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Inside ▸

Generic medicines: dealing with multiple brands

More often, consumers are being presented with the choice of a generic medicine because of increases in the number of generic medicines available, increased awareness about generic medicines and government strategies to enhance uptake. Generic medicines help spread the healthcare dollar, but some health professionals and consumers have reservations about using them. This *NPS News* considers some of the issues around generic medicines and brand substitution, and how health professionals can help consumers use generic medicines safely and appropriately.

Generic medicines are bioequivalent

"I don't prescribe generic medicines because I don't believe that they're all equivalent …" [GP][1]

"One can't help but wonder whether you are getting an inferior medication with generics" [Consumer][2]

Two products are considered bioequivalent when they produce similar plasma concentrations of the same active ingredient. Bioequivalence is usually assessed in healthy volunteers by administering the two products on separate occasions. The peak plasma concentration (C_{max}) and the extent of absorption (area under the concentration–time curve, AUC) of the generic medicine and the original brand are compared. To be bioequivalent, the 90% confidence intervals (CI) for the ratio of each pharmacokinetic variable must lie between 0.80 and 1.25. This is a numerical index that provides an indication of the certainty of the study results. It does not mean that the C_{max} and AUC ratios can vary by –20 to +25%.[3] In practice, the differences in the pharmacokinetic variables of the two products would have to be less than 10% to satisfy the 90% CI bioequivalence requirement.[3] The amount of active ingredient in the systemic circulation (bioavailability) is taken as a measure of the product's clinical efficacy.[4]

Bioequivalence between the original brand and the generic version of a medicine is the fundamental basis of generic substitution. However, in a survey of Australian GPs (N = 785) 27% believed that generic medicines are not always as effective as branded medicines and 30% were undecided about their bioequivalence.[5] Although there may be exceptions (e.g. medicines with narrow therapeutic indices), this lack of confidence in generic medicines is largely unfounded physiologically. For a generic medicine to be listed on the Pharmaceutical Benefits Scheme (PBS), a manufacturer/supplier must demonstrate that their product is bioequivalent to the original brand available in Australia.[6] Generic medicines must also adhere to the same quality of manufacturing codes as branded medicines.[7]

Inactive ingredients (e.g. binders and fillers) may differ between bioequivalent products. However, adverse reactions to inactive ingredients are rare.

Practical tip: Bioequivalent medicines are marked with the letter 'a' or 'b' on the Schedule of Pharmaceutical Benefits (see Figure 1, over).

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Education minimises confusion

The most common concern with brand substitution, shared by GPs and pharmacists alike, is consumer confusion — particularly among the elderly.[5,8,9] The concern is that confusion may lead to double dosing or reduced adherence.[10] Confusion can also arise when consumers receive a generic medicine in hospital or when travelling.

Practical tips to reduce potential confusion

Teach consumers how to identify the active ingredient in their medicines. Advise them that the packaging and appearance of the medicine may look different, but they contain the same active ingredient.

Be consistent in the selection of brands for consumers on long-term therapy (see Prescibing software tips).

Encourage the use of a **medicines list** (available at http://www.nps.org.au/resources/content/medicines_list.pdf; also see Prescibing software tips). This should record both brand and active ingredient names.

Arrange **periodic medication reviews** and Home Medicine Reviews to ensure the correct medicines are being taken.

In the pharmacy

Pharmacists can use Label 15, which states *"This medicine replaces … Do not use both"*, on the container whenever the brand is changed. Explain to the consumer when a medicine is being replaced with an alternative brand and draw their attention to Label 15. Advise them not to start the new pack until they have finished the previous pack.

Pharmacists should also explain any differences in appearance or form (e.g. colour, tablet vs capsule) and ensure the active ingredients appear prominently on pharmacy labels.

Pharmacy assistants should be educated about potential consumer confusion (particularly in the elderly) and how to avoid it (see Counter Connections, *inPHARMation* 2007;11(8): December special edition).

