Generic Medicines in Australia

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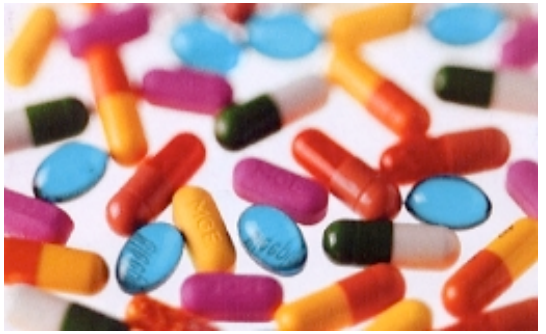


The aim of this presentation

- Overview of medicines policy and regulation in Australia
- Generic medicines in the Australia market
  - implications for sustainability of subsidized access to medicines
- Bioequivalence testing and its implication for generic medicines

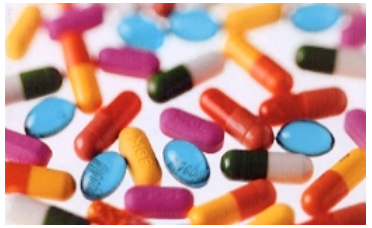
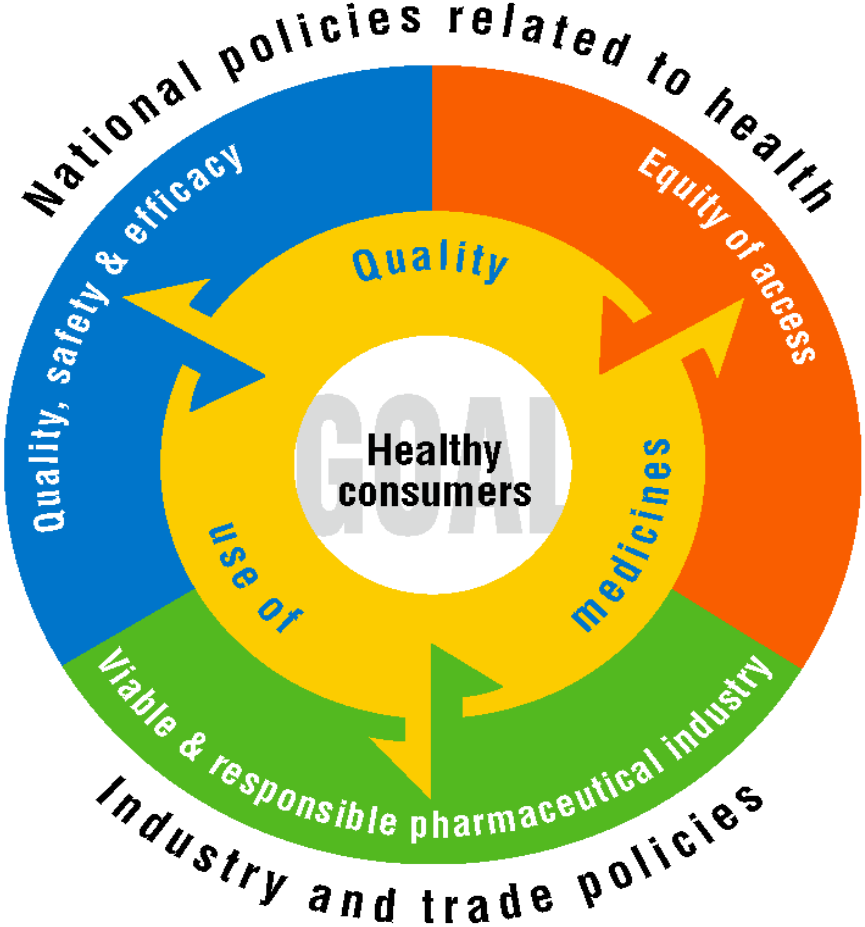


