BEST PRACTICE

Special Edition

March 2007

Paroxetine
MEDICATION
Brand Change

bpac nz
better medicine

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Best Practice Journal (BPJ)
ISSN 1177-5645

BPJ is published and owned by bpac^{nz}
Level 8 10 George Street Dunedin

BPJ Special March Edition 2007

Bpac^{nz} is an independent organisation that promotes health care interventions which meet patients' needs and are evidence based, cost effective and suitable for the New Zealand context.

We develop and distribute evidence based resources which describe, facilitate and help overcome the barriers to best practice.

Bpac^{nz} has four shareholders:

Procare Health, South Link Health, IPAC and The University of Otago

Bpac^{nz} is currently funded through contracts with PHARMAC and DHBNZ.

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Special Edition

Dear Colleague

Welcome to this special edition of best practice journal.

This edition has been produced as part of an education programme for community pharmacists to support the paroxetine brand change.

The brand of subsidised paroxetine hydrochloride 20 mg tablets is changing from Aropax to Loxamine, as a result of a recent agreement with generic supplier Pacific Pharmaceuticals. From 1 April 2007, Loxamine will be available fully subsidised without the need for endorsement, and Aropax will be delisted from the Pharmaceutical Schedule from 1st September.

The education programme accompanying this change has been funded by Pharmac. This is in recognition that increased interaction with patients affected by this brand change is likely to result in both a greater necessity and opportunity for you to discuss the treatment of depression with your patients.

The purpose of the education programme then, is to provide you with an update on the current approaches to the treatment of depression and with information designed to specifically assist with counselling patients through the change.

This is a significant change and we would like to evaluate both the change process and the usefulness of the education programme in supporting the change. Therefore to encourage you to participate in the education programme and the evaluation we will pay you $100 to review the bpac educational resources and then complete the depression quiz and the evaluation questionnaire.

The depression quiz is available online now at www.bpac.org.nz (or can be ordered in hardcopy by free faxing 0800 27 22 69). The evaluation questionnaire will be sent to you as the change campaign nears completion.

Bpac will also host a series of paroxetine change meetings throughout the country over the coming weeks. These meetings, which will include presentations from local psychiatrists, will be an excellent opportunity to learn more about the treatment of depression and we encourage you to attend. You will receive further information about the meetings including dates and locations over the coming weeks.

We hope you find this special edition of the best practice journal useful and as always we welcome your comments and suggestions.

Regards,

The bpac^{nz} team

Depression

causes, presentation and treatment

Depression is common, serious and treatable

The current National Depression Initiative aims to increase public recognition of this important condition, leading to earlier presentation and treatment.

Depression affects not only the individual, but also those around them. It decreases motivation, tolerance and concentration. This impairs parenting and relationships. It also affects productivity and safety at work. It causes the loss of over a million working days a year in New Zealand and decreased productivity on twice that number of days. The recent New Zealand mental health epidemiology study found nearly 6% of adults had experienced major depression in the last year, and 16% during their lifetime.[1]

Multifactorial causes

The final pathway for depression is presumably disturbed neurotransmission, but how a variety of stressors cause this is unclear. Some people are more vulnerable to depression due to genetic factors, past adversity or previous episodes of depression. Resilience built through overcoming challenges and good social support can reduce this risk. Whether a particular stressor triggers depression may depend on the meaning of the particular event for the individual; whether it occurs alone or along with other pressures; and the person's overall social context. Losses, such as a relationship ending, bereavement, unemployment, financial or legal problems, or loss of health, are common triggers. Physical illness, such as hypothyroidism or Parkinson's Disease, can lead to depression directly, while any chronic or life-threatening illness can cause considerable emotional strain. Some medications can cause depression, such as steroids, oral contraceptives and some beta-blockers.

Presentations vary

The core features of depression are EITHER low mood, **or** loss of all interest and pleasure in usually pleasurable activities, persistently and pervasively over at least two weeks **and** which significantly impairs a person's social or occupational functioning. Associated with this are other symptoms, summarised in the box below.

- significant weight loss or gain (when not dieting) or marked change in appetite
- insomnia or hypersomnia nearly every day
- psychomotor agitation or retardation nearly every day
- fatigue or loss of energy nearly every day
- feelings of worthlessness or excessive or inappropriate guilt nearly every day
- diminished ability to think or concentrate, or indecisiveness, nearly every day
- recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide

(Criteria summarised from DSM-IV)[2]

So, while one often thinks of a person suffering depression as being slowed up, sleeping poorly and losing weight, they can be gaining weight, sleeping excessively and agitated. Adolescents can present as irritable rather than overtly depressed.

Depression may also occur as part of other psychiatric disorders. The clinical presentation is very similar, but the distinction has important treatment implications.

Treatment

This must start with a thorough clinical assessment. This should establish the type of depression; the person's strengths and supports; contributing causes to their depression; and ways the person and those close to them can work to change or adjust to these. An assessment of risk of suicide, or risk to others through neglect of usual caregiving roles, is essential.

Information that depression is a clinical condition, not a moral weakness or personal failure, is important, as is the expectation of effective treatment. Clinical support to review current stressors and their resolution is essential. For mild to moderate depression, structured brief psychotherapies such as cognitive behaviour therapy are as effective as antidepressant medication. They may offer protection against future episodes by providing effective self-treatment. However its availability is limited, particularly in the public sector.