The pharmacy should also implement a brand substitution policy that should consider:

- when brand substitution will be offered
- obtaining consumer consent
- recording consumer brand substitution preferences
- brand consistency
- addressing consumer requests for brand substitution that go against the stated intention of the prescriber.[11]

An additional concern for some GPs is the possibility that multiple generic brands may be substituted during the life of a prescription.[12] A recent study of 533,279 prescriptions for 8 medicines for chronic conditions commonly dispensed on the Repatriation Pharmaceutical Benefits Scheme (RPBS) found that substitution occurred in only 7% of cases and only 1% had more than one substitution.[13] The findings of this study may not directly apply to the general population or for all types of medicines. However, it suggests that pharmacists are generally consistent in the selection of brands for consumers on long-term therapy, in accordance with their professional code.[13,14]

GPs can influence consumer choice

"I believe in sticking to what I've been prescribed before. I know the doctor and I feel safe with his choice of medication." [Consumer][15]

Health professionals, especially GPs, can have a strong influence on consumer acceptance of generic medicines. In a consumer survey (n = 310), 50% indicated they would not use a generic medicine without checking with their GP despite agreeing that the generic medicine contained the same ingredients as the branded medicine.[16]

Practical tip when prescribing

When brand substitution is acceptable to you as a prescriber, advise your patients of this. A brief mention that a generic brand might be offered by the pharmacy may be enough reassurance. (Leaving the 'Brand substitution not permitted' box blank may not be sufficient assurance for some consumers.)

Prescribing software tips

Prescribe using the active ingredient of a medicine to indicate that brand substitution is acceptable. Most prescribing software packages allow this.

To prescribe a generic brand*, enter the brand or generic name of a medicine. A list of alternative brands can then be viewed in the following programs by taking the steps shown below.

- *Medical Director:* click on the 'Brands' button. (Note: brands that are not registered as bioequivalent may also appear in the list).
- *Best Practice:* click on the 'Equivalent products' button. (Note: brands that are not registered as bioequivalent may also appear in the list).
- *Practix:* click on the 'Equivalences' button.

Prescriptions for **acute conditions**: Set up a 'favourites' list and populate the list with generic brands of medicines that are prescribed frequently. A well organised list saves time, permits consistent generic prescribing and reduces the risk of typing errors.

Prescriptions for **chronic conditions**: Set up an individual's current medicines list with generic medicines (when appropriate). This will be available indefinitely with no extra effort during subsequent consultations.

All programs allow an individual's **current medicines list** to be printed out.

* Although pharmacies are unlikely to stock all generic brands of a medicine, prescribing with a generic name or active ingredient will help indicate that brand substitution is acceptable.

Figure 1: Online PBS Schedule for health professionals (www.pbs.gov.au).

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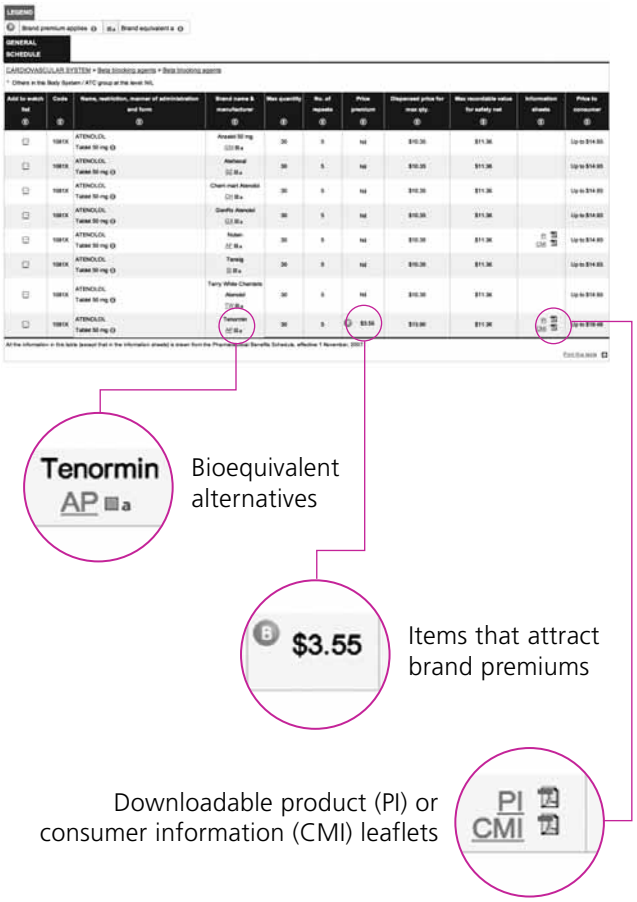

Pharmacists' role

A survey of 443 consumers taking medicines for chronic conditions showed that 79% trusted pharmacists' recommendations. Pharmacists play an important role in educating consumers about the efficacy and safety of generic medicines. Acceptance of generic medicines has been shown to be influenced by satisfaction with the communication and quality of information consumers receive from health professionals.[17,18]

Practical tips

Assess whether the patient is likely to be confused by a generic brand (see *When is brand substitution not appropriate?*).