Photo: Tourism Australia

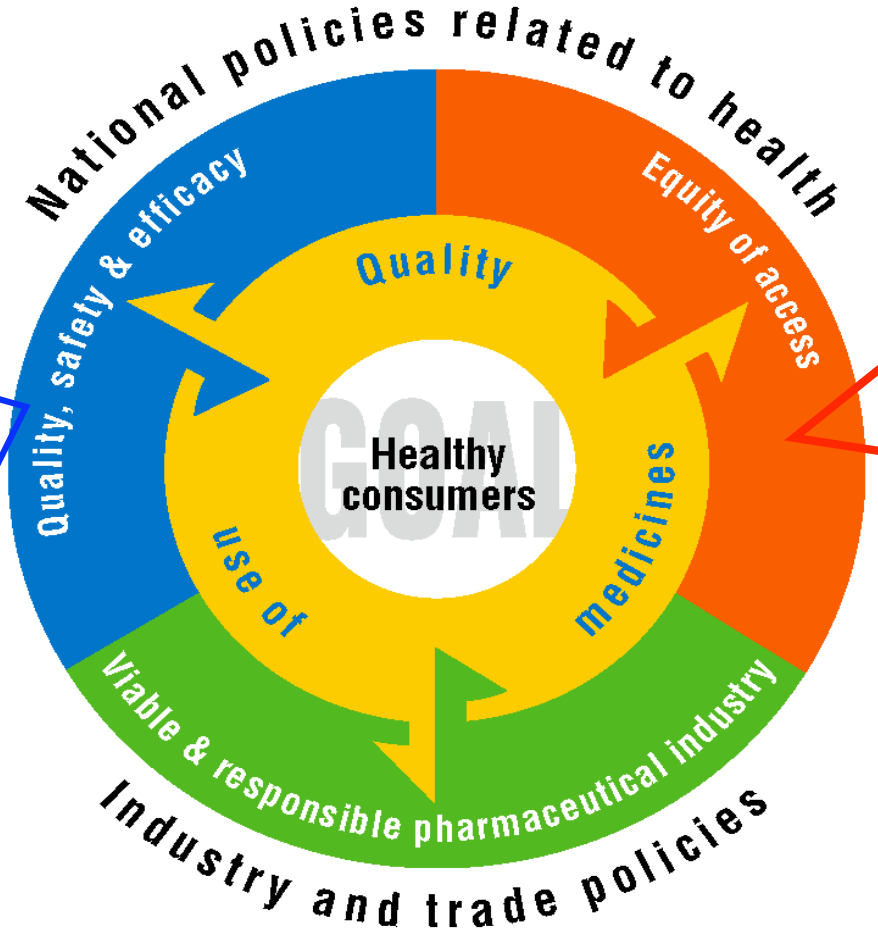
Australian's National Medicines Policy



"Better health through quality use of medicines"

Australian's National Medicines Policy

Therapeutic Goods Administration (TGA)
Evaluates and approves the use of medicines based on evidence of quality, safety and efficacy



Pharmaceutical Benefits Scheme (PBS)
Provide access to medicines based on evidence of cost-effectiveness

"Better health through quality use of medicines"

QUALITY USE OF MEDICINES

- **Quality Use of Medicines** is defined as:
  - selecting management options wisely;
  - choosing suitable medicines if a medicine is considered necessary; and
  - using medicines safely and effectively.

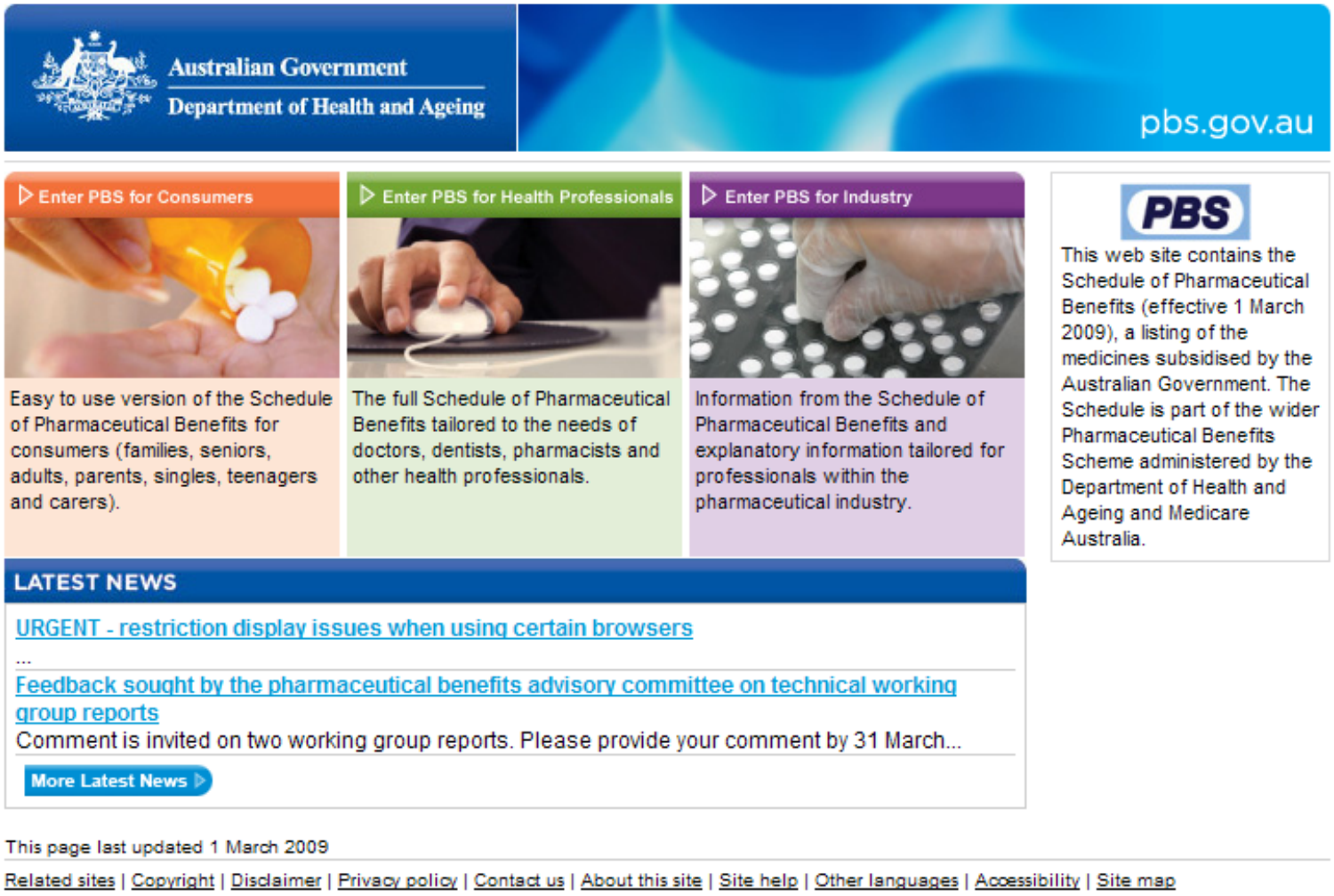
"Better health through quality use of medicines"