There is an increasing range of antidepressant medications. The major groups are:

- Selective Serotonin Reuptake Inhibitors (SSRIs)
- Tricyclic antidepressants (TCAs)
- Selective Serotonin and Noradrenaline Reuptake Inhibitors (SNRIs, e.g venlafaxine)
- Reversible Inhibitors of Monoamine Oxidase A (RIMAs, e.g moclobemide)
- Irreversible Monoamine Oxidase Inhibitors (older and now rarely used)

Most of these groups have recently been reviewed by bpac^{nz} in the best practice journal.[3] Newer agents are generally more tolerable than older ones, although there is a rare risk of agitation and increased suicidality with SSRIs.

Mechanism of action

Current theories of drug action emphasise interactions with subpopulations of serotonin and noradrenaline receptors. However, it is important to recognise that there are many other neurotransmitters affecting regulation of mood. Antidepressants also affect the levels of brain derived neurotropic factor, which is a locally active agent that influences the production of new axonal connections and may have a significant part to play in the recovery from depression.[4] Investigations into these other mechanisms controlling mood can be expected to lead to more effective treatments in the future.

Choosing an antidepressant

There is no compelling evidence that one drug or drug group is more effective or better tolerated than another so choice of antidepressant is based on individual patient factors and includes:

- **Previous response** If a patient has responded well to an antidepressant before, that drug should be considered as first choice.
- **Adverse effects** Drugs which have previously caused troublesome or unmanageable adverse effects should be avoided. The drug's adverse effect profile and its potential for aggravating any concurrent conditions should be considered. For example, avoiding TCAs in cardiac conduction abnormalities.
- **Assessment of potential for drug interactions** For example, citalopram has a much lower potential for interactions than fluoxetine or venlafaxine.
- **Individual tolerance to adverse effects** For some people the anticholinergic effects of TCAs will be unacceptable but others will not tolerate the stimulatory effects sometimes associated with SSRIs.
- **Co-morbid psychiatric or medical conditions may influence drug choice**
- **Starting and continuing treatment** If a person's drug taking is erratic and unreliable, fluoxetine may be the preferred SSRI as it has a long half-life and is less likely to cause discontinuation effects.
- **Suicide risk** The potential for fatal overdose is much higher with TCAs than with SSRIs. Suicidal thinking has been linked to SSRIs but this can also occur with TCAs and any antidepressant drug treatment.

Optimising response

Optimising the response to antidepressant treatment involves initial drug choice as outlined above, use of an adequate dose for sufficient duration, management of adverse effects, review of diagnosis, management of patient expectations and the use of concurrent non-drug treatment. It is very important to explain to patients the possibility of non-drug options to augment antidepressants and the expectations of antidepressant therapy. A person's expectations and beliefs about their condition and treatments can influence compliance.

Appropriate dose and duration

Antidepressants should usually be started at the recommended initial dose and the response reviewed after 4–6 weeks. With TCAs, gradual titration every 3–7 days is generally recommended to assess tolerance of dose related side effects. A smaller initial dose should be considered in some situations, e.g if there is associated panic disorder or anxiety or if the person has previously found drug treatment intolerable.

If response to an antidepressant is poor, partial or not sustained after 4–6 weeks, compliance and review of diagnosis needs to be checked before a change is considered. Some patients may also respond to an increase in dose according to the manufacturer's recommendations. Temporary dose reduction to manage adverse effects may be warranted. For example, if an SSRI causes initial mild restlessness (not associated with severe anxiety or suicidal ideation), reducing the dose or short term use of a benzodiazepine may be effective instead of switching to an alternative drug.

Changing drug therapy

If there is a partial response, or an initial response that has become attenuated, a further increase in dose may be effective. If there is no response at all to the usual maximum dose then a response may be obtained by changing to another drug.

There are no hard and fast rules to guide which drug to switch to. Similar factors that governed the initial drug choice may be relevant and there may be some logic in trying a drug from a different class. However, a response or better tolerability is often seen by changing to another drug from the same class, (e.g. switching from fluoxetine to citalopram). This may be explained by subtle differences in pharmacology or differences in drug metabolism and genetic polymorphism. When switching drugs, consideration needs to be given to washout periods, cross tapering and the management of discontinuation syndrome.

Getting well, staying well

Treatment of major depression aims to achieve complete remission of symptoms. This may require a trial of more than one agent. Response rates of about two-thirds can be expected with any of these agents in primary care, with an effective treatment possible for some 90% of depressed people. Relapse rates are high — up to 50% in the first year after recovery — so continued treatment at the effective treatment dose is important. After recurrent depression, there is evidence to support continued treatment for up to three years. Drug interactions are important. While CYP2D6 is a common mechanism of metabolism, some agents, such as citalopram, are metabolised by CYP3A4, with a different pattern of interactions. Strategies to cope with side-effects, or to change medication, help people continue with their treatment.

Interventions in the pharmacy

In the pharmacy, if there is concern about someone's safety when collecting their antidepressant, it can be helpful to ask the person how they are and if they feel safe. If they express concern, one can ask if they can get help for this. Are they planning to discuss this with the doctor or mental health team, or do they have friends, family or whānau to call on? All mental health services have crisis teams who can be contacted in emergencies, whether or not an individual is currently using their services.

