BIOAVAILABILITY AND BIOEQUIVALENCE – WHAT DO THEY MEAN?

CGPA
Making Patient Care Affordable

WHAT DOES BIOEQUIVALENCE MEAN?

All prescription drugs sold in Canada, both generic and brand-name, are reviewed and authorized for sale by Health Canada before they are available for use. A generic drug is manufactured using the same active ingredient that is in the brand-name equivalent.[1] Generic medicine is only available for prescription after the formulation has been determined to be bioequivalent and have the same effect in the body as the brand-name reference drug.[2]

WHAT ARE BIOAVAILABILITY STUDIES?

The evidence proving that a generic drug works the same way in the body is obtained through bioavailability studies.[3] They are preformed to verify that two different drug formulations with the same active ingredients, in the same amounts, will be absorbed into the body at the same rate and amount to reach the site where the drug is activated.[4] These studies are conducted to compare the efficacy of a generic drug to the reference brand-name drug.

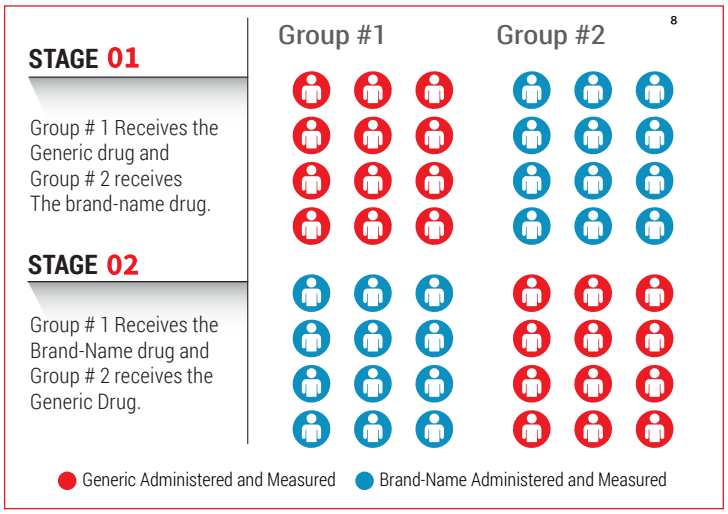
WHAT DOES BIOAVAILABILITY MEAN AND HOW ARE BIOEQUIVALENCE STUDIES CONDUCTED?

Bioavailability is a measure of the rate and extent to which therapeutically active ingredients in a drug are absorbed into the body. Bioavailability is assessed using two main variables: the concentration of the active ingredients in the blood over time; and, the maximum concentration of the active ingredient in the blood stream.[5]

The minimum number of people required for a bioequivalence study is twelve[6]; however, larger numbers are recommended and in typical bioequivalence studies between 32 and 72 people participate in the test. The individuals are separated into two groups and the study takes place in two separate stages. This is called a cross-over study design.[7]

In the first stage Group 1 is given the generic drug and Group 2 is given the brand-name drug. The drug absorption based on the blood concentration of the drug over time, the maximum observed concentration of the drug and the time it takes to reach that maximum concentration are all measured in both groups to assess and compare the bioavailability of the drugs.

At the second stage, the group that received the generic drug in stage one is given the brand-name drug, and the group that was given the brand-name drug is given the generic drug. The bioavailability of the drug in these two groups is assessed and measured in the same way as stage one. The bioavailability of the brand-name drug is then compared to that of the generic drug in each individual participating in the study. When these comparisons demonstrate a similar extent of absorption and a similar maximum drug concentration, bioequivalence is proven and the generic drug is confirmed to be as safe and effective as the brand-name version.



SCIENTIFICALLY ACCEPTABLE VARIABILITY

Every person's absorption rate of a drug is unique. No two people absorb the exact same amount of the active ingredient over the same time period, every time it is administered. Also, no one person absorbs the same amount of active ingredient every time the drug is administered to them. An individual's absorption rate can be influenced by external factors such as diet, and digestive changes. To account for these differences, health authorities have developed a concept called 'scientifically acceptable variability' which is a range within which marginal differences of absorption levels, over time and across study participants, are acceptable. This "*acceptable range of variability*" occurs when testing all drugs – both brand-name and generics.

"The bioequivalence standards we use in Canada have been in place for 20 years and are among the most rigorous in the world." [9]

— Eugenia Palylyk-Colwell, BScPharm, PhD; Member, Scientific Advisory Committee on Bioavailability and Bioequivalence, Health Canada

1. CGPA, Consumer Information Brochure, 2016
2. Ibid
3. Health Canada, [Internet] Guidance Document Conduct and Analysis of Comparitive Bioavalability Studies, p 2, Sec.4.1, 2012
4. Ibid
5. CADTH, [Internet] *What are Bioavalability and Bioequivalence*, 2016, p 1
6. Health Canada, Guidance Document Conduct and Analysis of Comparitive Bioavalability Studies, p 5, Sect 2.3.1.1
7. Ibid, p 5, Sect. 2.3.1
8. Dr. Jake J. Theissen (PhD.), The Efficacy, Safety and Quality of Generic Prescription Medicines, p 4, 2016
9. CADTH, [Internet] *What are Bioavalability and Bioequivalence*, 2016, p 1

Canadian Generic Pharmaceutical Association
4100 Yonge Street, Suite 501, Toronto (ON) Canada M2P 2B5