Provide the same generic brand whenever possible.[14]

Explain to consumers that:

- The generic medicine contains the equivalent dose of the same active ingredient as the branded medicine and is thus expected to be equally effective.
- Generic medicines have the same active ingredients and thus the same adverse effects as branded medicines.
- Inactive ingredients rarely cause adverse events but to seek medical advice if they experience any unexpected adverse events after substitution.
- Generic medicines must meet strict Australian standards, including the same manufacturing requirements, as branded medicines.

Affordability of generic medicines

"It's more based on cost factors because, you know, I have a lot of medication, so I'm trying to reduce my medication cost." [Consumer][15]

For the individual

A consumer's ability to pay for medicines can influence adherence.[10,19] Using generic medicines is one way consumers can minimise the cost of their medicines, particularly if they are using multiple medications for chronic conditions.

For the community

Extensive reforms were introduced to the PBS from 1 August 2007. The main aim of the reforms is to encourage competition within the medicines industry and thereby enable the PBS to get the most value for money.[20] Paying less for medicines that no longer have a patent allows the government to subsidise newer, more expensive medicines on the PBS (e.g. rituximab: $2309 for a 500 mg vial).

There are financial considerations for pharmacists associated with dispensing and supplying generic medicines. A payment of $1.50 per generic prescription will compensate pharmacists (from 1 August 2008) under the new PBS arrangements. However, the guiding principle in any brand substitution decision, as endorsed by the Pharmaceutical Society of Australia, is that the consumer's health should always be the pharmacist's prime consideration and that brand substitution should not place consumers at risk.[14]

How much can consumers save?

Brand premiums that are passed on to consumers who purchase the original brand of some medicines range from $0.06 to $79.46.[21] Most brand premiums are between $1.00 and $4.00, with an average of $2.76.[21]

Note: Not all generic medicines are necessarily cheaper than the original brand.

When is brand substitution not appropriate?

- Consumers with **clinically significant intolerances** to inactive ingredients included in the generic medicine (e.g. lactose, gluten, colours). Inactive ingredients may also be important for those who observe particular religious or cultural practices. Ingredients are listed at the end of the consumer medicine information (CMI) and at the beginning of the product information (PI) for each medicine.
- Consumers who are more **likely to become confused** (e.g. cognitive or vision impairment, non-English speaking background).
- **Critical dose** or narrow therapeutic index medicines (i.e. medicines for which relatively small variations in plasma concentrations can cause significant adverse effects or loss of efficacy). Examples include cyclosporin, digoxin and warfarin.
- Conditions in which **negative perceptions/attitudes** to substitution can impact on treatment adherence or response (e.g. people with mental illnesses).

Useful Resources

Schedule of Pharmaceutical Benefits (www.pbs.gov.au) – *online version for health professionals shows approximate price for consumers of all available brands and indicates whether brand premiums apply. CMIs and PIs are also available for some medicines.*

Counter Connections, *inPHARMation* 2007; 11(8): December special edition – *pharmacy assistants module, addresses how pharmacy assistants can help consumers avoid confusion.*

Medicines Talk: Generic medicines explained. August 2007. (Go to www.nps.org.au/consumers) – *contains examples of pharmacy labels for branded and generic medicines.*

Fact Sheet: Generic medicines. July 2007. (www.nps.org.au/consumers)

Consumer medicine information leaflets (www.nps.org.au/consumers)

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References available online at www.nps.org.au/healthpro

The information contained in this material is derived from a critical analysis of a wide range of authoritative evidence. Any treatment decisions based on this information should be made in the context of the clinical circumstances of each patient.

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