Pharmacists' responsibility and potential liability regarding generic substitution

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Abstract: The generic medicines market in Australia is continuously growing and there is a push by the government towards generic substitution. However, generic dispensing places additional time constraints on pharmacists. There is also an increased need for professional judgement, and hence increased risk of error. Generic dispensing consequently places an increased responsibility on pharmacists, with a subsequent increased practice and liability risk. It is therefore important that pharmacists implement good practice standards and guidelines in order to manage their liability with regard to generic dispensing in both community and hospital pharmacy practice.

Keywords: Generic Medicine; Generic Substitution; Australia; Bioequivalence; Community Pharmacy

1. INTRODUCTION

The number of generic medicines in Australia is growing, as is the case internationally. A generic medicine contains the same active ingredient as another product, but is marketed under a different name. The inactive ingredients that carry the active compound need not be identical to that contained within the original product and the bioavailability may hence be subject to changes. Generic medicines normally enter the market when the patent of an innovator medicine expires and other manufacturers then manufacture generic versions.

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Generic substitution saves the Australian government money through reduced tender prices for Pharmaceutical Benefits Scheme (PBS) listings. Australia’s Pharmaceutical Benefits Scheme (PBS) is regulated by the National Health (Pharmaceutical Benefits) Regulations 1960 (Cth), under the National Health Act 1953 (Cth). This Act relates to the provisions of pharmaceutical, sickness and hospital benefits, and of medical and dental services in Australia. Additionally, generic substitution results in consumer savings through reduced PBS co-payments. The increased dispensing of generic medicines, however, potentially causes increased risk for pharmacists through the medicine selection process\(^3\), as well as through the increased need to discuss the substitution with the patient.

2. THE POLICY AND REGULATORY FRAMEWORK

2.1 The definition of bioequivalence

The responsibility to ensure bioequivalence of generic medicines in Australia lies with the pharmaceutical companies and the Therapeutic Goods Administration (TGA). Two medicines are considered bioequivalent when they produce such similar plasma concentrations of the active ingredient that their clinical effects can be expected to be the same.\(^4\) Bioequivalence is usually assessed in a small number of healthy volunteers through administering the two products on separate occasions. The peak plasma concentration (C\(_{\text{max}}\)) and the extent of absorption (area under the concentration–time curve, AUC) of the generic medicine and the original brand are then 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.\(^5\)

The amount of active ingredient in the systemic circulation is hence used as a measure of the medicine’s clinical efficacy. However, the inactive ingredients also referred to as excipients, can differ and this may have an impact on patient

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tolerability. These include diluents, binders, fillers, surfactants, lubricants, coatings and dyes. Generic medicines must adhere to the same quality of manufacturing codes as branded medicines.

Therefore, for a generic medicine to be listed on the PBS, a manufacturer must demonstrate that their product is bioequivalent to the original brand in Australia. There is, however, no readily identifiable and authorised source of bioequivalence to support brand substitution of private, non-PBS prescriptions.

2.2 Changes to the Pharmaceutical Benefits Scheme (PBS)

There has been increased support by the Australian government towards the use of generic medicines in an attempt to contain the growth of the PBS budget. This support is demonstrated by that fact that generic dispensing and prescribing, over recent years, had been facilitated by the government through the following initiatives:

- The introduction of the Brand Premium Policy (Brand Pricing) in December 1990 to increase price competition between pharmaceutical manufacturers;

- The introduction of generic substitution in 1994, allowing a pharmacist to supply an interchangeable brand in place of the one prescribed under the PBS. Patients need to pay the price difference if they choose the more expensive brand; and

- Amendments to the National Health (Pharmaceutical Benefits) Regulations 1960 (Cwlth) to promote increased generic prescribing. These changes required, as of February 2003, that computer prescribing programs must by default permit brand substitution for PBS prescriptions.

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6. McLachlan, n 2


However, despite these initiatives, the government’s expenditure towards the PBS continued to grow. Therefore, in an attempt to sustain the PBS, significant PBS reforms were passed through Parliament in August 2007. These reforms included changes to the pricing of generic medicines on the PBS as well as new financial incentives for pharmacists to dispense generic products when available. This involves the payment of an additional $1.50 to pharmacists when dispensing generic medicines, which was implemented on 1 August 2008. Pharmacists are therefore strongly encouraged to dispense generic medicines, provided that the doctor has approved substitution to occur.

2.3 Generic dispensing requirements

Various practice standards and guidelines directly or indirectly apply to generic dispensing. These include the Pharmaceutical Society of Australia (PSA) Professional Practice Standards for Dispensing and Counselling, the Guidelines for pharmacists on PBS brand substitution and when to issue a Consumer Medicine Information (CMI) leaflet. The PSA is the national professional organisation for all pharmacists in Australia and the requirements and criteria as specified in these documents need to be implemented by all pharmacists, regardless of the setting, as these documents had been endorsed or adopted by the pharmacy registering authorities with the responsibility for the registration and discipline of registered pharmacists through state and territory legislation that provides for the regulation of the profession throughout Australia. The authorities use these standards and guidelines as admissible


evidence in disciplinary proceedings and it is therefore important that pharmacists implement the criteria as specified in these documents during generic dispensing. However, the implementation of certain criteria may be challenging to apply in practice all the time due to time pressures.

In addition to these practice requirements the National Prescribing Service (NPS) has also developed criteria regarding the dispensing of generic medicines and recommends that substitution should occur only after consultation with the patient, with their informed consent, and after considering the following:

1. The patient’s ability to understand and manage the change;
2. Whether the presence of particular inactive ingredients (e.g. lactose) limits their choice of brands; and
3. Whether packaging differences might present problems.