Pharmaceutical Benefits Scheme (PBS)

- provides reliable, timely and affordable access to a wide range of medicines for all Australians.
- only medicines approved by the TGA
- requires evidence of cost-effectiveness
- subsidized access – with co-payment
  - up to $AUS 32.90 (January 2009)
  - $AUS 5.30 (concession card holder)
  - Government pays the remaining medicines cost

www.pbs.gov.au

Pharmaceutical Benefits Scheme (PBS)



www.pbs.gov.au

Generic medicines in Australia

Generic medicine products have the

- same qualitative and quantitative composition in terms of active ingredients
- Same pharmaceutical form (eg tablet)
- Same bioavailability (related to rate and extent of absorption – established in a bioequivalence study)

Australian guidelines for the registration of drugs / Therapeutic Goods Administration, Commonwealth Department of Human Services and Health 1994

- May include products marketed under a different brand (so called “Authorised” generic medicines)

Generic medicines in Australia

- Available in Australian since the 1950s
- Widely used in hospitals by competitive tendering
  - generic products supplied at a lower cost
- Community competition increased in 1990s
- Supported by government policies
- Opportunity to slow increasing growth in health expenditure

Hassali MA, Stewart K, Kong DC. Ultilisation of generic medicines in the Australian healthcare system *J Generic Medicines* 2004

Australia Government Policies to support generic medicines

Brand Premium Policy

- Government funds a base price for medicines
- Originator brand may attract a **price premium** paid by the patient

Brand Substitution Policy

- Pharmacists (with patient consent) may **switch** branded and generic medicines where they are proved to **bioequivalent**

Therapeutic Group Premium

- Medicines are grouped together (based on their therapeutic effects at a population level)
- Price is set by the lowest priced medicine in the group

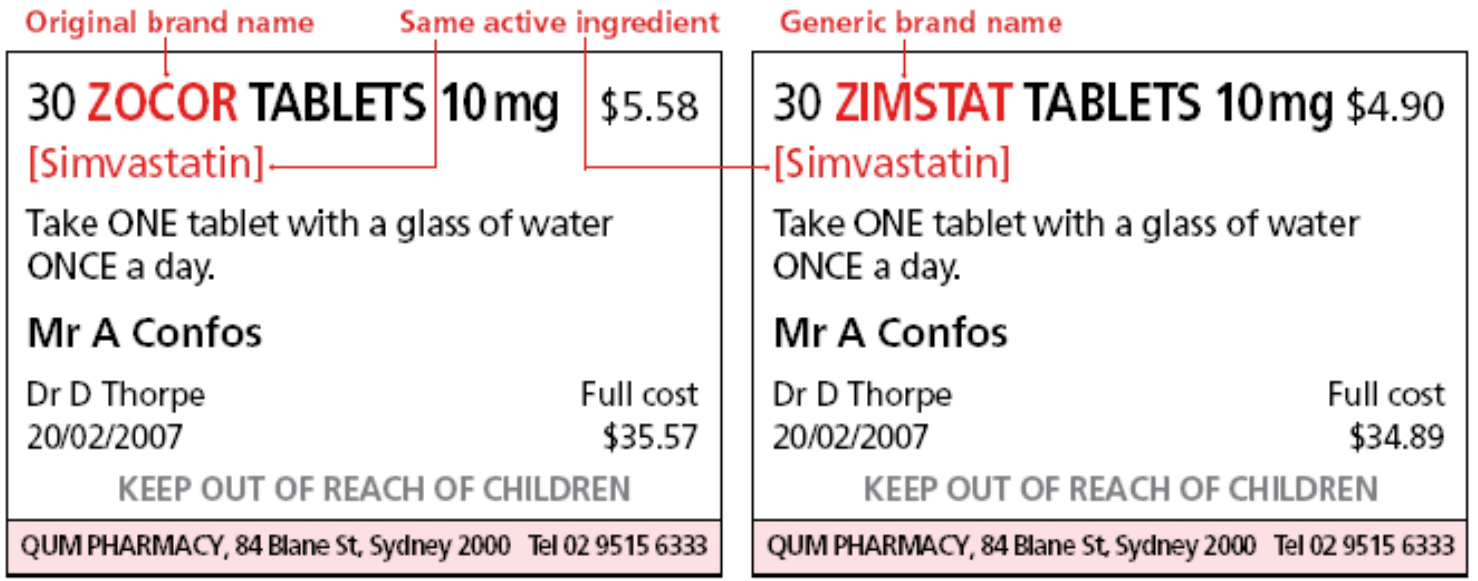
Hassali MA, Stewart K, Kong DC. Ultilisation of generic medicines in the Australian healthcare system *J Generic Medicines* 2004

