FDA's Orange Book Therapeutic Equivalence Codes

Code	Interpretation
AA	No bioequivalence problems in conventional dosage forms
AB	Meets necessary bioequivalence requirements
AB1	Meets bioequivalence requirements to AB1 rated reference drug
AB2	Meets bioequivalence requirements to AB2 rated reference drug
AB3	Meets bioequivalence requirements to AB3 rated reference drug
AB4	Meets bioequivalence requirements to AB4 rated reference drug
AN	Solution or powder for aerosolization
AO	Injectable oil solutions
AP	Injectable aqueous solutions
AT	Topical Products
BC	Controlled-release tablet, capsule, or injectable
BD	Documented bioequivalence problems
BE	Enteric coated oral dosage forms
BN	Product in aerosol-nebulizer delivery system
BP	Potential bioequivalence problems
BR	Suppository or enema for systemic use
BS	Testing standards are insufficient for determination
BT	Topical products with bioequivalence issues
BX	Insufficient data to confirm bioequivalence
B*	Requires further FDA investigation and review
EE	This entry has been evaluated by the FDA, but a rating is not available for this labeler's product
ZZ	FDA standard with no orange book code

Acknowledgements

Besides teaching, author also works as a community pharmacist at Harmons Grocery.

Conflict of interest

We declare that author has no conflict of interest.

References

1. FDA. Approved drug products and therapeutic equivalence evaluations. 35th ed. USA: Orange book preface, FDA; 2015.
2. Pipho RW. Therapeutic interchange and equivalence: focus on antihypertensive agents. 2015.
3. Clinical Pharmacology Important Terms. USA: Orange Book Therapeutic Equivalence.

Citation: Kale VM. FDA's orange book and ab ratings of pharmaceutical drug products: a guide to community pharmacist. MOJ Bioequiv Availab. 2015;1(3):54–55. DOI: 10.15406/mojbb.2015.01.00013