NPS further identified the following points that should be discussed and clarified with patients:

1. Advise that alternative brands contain the same amount of the same active ingredient and are as effective and safe;
2. Reassure that all medicines registered in Australia are required to meet the same strict quality standards;
3. Explain which medicine the new brand will replace and that the patient should not take both medicines at once;
4. Identify and discuss any differences in appearance between the old brand and the new one;
5. Provide the active ingredient name and point it out on the packaging and/or Consumer Medicine Information (CMI); and
6. Provide the CMI for the new brand.

Generic dispensing therefore places additional responsibility on pharmacists as they need to ensure the systems are in place to determine which patients agree to have generic medicines dispensed and that those patients receive the appropriate counselling.

3. INCREASED ERROR RISK

Generic substitution does increase the risk for medication errors to take place. This risk is increased at all levels, namely at the hospital, pharmacy, or at patient level.

A recent Victorian pharmacy error clearly indicates the importance of public education on the necessity to check the active ingredients of medicines. This error, which led to the hospitalisation of a seven-year-old asthmatic boy, involved the incorrect dispensing of Risperdal® (risperidone) instead of Redipred® (prednisolone). The boy’s parents subsequently gave him large doses of risperidone for his asthma. An important factor that contributed to this potentially fatal incident was the fact that the parents did not identify the error, even though the boy’s father said that they had been issued at least two bottles of the wrong medication by their pharmacy. He further commented: ‘It comes in the same size bottle; it’s liquid and looks the same. We just thought this other drug was a generic brand of the same drug.’ These comments suggest system failures in both the dispensing and patient counselling processes and the need to educate patients to focus on active ingredients rather than on the brand names.

An analysis of the Pharmacists Board of Queensland disciplinary case data similarly indicates that generic substitution contributes to errors. In one case the patient specifically indicated that the substitution of a generic substance directly contributed to her confusion:

[the patient] noticed the label underneath stated Aldazine 100 (thioridazine tablets) and assumed that she had been given a generic brand as she was always asked a question regarding dispensing a generic equivalent when presenting prescriptions at the pharmacy.

This case emphasises the important role pharmacists have in the counselling of patients when substitution has taken place.

The increased error risk involved with generic substitution is also a reality in hospital practice. This was demonstrated by a case reported to the United


States Agency for Healthcare Research and Quality. The case involved a patient suffering from toxic doses of the antiepileptic carbamazepine. This was a result of a change in the carbamazepine brand to a generic formulation that tended to settle out of suspension significantly faster than the original brand. Failure to shake the bottle prior to administration resulted in the initial doses being diluted with the remaining solution becoming increasingly concentrated and subsequently resulted in a toxic dose. This case specifically highlights the importance of having a very cautious approach with regard to substitution of anti-epileptic medicines.

4. INTERNATIONAL CASE LAW

Legal commentaries in the United States of America (USA) have suggested that courts should more closely examine pharmacists’ expanded role in selecting an appropriate generic substitute. This is a result of two reported appellate court cases involving drug product selection in which pharmacists were sued for damages. In *Ulman v Grant* (1982) 450 NYS 2d 955, the patient presented a prescription to a pharmacy for Septra DS®, a specific brand of sulphamethoxazole/trimethoprim. The prescriber wrote ‘substitution permitted’ on the prescription, and the pharmacy dispensed Bactrim DS®; the plaintiff suffered an adverse reaction and sued against the pharmacy. In *Bichler v Willing* (1977) 397 NYS 2d 57 a pregnant mother was prescribed diethylstilbestrol (DES) and the pharmacy dispensed the Eli Lilly brand. The daughter of the mother claimed severe and permanent injury due to the medicine, and sued the pharmacy.

In these two cases the courts had to consider whether the pharmacist’s choice of a specific brand would have made a difference in determining their liability. The courts held that a pharmacist is not negligent unless the pharmacist knowingly dispenses a medication that is inferior or defective. Hence, if the generic medicine is not inferior or defective, the injury is not foreseeable. Therefore, both plaintiffs in these cases were unsuccessful in establishing...


pharmacist liability. However, it has been argued that these cases were considered before the role of pharmacists had expanded, and that today’s courts would give closer examination to pharmacists’ expanded role in selecting an appropriate generic product.\(^{22}\)

An in-depth analysis of the theories of potential pharmacist liability and claims of professional negligence had subsequently been undertaken by legal and pharmacy practice experts in the USA.\(^{23}\) The authors concluded that pharmacists undertake new responsibilities under medication selection law (common law and legislation), and might be exposed to liability if injuries were to occur when generic medicines were substituted for prescribed brand medicines. Three possible theories were identified under which pharmacies might be held liable for injuries sustained in medication product selection situations, namely: (1) negligence; (2) express or implied warranties; or (3) strict product liability.

5. DISCUSSION

It is not known which theories would apply in Australia, as there is a lack of case law, and therefore precedent. However, it is clear that the increase in generic dispensing places additional time constraints on pharmacists. There is also an increased need for professional judgement, and an increased risk of error. It is particularly important that pharmacists keep proper record of substitution processes with sufficient detail to demonstrate at a later stage that informed consent had been obtained.

Pharmacists are required to use professional judgement and not supply a generic brand if there is any doubt the generic will cause patient harm, as the patient’s health outcome should be the prime consideration in any brand substitution decision. Pharmacists would be placed in a difficult legal position when basing substitution decisions solely on cost. Other issues, such as the potential for patient confusion, must also be considered as well as the appropriateness of the non-active ingredients. For example, in patients with specific food allergies. The growing generic market and government push towards substitution therefore places increased responsibility on pharmacists, with a subsequent increased risk that must be managed in community pharmacy practice.

\(^{22}\) Christensen \textit{et al}, n 3.

\(^{23}\) Christensen \textit{et al}, n 3.