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An Evaluation of Health Service Impacts Consequent to Switching from Brand to Generic Venlafaxine in New Zealand under Conditions of Price Neutrality

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ABSTRACT

Objective: To study the health impact on adult New Zealand patients who switch from originator brand to generic venlafaxine. **Methods:** The national pharmacy database was used to select patients using venlafaxine for at least 6 months. Switchers and nonswitchers were identified, and switch behavior was compared for a 12-month follow-up period. Change in health service use following switching was also compared between switchers and nonswitchers including use of the emergency department, hospital, and specialist outpatient services over the same period. **Results:** Approximately 12% of all originator brand users switched to generic venlafaxine, at least half of whom continued to use the generic throughout the follow-up period to August 1, 2012. Almost 60% of new users of the generic venlafaxine, however, switched to using the originator brand. Aside from a slight reduction in the use of outpatient services among switchers, there were no significant differences in health services use between switchers and nonswitchers for either existing or new venlafaxine users. **Conclusions:** Although both products remain fully subsidized and available, there is little incentive for prescribers, pharmacists, or patients to switch to the less expensive generic brand. If savings to the national New Zealand budget are to be realized, additional policy measures should be implemented to minimize incentives for multiple and reverse switching, and prescribers, as key opinion leaders, could take the lead in promoting generics to their patients.

Keywords: generic, pharmaceutical pricing, substitution, venlafaxine.

Introduction

Depression affects more than 130 million people worldwide, with an estimated lifetime prevalence of 10% to 15%. It carries a burden of illness in itself and has been associated with greater rates of mortality following myocardial infarction and stroke, and 20-fold increases in the rate of death from suicide [1]. In addition, decreased workplace productivity and psychosocial disability are key features of depression [1]. The World Health Organization suggests that by 2030 depression will be the leading cause of disease burden, with the disease affecting both developed and developing countries [1,2].

The lifetime risk for a major depressive illness in New Zealand has been estimated to be approximately 25%, with a median age of onset occurring in the early 1930s. It is expected that one in four adults will experience an episode of major depression in his or her lifetime [3]. Alongside psychosocial therapy, antidepressant medicines form the mainstay of treatment, with selective serotonin reuptake inhibitors (SSRIs) usually being the first choice of antidepressants. The advent of venlafaxine—a serotonin-noradrenaline reuptake inhibitor—in the late 1990s offered an additional treatment option in the antidepressant armory alongside related SSRIs, despite higher rates of adverse events [4].

In New Zealand, the use of venlafaxine has generally been reserved for "treatment-resistant" depression when a trial of at least two other antidepressant medicines has not been successful [5,6]. The originator brand Efexor-XR was introduced in the New Zealand market and subsidized by the government in early 2004, with special restrictions requiring prescriptions to be initiated only by a psychiatrist to limit usage while increasing experience with the medicine. In 2007, access was widened to include psychiatric registrars and vocationally registered general practitioners and usage of the medicine increased. In mid-2011, a less expensive generic version of venlafaxine (Arrow Venlafaxine XR) became available, subject to the same prescribing and subsidy conditions as the originator brand [7]. No incentive, however, was given to pharmacists or prescribers to encourage their patients to switch to the generic. Indeed, a reverse incentive remains in place for pharmacists to both commence new patients and continue existing ones on the more expensive originator brand because the pharmacy fee is made up in part of a percentage of the base cost of the medicine.

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The clinical justification for switching between brands of the same pharmaceutical preparation rests on an assumption of bioequivalence, that is, both medicines' overall bioavailability and maximum plasma concentrations being the same [8]. A limited number of medicines are traditionally considered noninterchangeable, either when bioequivalence has not been established or the therapeutic index is narrow and the risk of toxicity high. Despite this, successful substitution with generic cyclosporine, long considered the archetypical noninterchangeable medicine, has been recently reported in heart transplant patients [9]. Establishing bioequivalence, however, does not guarantee acceptance of the "same-but-different" generic medicine by health professionals or patients, and concerns linger around the interchangeability of generic medicines with their originator counterparts [10,11]. Literature related to brand switching of SSRI and serotonin-noradrenaline reuptake inhibitor medicines focuses mainly on the market share of the brands, especially in insurance settings with tiered-pricing plans that favor generic equivalents for full subsidy [12]. Studies evaluating health outcomes of SSRI brand switching are limited in number and methodology. A US-based study reported increased health care costs associated with therapeutic brand switching (changing from one chemical entity to another), yet reported on brand-to-generic switching of SSRIs as a whole. The switcher patients included in this study also had significantly different baseline scores for depression than did their matched nonswitcher counterparts [13]. Available reviews of brand-to-generic switching of psychotropic medicines include literature on a diverse range of medicines including older and newer antidepressives, antipsychotics, and antiepileptic medicines, blurring the picture on these distinct pharmacological entities and contributing to misperceptions [14,15].