Generic medicines in Australia

- 40% of PBS subsidized prescriptions are for a generic medicine (approximately 30% of the cost)
- 20% of the generic medicines on the Australian market are “authorized generic medicine products”
  - Identical to originator pharmaceutical product but are labeled and sold by the generic medicines manufacturer
- Many major pharmaceutical companies also have a commercial subsidiary that markets generic medicines (eg Novartis and Sandoz)

Generic Medicines Industry Association
http://www.gmia.com.au/

Finding the name of the active ingredient on the pharmacy label



This diagram shows the pharmacy labels of two brands of the cholesterol-lowering medicine simvastatin. The left-hand one is the original brand Zocor, and the right-hand one is one of the generic versions with the brand name Zimstat. In this example, the patient Mr Confos is a concession card holder. He pays $5.58 for the original brand Zocor, including a brand premium of $0.68, or $4.90 for the generic brand Zimstat.

ZOCOR – originator medicine with a Brand Premium
ZIMSTAT – generic medicine

PROVEN to be **BIOEQUIVALENT**
EXACT **SAME QUALITY** STANDARDS APPLY

Medicine Talk, Autumn 2007

Generic medicines in Australia

"Have delivered savings to the PBS through generic price reductions of substantially over $AUS 3 billion to date"

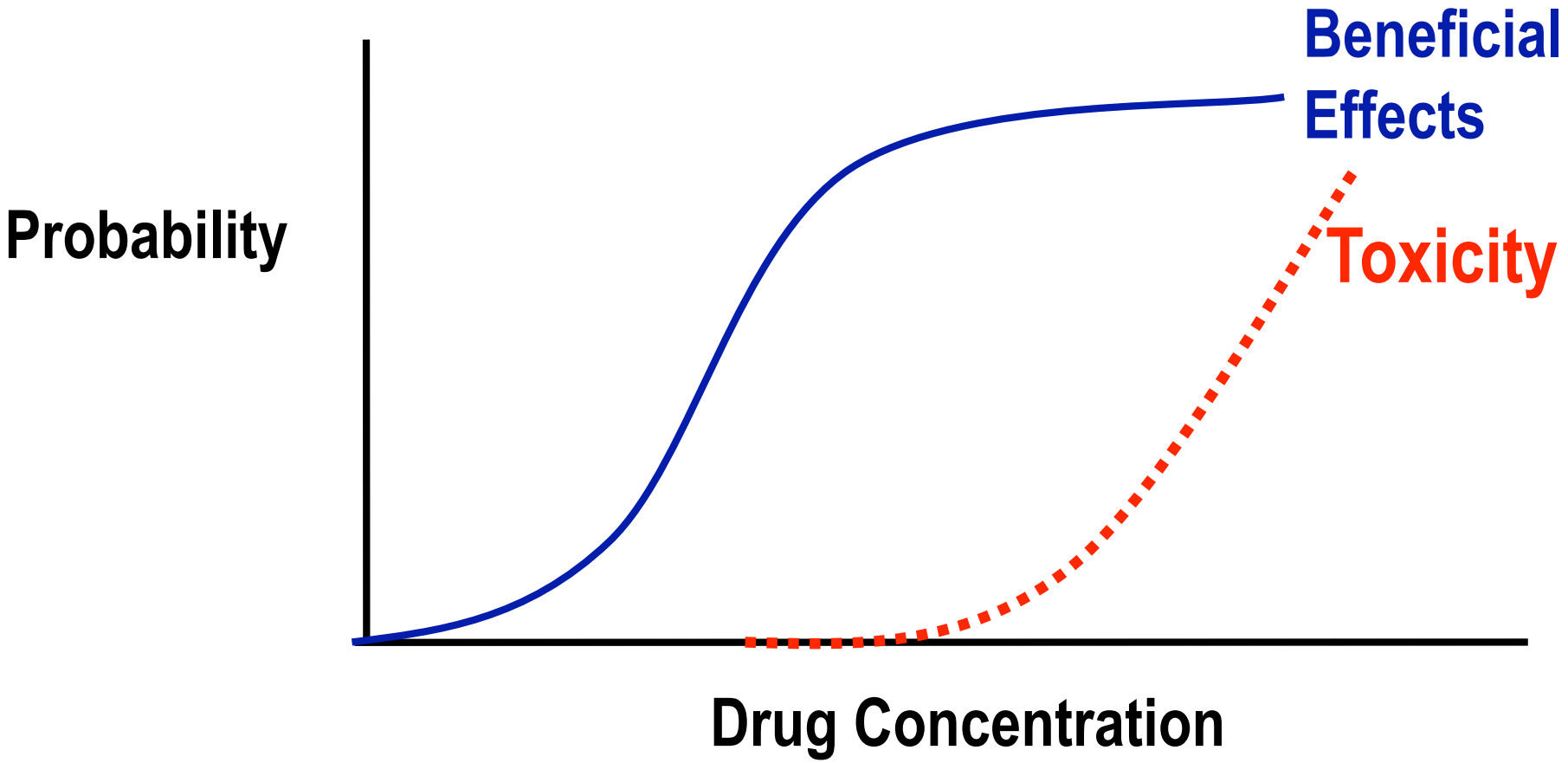
Date from 2008
Generic Medicines Industry Association
http://www.gmia.com.au/

