GMiA Generic Medicines Industry Association Pty Ltd

Making medicines affordable

FACT SHEET

CHOOSING GENERIC MEDICINES

What is a generic medicine?

A generic medicine contains the same active ingredient as another product but may be marketed under a different brand name.

A generic medicine is equivalent to the original medicine in dosage form, safety, strength, route of administration, quality, performance characteristics and intended use.[i]

Generic medicines meet the same standards as the original brand

Generic medicines must meet strict Australian standards, including the same quality criteria and manufacturing standards as the original medicine.

Before they can be sold in Australia, generic medicines are independently assessed by government, through the TGA to ensure they contain the same active ingredient, in the same dose and deliver the active ingredient in the body in the same way as the original brand.[ii]

Do generic medicines deliver the same effect in the body?

A generic medicine can only qualify for market authorisation if it is accepted as equivalent to the originator product, that is, it must work in the same way in the patient's body.

Equivalence can be established in two ways:

- By directly measuring the safety and efficacy response to a generic medicine compared to the original in a clinical trial. This is termed therapeutic equivalence.
- By measuring the amount of medicine in the blood following administration of the generic or original medicine in a clinical trial. This is termed bioequivalence.

Based on established scientific principles and over long experience, demonstrating bioequivalence also establishes therapeutic equivalence.

What is bioequivalence?

Bioavailability is a measurement of the rate and extent that the active medicine reaches the systemic circulation and is therefore available at the site of therapeutic action. If two medicines are bioequivalent, there is no clinically significant difference in their bioavailability.[iii] Using bioequivalence to measure the effect in the body of two medicines is accepted internationally and supported by rigorous scientific evidence.

Are generic medicines as effective as the original medicine?

YES

A generic medicine is equivalent to the original medicine in dosage, safety, strength, quality, the way it works, the way it is taken and the way it should be used. [i]

The Therapeutic Goods Administration (TGA) requires that generic medicines meet the same quality criteria and manufacturing and performance standards as the original medicine. [ii]

Generic medicines must be equivalent to the original medicine and the two medicines therefore work in the same way. A review of 38 clinical trials comparing the effect of generic and original cardiovascular medicines found no evidence that original medicines were more effective than generic medicines.[iv]

Before the government will allow a generic medicine onto the Australian market, evidence of bioequivalence must be thoroughly evaluated by the TGA. That is, the generic medicine must reach the systemic circulation and be available at the site of therapeutic action at the same rate as the original medicine.

Other ingredients in medicines

The formulation of a medicine will contain the active ingredient(s) as well as other inactive ingredients, called excipients. Generic medicines can have inactive ingredients that may be different from those in the original medicine. These must also meet the TGA's quality and safety criteria. The current Handbook of Pharmaceutical Excipients list is limited to 91 inactive ingredients that may be used in tablets.

In addition, the type of inactive ingredients used in a generic medicine must be very carefully chosen so that the medicine continues to meet the bioequivalency test.

Patients are advised to seek the advice of their doctor or pharmacist on issues related to their medication.

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Can a generic medicine work differently?

One valid concern in relation to generic medicines is that individual patients could have idiosyncratic sensitivity to specific excipients. This can occur but is very rare and is not a problem limited to generic medicines. Remember that all excipients approved for use in medicines must have acceptable standards of quality and safety, and consequently a low probability of causing harm. Changes of excipients in the original medicine can cause similar outcomes.[v]

Why do some generic medicines look different from brand drugs?

Sometimes generic medicines may look different from the original medicine. Don't be fooled by appearances. Although the shape, colour or taste may differ, they are just as safe and effective. Differences in appearance may be due to reasons such as trademark regulation, or simply to take advantage of newer excipients.

Which medicines should not be substituted?

If a medicine is listed as equivalent to another brand on the Pharmaceutical Benefits Scheme, it is expected that these brands may be interchanged without differences in clinical effect.[vi]

Medicines should not be substituted if the "*brand substitution not allowed*" box on the prescription is ticked.

Medicines that are not equivalent should not be substituted for each other.

There has been considerable debate regarding the bioequivalence of medicines for which a small change in blood drug concentration leads to significant change in therapeutic response or toxicity, that is, medicines with a narrow therapeutic index.

In Australia, bioequivalence principles and criteria equally apply to medicines with a narrow therapeutic index.[vii]

Why do generic medicines cost less?

Generic medicines are less expensive than the original medicine because the generic medicine manufacturers do not face the as high research and investment costs of the company manufacturing the original medicine AND spend far less on sales, advertising and promotion. The associated savings are substantial and are passed along to you in lower prices.

Generic medicines are NOT less expensive than original medicines because they have inferior ingredients, contain or deliver less active medicine or are manufactured to lesser standards. In fact, the costs of ingredients and manufacturing are typically similar for original and generic medicines.

Increased use of generic medicines stimulates price competition among manufacturers and lowers the price to the purchaser, that is, to the healthcare system and to the consumer.

Generic medicines are a smart choice that drive savings

Every time a consumer chooses a generic medicine there are substantial benefits to national savings. Sometimes there are also direct savings for the consumer. Generic medicines can ease the cost of living by providing consumers access to more affordable, high quality medicine.

Bioequivalency studies

The standard method of measuring bioequivalence accepted by the TGA and regulators in other countries is a clinical study with a cross-over design. The method involves healthy volunteers (or patients) receiving the original or generic product on separate occasion and then comparing the rate and extent of absorption by measuring:

- the time taken for maximum plasma concentration (T_{max})
- the maximum plasma concentration (C_{max})
- the area under the plasma concentration–time curve (AUC)

The generic:original product ratios and 90% confidence intervals (CI) are calculated for each parameter. Two products are considered bioequivalent if the 90% CIs around the ratio point estimates fall within specified limits (0.8 to 1.25).[viii]

The 90% CI of 0.8-1.25 is a numerical index and not a direct measure of the difference in systemic concentrations of the active ingredient resulting from administration of the two products. It does NOT mean that the C_{max} and AUC ratios estimated for each formulation can vary by -20 to +25%.

The robustness of this standard has been evaluated in a US Food and Drug Administration review which found the average difference in C_{max} and AUC ratios for generic and original products was 4.57% and 3.17%, respectively.[x]

This amount of difference would be expected and acceptable, whether for one batch of an original medicine tested against another batch of the same original medicine, or for a generic medicine tested against the original medicine. As a rule, the difference for the generic-to-original comparison was about the same as the original-to-original comparison.[ix]

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