Bioequivalence and generic medicinal products: The levothyroxine case

Teresa Torres Moral, Universitat Autònoma de Barcelona
Mentor: Nuria Maria Vivas Sabido

Introduction

Levothyroxine

Levothyroxine is a levoisomer of the thyroid hormone thyroxine, prescribed in many cases of hypothyroidism. It is metabolized in Thyroxine when ingested and has the same effects as the endogenous hormone. Thyroxine (also known as T4) is synthesized in the thyroid gland and becomes triiodothyronine (also known as T3) when leaving the gland. T3 is a molecule with a shorter average life but with more biological activity. This hormone is governed by the hypothalamic-pituitary-thyroid system and its synthesis inhibits other hormones as TSH and TRH. The regulation is represented in figure 3.

Definitions:

BIOEQUIVALENCE

‘Two medicinal products are bioequivalent if they are pharmaceutically equivalent or pharmacologically active and if their bioavailabilities after administration in the same dose are similar to such degree that their effects with respect to both, efficacy and safety, will be essentially the same.

GNERIC MEDICINAL PRODUCT

‘Medicinal product which has the same qualitative and quantitative composition in active substances and the same pharmaceutical form as the reference medicinal product, and whose bioequivalence with the reference medicinal product has been demonstrated by appropriate bioavailability studies. The different salts, esters, ethers, mixtures of isomers, complexes or derivatives of an active substance must be supplied by the applicant. The various immediate-release oral pharmaceutical forms shall be considered to be one and the same pharmaceutical product, if the various immediate-release oral pharmaceutical forms shall be considered to be one and the same pharmaceutical product.

Bioequivalence studies

Bioequivalence studies vary depending on the type of drugs, and on some occasions they are not necessary. However, most of them have the following characteristics.

CHARACTERISTICS

Randomized block: They use a systematic and replicable procedure, in which the participants are distributed randomly in different treatment groups.

Crossover: Both, the treatment and the control are administered to the patient in randomly successive periods, which allows each participant his own control.

In two periods: Two doses are taken, separating the two periods.

Double blind: Both, the patient and the researcher ignore whether the patient is having the treatment or the control.

PARAMETERS

AUC

It’s the area under the curve in the graph of drug concentration versus time. This gives information about the total quantity of active substances that reaches the bloodstream, that is, the absorption rate.

Cmax

It’s the highest concentration in blood acquired. It gives information about efficacy.

Tmax

It’s the time needed to reach Cmax. It gives information about absorption velocity.

ANALYSIS OF RESULTS

The values of each patient are logarithmically transformed so as to compare the average values of generic and reference drugs. The quotient between these medicines must be within the limits 80-125%, because they have been logarithmically transformed, and with these percentages they are within a range of symmetric acceptance in logarithmic scale.