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Key messages on the use of SSRIs

- Most guidelines now recommend an SSRI as the first choice antidepressant if a patient does not respond to non-pharmacological interventions or has a history of moderate or severe depression.
- SSRIs are usually the first choice antidepressant in older people but specific adverse effects and drug interactions require monitoring.
- The clinical effects of antidepressants may start after 2–3 weeks treatment but the response should be assessed by an adequate trial, i.e appropriate dose for at least 4–6 weeks. At this stage if there is a partial response a dose increase may be appropriate. If there is no response an alternative may be considered.
- Citalopram is a good first choice SSRI as it has a lower potential for drug interactions than fluoxetine or paroxetine.
- Paroxetine requires a shorter washout period when switching SSRIs. However, discontinuation syndrome is common. For information on washout periods and switching see BPJ Issue 1.
- It is often possible to manage adverse effects before switching treatment, e.g dose reduction in anxiety.
- Fluoxetine has a longer half life so there are fewer concerns when doses are missed, and discontinuation syndrome is not usually a problem. However, longer washout periods may be required.
- All SSRIs are likely to be beneficial in treatment of anxiety disorders, despite some having more indications listed on their data sheet than others.
- SSRIs may be associated with an initial increase in anxiety that peaks over the first week of treatment and then subsides as the treatment effect emerges. Counselling patients about this possibility is important to prevent withdrawal from treatment.
- SSRIs have a number of significant drug interactions and adverse effects. Some of current interest include; increased risk of bleeding – the risk is higher when SSRIs are used concomitantly with NSAIDs, aspirin, warfarin or low molecular weight heparins; serotonin syndrome especially if taken with other serotonergic agents and hyponatraemia especially in the elderly also taking diuretics.

SSRIs have other indications

All SSRIs are licensed to treat depression. Some have additional indications, reflecting manufacturer's additional applications based on demonstrated efficacy. Fluoxetine is also licensed for bulimia nervosa, obsessive-compulsive disorder (OCD) and premenstrual dysphoric disorder (severe pre-menstrual syndrome); and sertraline for OCD, panic, post-traumatic stress disorder (PTSD) and social phobia. Paroxetine has the broadest range of additional licensed indications: OCD, panic, Social Phobia, Generalised Anxiety Disorder and PTSD. The necessary period of treatment, and dose, may differ between indications. For example, OCD generally responds only to higher doses of SSRI maintained over at least 12 weeks.

what is bioequivalence?

Bioequivalence is defined as the absence of a significant difference in the rate and extent of absorption into the systemic circulation, of two pharmaceutically equivalent medicines, when administered in the same dose under similar conditions. Therapeutic effect (in terms of efficacy and safety) of bioequivalent medicines is considered to be essentially the same.[1]

The rate and extent of absorption of an active ingredient in a medicine is defined as its ***bioavailability***.[2] Pharmacological response is related to the concentration of an active ingredient at the site of action (receptor site). Drug concentrations cannot usually be measured at the site of action so it is assumed that the drug concentration at the receptor site is in equilibrium with that in the blood. Most bioavailability studies therefore measure the drug concentration in blood. The bioavailability of the active ingredient is what determines a product's clinical efficacy.[3]

Bioavailability is measured using three main parameters – the area under the plasma drug concentration versus time curve (AUC), the maximum plasma concentration (C_{max}) and the time to reach maximum concentration (T_{max}).

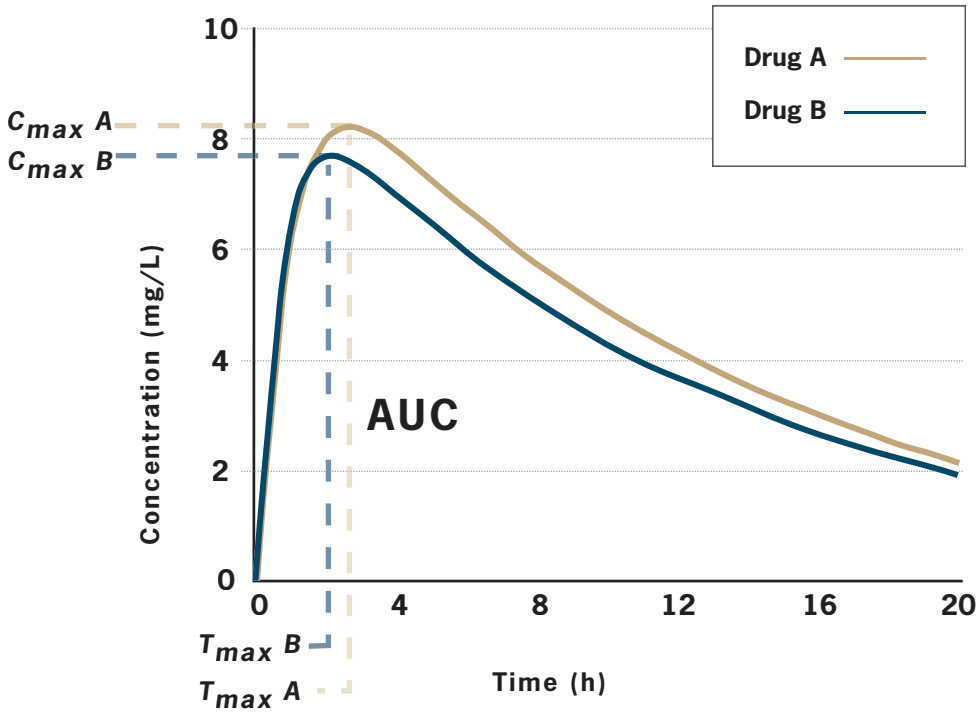
Bioequivalence can be determined by a comparison of the bioavailability of two formulations of the same drug given at the same dose. The generic (or new brand) is always compared with the innovator (or reference) product. Wherever possible, both products are tested in the same group of subjects in a randomised cross-over study. The two medicines may be said to be bioequivalent if the 90% confidence intervals for the ratios of the geometric means (generic:innovator) of the AUC and C_{max} fall between 0.8 and 1.25 (80% and 125%). The T_{max} of the generic and innovator version of the drug must also be similar and there should not be a marked difference in inter-subject variability.[2]