Bioequivalence

- Pharmacological basis of drug response

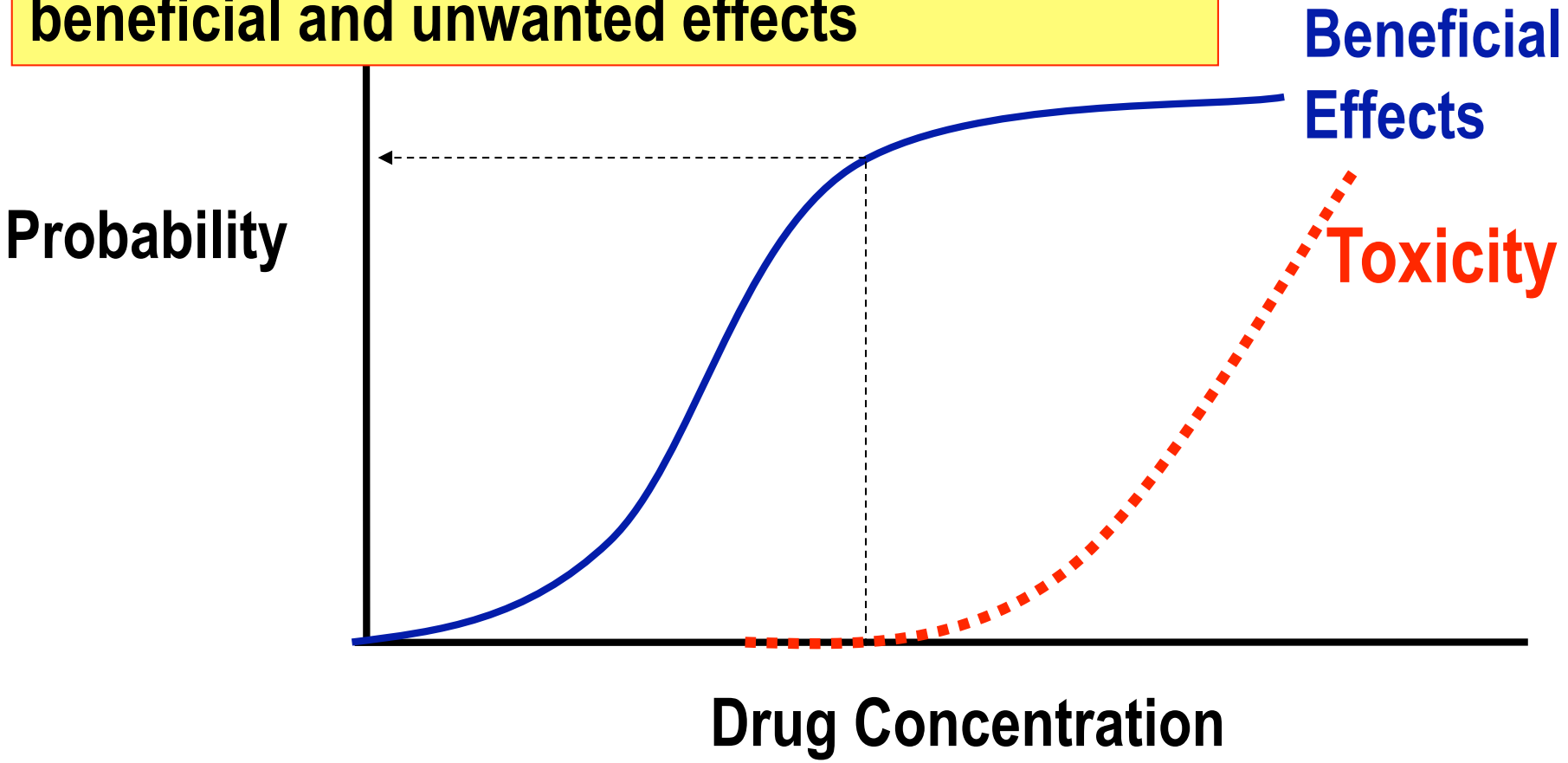
- Key principle in drug development and regulation of originator and generic medicine products