New Zealand's Pharmaceutical Management Agency (PHARMAC) is the agency responsible for making funding decisions regarding which pharmaceutical preparations will be listed in the Pharmaceutical Schedule and thus provided largely free to all New Zealanders (outside of a co-payment of $5). Within a fixed annual budget, PHARMAC purchases around 2000 prescription preparations. Evidence-based appraisals are used by PHARMAC in funding decisions for novel medicines, as they are in similar agencies in England, Canada, and Australia. In making funding decisions on generic medicines, however, PHARMAC and its sister agencies must rely on bioequivalence studies as submitted with product registration.

Although the bioequivalence and substitution of some medicines, for example, of originator brand aspirin with generic aspirin, has long been accepted, substitution of medicines for chronic illnesses with generic equivalents is viewed with suspicion by patients as well as by pharmacists and doctors [16,17]. With the availability of a generic brand of venlafaxine in New Zealand, PHARMAC has included both generic and originator brand in the Schedule, rather than adopting a more stringent funding decision that might have seen only generic venlafaxine fully subsidized and the originator brand partially or unsubsidized. Over time, use of the generic brand would be expected to increase through the use of venlafaxine by new patients as well as through incidental switching from originator to the generic brand (known to occur for risperidone, olanzapine, and quetiapine at least) [18].

It is the patients using the generic option in a setting of price neutrality who offer an opportunity to evaluate the consequences of venlafaxine brand switching, with the aim of identifying opportunities or risks of brand switching within the New Zealand context.

Methods

A retrospective study using the national health and pharmacy claims data sets was undertaken of all adult patients in New Zealand using venlafaxine during the period from February 1, 2011, to August 1, 2013.

Data Sources

Prescription records are kept in a centralized government database, the "PHARMS data set," and form the basis for reimbursement to pharmacies for the dispensing of prescription medicines and service provision. In addition, all contacts with the public health sector made by a patient are documented within a number of other databases held by the Ministry of Health. The National Minimum Dataset is a national collection of public and private hospital discharge information, including coded clinical data for inpatients and day patients, whereas the National Non-Admitted Patients Collection information includes event-based purchase units of medical and surgical outpatient events and visits to the emergency department (ED). The Mortality Collection records the underlying cause of death for all deaths registered in New Zealand. Linkage of these data sets via an encrypted National Health Index has been validated and is the basis of many New Zealand health services studies [19].

Patients' demographic characteristics that were extracted include age, sex, ethnicity, and home address. An individual's home address is further associated with a place of domicile index —the New Zealand small-area index of relative socioeconomic deprivation ("NZDep"), which is derived from census data. The NZDep is a 10-point scale, with an index of 10 indicating the area of domicile is lived in by the least socially and materially well-off people. It is widely used in health research as well as by planners and for the allocation of health funds in New Zealand [20], and was also extracted for inclusion in the analysis.

Information on the cost and availability of venlafaxine was sourced from publicly accessible information from PHARMAC Annual Reports and the Pharmaceutical Schedule. Adverse reaction reports were obtained from the national Centre for Adverse Reactions Monitoring (CARM).

Cohorts

On August 1, 2011, generic venlafaxine became available for prescribing with full subsidy, although advance notice of its availability had been given to prescribers and pharmacies for at least 6 months (to allow for a period of stabilization of both drug choice and dosage) and in keeping with New Zealand guidelines [6]. Thus, from this date onward, it was anticipated that there would be new users of both the originator and the generic brands as well as existing users of the originator brand. Accordingly, study cohorts were constructed using the pharmacy data set to identify both new users of venlafaxine (either brand) and patients using originator venlafaxine continuously for at least 6 months before the introduction of the generic on August 1, 2011 (see Fig. 1). Adult patients who received a continuous supply of originator venlafaxine (prescriptions dispensed covering at least 168 days) in the 6 months preceding August 1, 2011, formed the "existing user" cohort (n = 10,212). Two further cohorts were constructed from patients using venlafaxine for the first time between August 1, 2011, and July 31, 2012, and for 6 successive months: one of new users of the originator venlafaxine (n = 3819) and another for the generic venlafaxine (n = 201).

Switch dates were recorded for all switchers and the time taken to switch calculated (days), this being the difference from the start date in the case of new users and from the policy date of August 1, 2011, in the case of existing users. Nonswitcher patients were assigned an "index date" upon which outcomes preindex and postindex date could be measured. Assigned index dates proportionally matched switch dates of switchers, and were randomly allocated. Follow-up was conducted for a period of 12