In practice, the generic company tries to achieve a ratio of bioavailability (AUC,C_{max}) close to 1. If the ratio is closer to 0.8 or 1.25, then the data would have to be very uniform for the 90% confidence intervals of the ratios to lie in the 0.8 to 1.25 range and therefore achieve bioequivalence.[2]

According to FDA guidelines for bioequivalence, a generic copy of a drug must contain identical amounts of the active ingredient in the same dose formulation and route of administration. Some inactive ingredients (excipients) are allowed to differ but must occur in a similar ratio to the active ingredient as that observed in the innovator drug.[4]

Simulation of a drug concentration versus time curve for two drug products

Adapted from Birkett D, 2003



C_{max} *maximum plasma drug concentration,* T_{max} *time required to achieve a maximal concentration,*

AUC total area under the plasma drug concentration-time curve

Drug A is the innovator product and Drug B is the generic product.

Drug A: C_{max} = 8.1 mg/L; T_{max} = 2.6 h; AUC = 124.9 mg.h/L

Drug B: C_{max} = 7.6 mg/L; T_{max} = 2.1 h; AUC = 112.4 mg.h/L

The ratio of areas (generic:innovator), and therefore the relative bioavailability, is 0.9. To be accepted as bioequivalent, the 90% confidence intervals for the area ratio would need to fall within the range 0.8–1.25.

How is bioequivalence regulated in NZ?

Adapted from Medsafe Bioequivalence Guidelines.[1]

In New Zealand, Medsafe is responsible for determining that a generic copy of a drug is bioequivalent to the innovator version, before it is released onto the market. Medsafe bases bioequivalence testing guidelines on overseas regulations and on what they regard as best current international practice.

Guidelines from the following regulatory authorities are currently used by Medsafe:

- European Commission Rules Governing Medicinal Products in the European Community Volume III and CPMP Notes for Guidance
- United States Food and Drug Administration (FDA)
- Australian Therapeutic Goods Administration (TGA)
- Therapeutic Products Directorate, Health Product and Food Branch, Health Canada
- World Health Organisation (WHO)

Any company wishing to manufacture or distribute a generic version of an innovator drug in New Zealand must submit a Comparative Bioavailability Study report, in compliance with international standards, to be considered by Medsafe.

Variables included in a bioequivalence study

Ideally the bioavailability of systemic medicines should be measured using blood plasma or serum concentration of the active ingredient. Where this is not possible, the quantity of the active ingredient or its metabolites excreted in urine, or pharmacodynamic variables (e.g. heart rate) may be measured. However this results in a less accurate measure of bioavailability.

Single dose studies are appropriate in most cases. A steady-state study may be used in certain circumstances including; medicines with a long terminal elimination half-life, highly toxic medicines, modified release products, medicines which induce their own metabolism, enteric coated preparations (if coating is innovative), combination products, medicines that exhibit non-linear pharmacokinetics and medicines which are likely to systemically accumulate.

Bioavailability studies are usually carried out in healthy adult human volunteers of both genders (where appropriate), of average weight and between eighteen and sixty years of age. The number of subjects needed should be based on the number required to reach statistical significance. The acceptable number of subjects is usually greater than twelve and less than forty.

Experimental conditions should be standardised including gastrointestinal conditions, posture, physical activity and timing of samples. The test formulation of tablets or capsules should originate from a batch of at least 10% of full production scale or 100 000 units (whichever is greater) and should be manufactured using full production scale equipment. The mean potencies (actual drug content) of the generic and innovator product should not differ by more than 5%.

What are the main issues with the validity of bioequivalence?

The introduction to the market of a generic drug, especially when replacing the innovator counterpart, is often met with suspicion and concern by health care providers and patients. Concerns mainly surround the issue of bioequivalence and whether use of the generic drug will result in unforeseen effects. Generic drugs are often perceived as being inferior due to their lower cost and the lesser extent of development that goes into manufacturing these drugs compared to the innovator version.[5]

The measure of bioequivalence

There has been some criticism of the use of the 80–125% reference range for bioequivalence in drugs which have a narrow therapeutic range such as carbamazepine, phenytoin and digoxin.[6] A relatively small change in systemic concentration of these drugs can lead to a markedly different therapeutic response or even toxicity. Warfarin also has a narrow therapeutic range and bioequivalence has not been established between the two main brands of this drug. Therefore the two variants are not considered interchangeable.[2] Similarly, concerns have been raised over using this reference range for drugs with a wide therapeutic range, for example antibiotics and antihistamines.[5]