Concentration-effect relationship



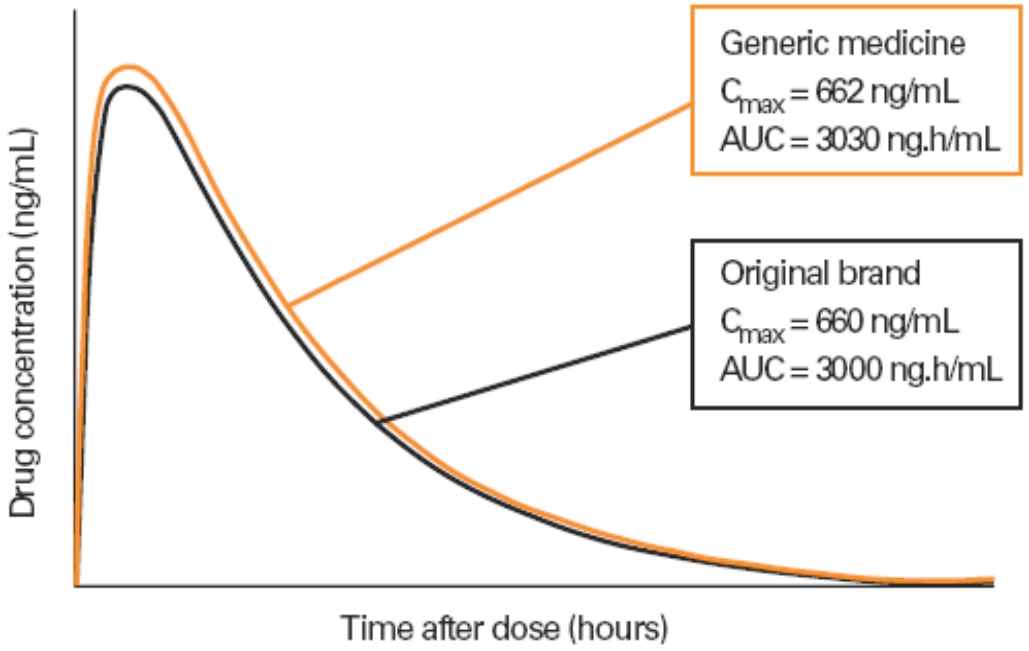
Concentration-effect relationship

A medicine product that achieves the **same concentration** in the body will lead to the **same beneficial and unwanted effects**



Bioequivalence analysis – a hypothetical bioequivalence study

Mean concentration–time curves for two brands of a drug after single oral doses



The original brand:generic medicine ratio for AUC is 0.99 (90% CI 0.91 to 1.04) and for C_{max} is 0.99 (90% CI 0.92 to 1.07).

C_{max}	peak plasma concentration
AUC	area under the concentration–time curve
CI	confidence interval