Testing bioequivalence in a "normal and healthy" population

When an innovator drug is developed, evidence is required of its pharmacokinetics, efficacy and tolerability in volunteer study subjects as well as the target population. However the development of a generic equivalent requires only evidence of its bioequivalence with the innovator drug in the study subjects. This leaves some doubt as to whether the generic drug would perform differently in a patient population, taking into consideration factors such as co-morbidities, concurrent prescriptions and physiological factors such as differences in first pass metabolism, gastric pH and bacterial flora.[5]

Older patients may also experience unique difficulties with a switch to a generic drug. Many suffer from multiple medical conditions and receive multiple drugs which may affect pharmacokinetic properties. Physiological changes associated with ageing may also affect drug absorption, distribution, metabolism and excretion.[7] Bioequivalence is generally tested in healthy subjects under the age of sixty.

Use of single-dose studies and the potential effect of excipients

Bioequivalence studies most often involve single doses of a drug.[1] In clinical practice, most drugs are administered in multiple doses and require maintenance of a steady-state. The maximum drug concentration attained at a steady state is often higher than that achieved after a single dose.[5] It is possible that excipients used in the generic formulation (preservatives, pH adjusters, thickening agents etc) could affect the absorption, and metabolism at steady state without producing these differences from a single dose.[8] Excipients can not always be considered inactive or inert.[3] Some patients could have individual reactions or sensitivity to a change in excipient.[2] The potential effects of drug accumulation may also not be seen with a single dose study.

Has the validity of bioequivalence been tested in NZ?

Adapted from Medsafe Media Release.[9]

In 2002 a drug company brought a challenge to the High Court against Medsafe's procedures in evaluating the safety and efficacy of a generic version of the drug, paroxetine mesylate. The company claimed that Medsafe had not followed its own procedures for assessing the generic drug and that clinical trials may be required to confirm that paroxetine mesylate was safe and effective.

The court case reviewed Medsafe's handling of the process for approval of the generic drug. This was supported by chemical, pharmaceutical and bioequivalence data which established the product's quality, safety and efficacy. The data showed that the generic version of paroxetine did not solely rely upon pre-existing toxicological data for the innovator product. The data also demonstrated bioequivalence between the generic and innovator product, with respect to the same amount of active substance being absorbed to the same extent.

The High Court rejected all grounds of challenge by the drug company and found in favour of Medsafe. It was ruled that the evaluation process for the generic drug was robust and followed correctly and that Medsafe properly considered all information about the drug.

The outcome of this challenge can provide reassurance that Medsafe applies rigorous procedures to evaluate the safety and quality of medicines before they are made available to the public.

So what does this mean?

There is no recent documented evidence of proven failure of a generic formulation of a drug, due to issues of bioequivalence. There are some reports of therapeutic inequivalence, however most of these cases were determined to likely be the result of progression of disease rather than lack of bioequivalence of a generic and innovator formulation of a drug.[10]

Given the fact that distributors of generic drugs in New Zealand must provide scientific evidence of bioequivalence in accordance with Medsafe's guidelines, it can be assumed that if a generic drug is on the market, it can be considered therapeutically equivalent to the innovator counterpart, unless classified as non-interchangeable.

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Developed with the assistance of Dr Dorothy Saville - Senior Lecturer University of Otago, School of Pharmacy

bioequivalence
of Loxamine vs Aropax

Can Loxamine and Aropax be considered bioequivalent?

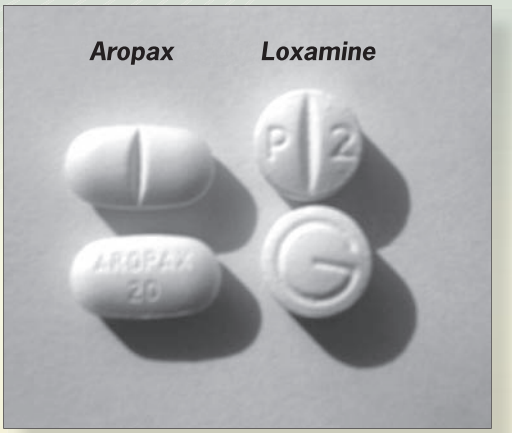
Yes, information received from Pacific Pharmaceuticals shows that the results of the studies on Loxamine are well within the bioequivalence acceptance limits. This means that any variation in bioavailability (AUC, C_{max}) between Loxamine and Aropax is very unlikely to be any different from variations between different batches of the same brand.

Loxamine vs Aropax: Bioequivalence study results

90% confidence intervals for ratios of geometric means

C_{max}	0.978 to 1.117
T_{max}	0.968 to 1.020
AUC 0–t	1.000 to 1.139
AUC 0–infinity	0.998 to 1.136

Loxamine and Aropax are bioequivalent (90% CI's within 0.8–1.25)



Loxamine vs Aropax: Inactive ingredients (excipients)

Both tablets contain 20 mg paroxetine hydrochloride

Aropax tablets also contain; the colouring agent titanium dioxide (white, E171), calcium hydrogen phosphate, hypromellose, sodium starch glycolate (potato starch), magnesium stearate, polysorbate 80 and macrogol 400.

Loxamine tablets also contain; calcium hydrogen phosphate anhydrous, sodium starch glycolate, colloidal anhydrous silica, magnesium stearate, purified talc, titanium dioxide and Eudragit 100.

Loxamine contains silica, talc and Eudragit 100 which are not present in Aropax tablets. Silica and talc are widely used, relatively inert compounds used as tablet fillers. Eudragit 100 is a polymethacrylate which is extensively used as tablet film coating. These agents are selected on the basis that they are very unlikely to cause adverse effects but the remote possibility of sensitivity to these excipients cannot be completely excluded.

Mental Health Foundation

Making mental health everybody's business

That's the mission of the Mental Health Foundation. The foundation is a charitable trust, established in 1974, that provides an information service, and promotes mental health and wellbeing throughout Aotearoa New Zealand.

The foundation's vision for New Zealand is for it to be a nation where collectively and individually we recognise the importance of approaches that sustain and improve our mental health.

In the last year, the Mental Health Foundation has taken on the role of co-ordinating and managing aspects of high profile Ministry of Health –funded campaigns such as 'Like Minds, Like Mine', and the National Depression Campaign, which features television messages by All Black legend John Kirwan.

The **National Depression Campaign** was launched in October 2006. The key messages of this campaign are:

If you think someone you care about is depressed, early acknowledgement is important so that practical help can be given.

There are ways to help people with depression, and self help strategies such as physical activity can be very effective.

If you are worried about being depressed, get help, there are effective treatments and therapies; there is a way through it.

Contact the National Depression Initiative on 0800 111 757 or www.depression.org.nz

Mental Health Foundation key services

National Information Service and Resource Centre

www.mentalhealth.org.nz
09 300 7030

Mental health promotion programmes

The Mental Health Foundation's youth mental health work, focuses on training the trainers and includes rangatahi programmes, resilience building and depression awareness.

The foundation produces a number of high quality, interactive, arts based resources and training programmes for people who work with young people.

Their work with adults includes supporting workers on issues of self-care and supporting vulnerable groups and sectors in the community such as refugees and migrants. For example, they have a range of programmes focusing on older people's mental health including raising awareness of depression in later life and strategies for making a successful transition to retirement.

MindNet

www.mindnet.org.nz

An internet-based resource and e-bulletin to help keep you informed about the latest developments in mental health promotion and prevention in Aotearoa New Zealand.

Suicide Prevention Information NZ (SPINZ)

www.spinz.org.nz

SPINZ provides high quality information on suicide prevention. Services include:

- Suicide prevention workshops throughout New Zealand.
- Face-to-face community liaison and support.
- Networking and participation in community hui.
- Dissemination of best practice information.