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Bioequivalence studies

- **use healthy subjects**
- **cross-over design**

Cmax -

A measure of absorption rate

AUC –

A measure of the extent of drug absorption

http://www.australianprescriber.com/upload/pdf/articles/873.pdf

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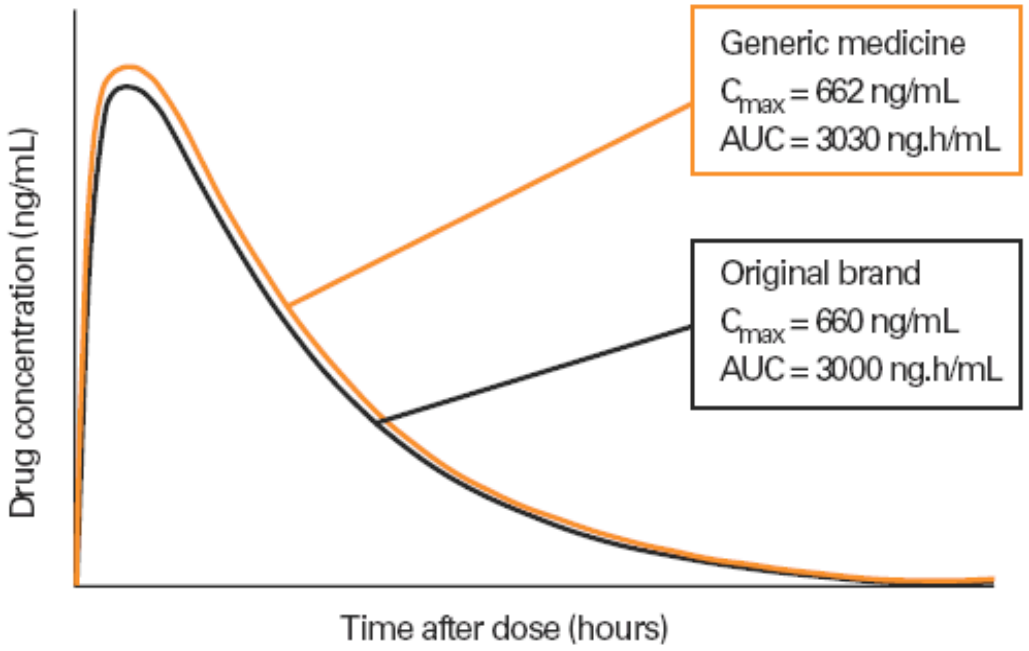

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C_{max}	peak plasma concentration
AUC	area under the concentration–time curve
CI	confidence interval

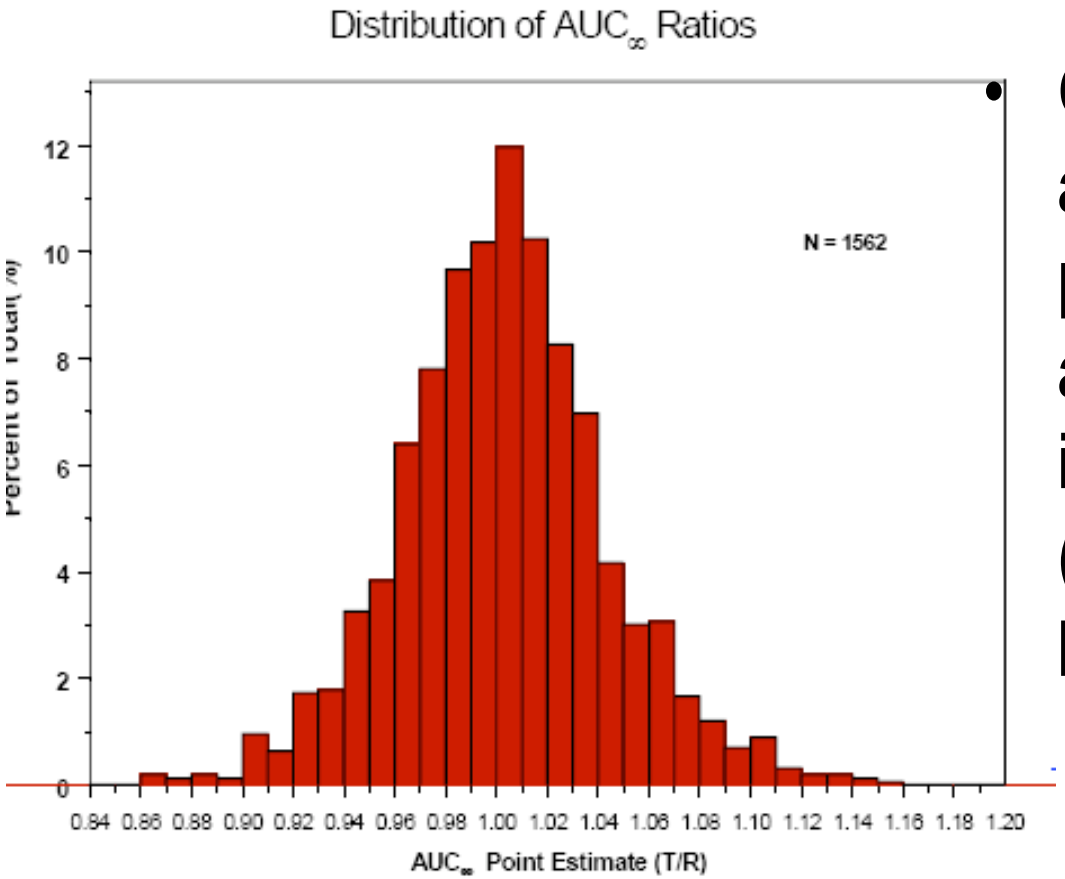
Reprinted with permission from NPS News 2006;44:3.

Bioequivalence compares the 90% confident interval of Cmax and AUC

This must conform with strict statistical limits within
0.80 to 1.25

http://www.australianprescriber.com/upload/pdf/articles/873.pdf

How different can AUC be for bioequivalent medicines?