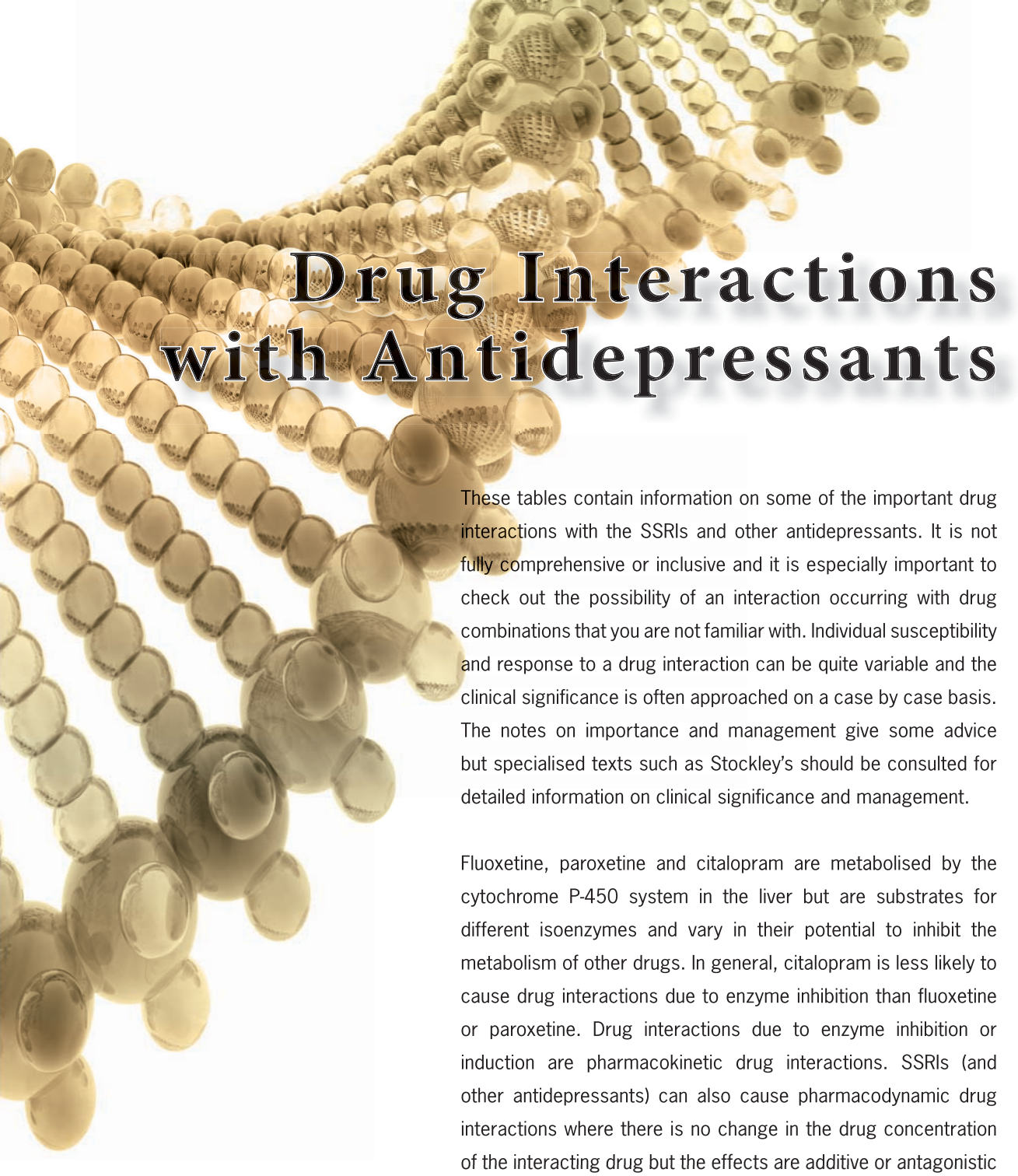
Working Well

www.workingwell.co.nz

Working Well supports employers and managers to create more mentally healthy work places.

The Mental Health Foundation also:

- Undertakes research into discrimination, employment and family attitudes as they effect people with mental illness.
- Campaigns for services which are non-discriminatory and a society which is fully inclusive of people with experience of mental illness.
- Is involved in advocacy and policy-making for improving mental health services and reducing stigma and discrimination against people who experience mental illness.



Drug Interactions with Antidepressants

These tables contain information on some of the important drug interactions with the SSRIs and other antidepressants. It is not fully comprehensive or inclusive and it is especially important to check out the possibility of an interaction occurring with drug combinations that you are not familiar with. Individual susceptibility and response to a drug interaction can be quite variable and the clinical significance is often approached on a case by case basis. The notes on importance and management give some advice but specialised texts such as Stockley's should be consulted for detailed information on clinical significance and management.

Fluoxetine, paroxetine and citalopram are metabolised by the cytochrome P-450 system in the liver but are substrates for different isoenzymes and vary in their potential to inhibit the metabolism of other drugs. In general, citalopram is less likely to cause drug interactions due to enzyme inhibition than fluoxetine or paroxetine. Drug interactions due to enzyme inhibition or induction are pharmacokinetic drug interactions. SSRIs (and other antidepressants) can also cause pharmacodynamic drug interactions where there is no change in the drug concentration of the interacting drug but the effects are additive or antagonistic due to the drug's pharmacological properties. Examples include additive sedation with CNS depressants and serotonin syndrome with other serotonergic drugs.

In Table 1 "All' refers to the three SSRIs available in New Zealand; paroxetine, fluoxetine and citalopram. Table 2 refers to TCAs in general although individual drugs have different properties which can increase the risk of an interaction; for example amitriptyline is one of the most sedative TCAs and clomipramine has marked serotonergic properties which increase the risk of serotonin syndrome if given with SSRIs.

Table 1: Some important drug interactions with Antidepressants

SSRI	Interacting Drug	Possible Effect(s)	Importance and Management
All	Alcohol	Increased CNS sedation	Advise vigilance in early stages of treatment
All	Benzodiazepines	Increased sedation possible. Fluoxetine and paroxetine may reduce metabolism of some benzodiazepines	Warn that increased sedation is possible
All	Warfarin	Increased INR and increased bleeding risk due to antiplatelet effect	Monitor INR and advise patients to report signs of bleeding
Fluoxetine & paroxetine	Metoprolol and propranolol	Increased beta-blocking effects, bradycardia	Monitor heart rate. Interaction not reported with citalopram
All	Buspirone	Serotonin syndrome and lowering of seizure threshold theoretically possible	Monitor concurrent use
All	Antiepileptics	SSRIs may lower the seizure threshold	Unlikely to be a problem if epilepsy well controlled. Observe seizure frequency
Fluoxetine	Antiepileptics, carbamazepine and phenytoin	Increased plasma concentrations of carbamazepine and phenytoin with fluoxetine	Monitor plasma concentrations of carbamazepine and phenytoin. Adjust dose if necessary. No similar reports with paroxetine and an interaction appears unlikely with citalopram.
Paroxetine	Antiepileptics, carbamazepine and phenytoin	Reported to decrease plasma concentration of paroxetine	Clinical significance not clear. Monitor clinical response
All	NSAIDs including aspirin	Increased risk of GI bleeding	Concurrent use not contraindicated but be aware of increased risk of bleeding especially in those with additional risk factors
All	Monoamaine oxidase inhibitors (MAOIs), including moclobemide	Hypertensive crisis	Avoid concurrent use. Washout periods essential when switching. Refer to product prescribing information and reference texts.
Fluoxetine & paroxetine (possibly citalopram)	Clozapine, haloperidol and risperidone	Increased plasma concentrations of antipsychotics	Monitor for dose related adverse effects and reduce dose of antipsychotic if necessary