Generic drug products approved over the 10-year period differed by an average of **less than 4%** in extent of absorption (AUC) relative to their branded comparator

Analysis of 1636 crossover fasting BE studies from approved ANDAs (1996-2005)

Haidar SH et al, A Review of ANDAs Approved 1996 – 2005 Reveals Small Differences in Bioavailability for BCS Class I and Other Generic Drug Products Relative to the Brand Name Equivalents
AAPS conference 2006 San Antonio

Bioequivalence principle

- Used by *Australia* (and USA and Europe) to approve the marketing of thousands of generic medicine products

- For some dose forms, *in vivo* studies may be waived and market access is granted based on *in vitro* studies

- Large amount of empirical and safety evidence suggests that generic medicines are used regularly without problems of safety or efficacy

Lawrence J. Lesko, Advisory Committee for Pharmaceutical Science
Rockville, Maryland, November 29, 2001

Bioequivalence is the foundation on which Australia's generic medicines industry is built

Avoiding patient confusion when using medicines

- Patients should be encouraged to know and record the name of the active ingredient in the medicine
- Patients should understand that the same medicine may be available in different brands
- active ingredient in the product should be displayed with greater or equal prominence to the brand name

MedicinesTalk

Information for consumers and consumer groups about using medicines wisely

Autumn 2007
No. 21

Generic medicines explained

When a pharmaceutical company first develops a new medicine, it takes out a patent to ensure that no other company may make and sell the medicine. It is only after the patent has expired that other companies may make copies of it. These copies are known as generic medicines.

Generic medicines are now more widely available than previously, because the patents of many medicines have expired recently.

Same active ingredient, different brand names

Prescription medicines have two names. The first is the name of the active ingredient. The second is the brand name. The active ingredient is the chemical that makes the medicine work as intended.

When a company produces a new medicine, it gives the active ingredient a name. It also gives the medicine a brand name, which is the name the company uses when promoting and selling the medicine.

When a company produces a generic version of a medicine, it gives the generic version a different brand name. However, the medicine always contains the same active ingredient as the original medicine.

For example, simvastatin is the active ingredient of a commonly used cholesterol-lowering medicine that was first sold under the brand name of Zocor, and is now available under many other brand names, including Lipex, Simvar 10, Simvastatin-DP, Terry White Simvastatin and Zimstat.

Different inactive ingredients

Medicines also contain inactive ingredients. For example, these ingredients hold tablets together, cont >

It is important to help patients understand that generic medicines have the same quality as originator branded medicines

Conclusions

- Generic medicines in Australia provide a considerable cost saving without compromising quality, safety and efficacy of medicines
- Bioequivalence is a well stabled principle for testing and approving generic and originator medicines
- Clear communication is needed to ensure patients do not confuse generic and originator medicines

Frequently asked questions about generic medicines

Andrew J McLachlan, Professor of Pharmacy (Aged Care), Centre for Education and Research on Ageing, Concord Repatriation General Hospital and Faculty of Pharmacy, University of Sydney; Iqbal Ramzan, Professor of Pharmaceutics, Faculty of Pharmacy, University of Sydney; and Robert W Milne, Associate Professor, Sansom Institute, School of Pharmacy and Medical Sciences, University of South Australia, Adelaide

Summary

In Australia, generic products must be bioequivalent to the innovator brand name product, or the market leader, before they are approved. Australia has rigorous scientifically-based evaluation procedures for generic medicines based on the internationally accepted principle of bioequivalence. Under the Pharmaceutical Benefits Scheme, generic substitution is only permitted if two products are bioequivalent. Consumers should be encouraged to know and record the name of the active ingredient in the medicines they are receiving to avoid confusion between different brands of medicines. Healthcare professionals have a key role in helping consumers understand any real or perceived differences (or lack thereof) between different brands of medicines. Prescribing generics helps to contain health costs.

Key words: bioequivalence, pharmacokinetics.

(Aust Prescr 2007;30:41–3)

Bioequivalence is then determined by comparing the peak plasma concentration (C_{max}), time to achieve a maximal concentration (T_{max}) and the extent of absorption (area under the concentration-time curve, AUC) of the products (Fig. 1).

These studies are well suited to identifying potentially significant differences in the delivery characteristics of the active substance of different products. The same bioequivalence principles apply to new drugs when different formulations of an active ingredient are compared.

Bioequivalent products are marked with a superscript a or b in the Schedule of Pharmaceutical Benefits.[5]

Is bioequivalence clinically important?

Yes, only those products that have been **proven to be bioequivalent** should be used interchangeably. On **scientific** grounds there is no reason to be concerned about substituting a generic product for a branded product that is flagged as being bioequivalent.[5]

Fig. 1

Bioequivalence analysis – a hypothetical bioequivalence study

Mean concentration–time curves for two brands of a drug after single oral doses