All	Tramadol	Both tramadol and SSRIs lower seizure threshold. Serotonin syndrome reported with concurrent use	Use the combination of tramadol and an SSRI very cautiously especially at high doses. Alternative analgesic may be preferable
All	Tricyclic antidepressants	Increased plasma concentrations of TCA and increased adverse effects. Risk of serotonin syndrome especially with clomipramine	Increases are variable but can be in the order of 3–4 times and more. Increases usually less significant or negligible with citalopram. If the combination is judged necessary, start with the lowest dose of TCA and monitor for dose related adverse effects, e.g sedation, or anticholinergic symptoms
All	Sibutramine	Increased risk of CNS toxicity	Avoid
All (especially fluoxetine & paroxetine)	Perhexilene, flecainide and other antiarrhythmic drugs	Plasma concentrations can be increased leading to toxicity.	Refer to individual product prescribing information and reference texts
Fluoxetine & paroxetine	Protease inhibitors (ritonavir)	Fluoxetine increases ritonavir concentrations and ritonavir may increase fluoxetine and paroxetine concentrations. Cases of serotonin syndrome with fluoxetine reported	Monitor for symptoms of serotonin syndrome. Reduce dose if necessary
All	Lithium	Neurotoxic symptoms and serotonin like syndrome occasionally reported	Addition of lithium to an SSRI can be beneficial and is usually uneventful. Observe for adverse effects
All	Selegiline	Hypertension, CNS excitation, serotonin syndrome	Avoid this combination as serious interactions have been reported. Manufacturers advise to avoid. N.B. apparent safe use of this combination has also been reported in the literature
All	St John's Wort	Serotonin syndrome	Avoid this combination
All	Sumatriptan	A few cases of dyskinesias with fluoxetine. Occasional reports of serotonin syndrome	Concurrent use of sumatriptan and SSRIs not usually a problem but monitor for any adverse effects when the combination is started

Table 2: Some important drug interactions with tricyclic antidepressants (TCAs)

Interacting drugs(s)	Possible effect(s)	Importance and management
SSRIs	Increased plasma concentrations of TCA causing increased adverse effects. Serotonin syndrome possible, especially with clomipramine	Increases are variable but can be in the order of 3 – 4 times and more. Increases usually less significant or negligible with citalopram. If the combination is judged necessary, start with the lowest dose of TCA and monitor for dose related adverse effects, e.g. sedation, or anticholinergic symptoms
Alcohol	Increased CNS depression, sedation	Warn patient about increased drowsiness. Limit alcohol intake
Antiarrhythmic drugs, e.g. amiodarone, flecainide, quinidine	Increased risk of ventricular arrhythmias	Avoid concurrent use. Refer to specialised texts.
CNS depressants e.g. Benzodiazepines Antihistamines Antipsychotics	Increased CNS depression, sedation	Warn patient about increased drowsiness
Clonidine	Antihypertensive effects of clonidine are reduced or abolished	Avoid concurrent use
Warfarin	Occasional reports of changes in INR	Evidence for an interaction is poor and inconclusive. Monitor INR as normal
Lithium	Neurotoxic symptoms and serotonin-like syndrome occasionally reported	Concurrent use can be beneficial and is usually uneventful. Observe for adverse effects
Antipsychotics	Increased sedation, additive anticholinergic effects Plasma concentrations of phenothiazines and/or the TCA may be increased	Often used together in clinical practice but be aware of the possibility of additive pharmacological and adverse effects
Selegiline	CNS excitation, serotonin syndrome	Interaction appears less likely than with an SSRI Caution and awareness of possible symptoms advised
Ritonavir	Plasma concentrations of TCAs may be increased.	Monitor for increased dose related adverse effects. Reduce dose of TCA if necessary.
Tramadol	Increased risk of seizures. Possibility of serotonin syndrome especially with clomipramine	Adverse effects unlikely but be aware of symptoms

The CYP450 System

Many drugs are metabolised by the cytochrome P-450 (CYP450) enzymes in the liver. The end result is either inactive compounds that can be excreted, or active compounds which can be further metabolised leading to eventual removal from the body. The CYP450 system consists of many enzyme subtypes each metabolising a specific range of drugs (substrates).

Some of the enzymes (e.g. CYP2D6 and CYP2C19) exhibit genetic polymorphisms and the frequency of these polymorphisms varies between ethnic groups. These genetic differences mean some people have an enzyme with reduced or no activity. In the case of CYP2D6 there are at least 3 variants giving phenotypes who are poor metabolisers, extensive metabolisers (the majority of people) or ultra fast metabolisers.

People who are poor metabolisers may have an increased risk of adverse reactions to a drug metabolised by the affected enzyme or reduced capability to convert a parent drug into the active drug. As an example of genetic variation, the frequency of CYP2D6 poor metabolisers is 5–10% in Caucasians and 1% in East Asians.

Some CYPs (CYP3A4) can have their activity increased (induced) by other drugs leading to increased substrate metabolism. Conversely some drugs can block (inhibit) the activity of a CYP enzyme and reduce substrate metabolism.

Examples:

- Fluoxetine is a substrate for CYP2D6 and a potent inhibitor of this enzyme. TCAs such as amitriptyline are also metabolised by CYP2D6. Fluoxetine will inhibit this and increase plasma concentrations of the TCA and increase dose related adverse effects.
- The activity of codeine is mainly due to conversion to morphine by CYP2D6. A poor metaboliser for this enzyme will have poor analgesic response due to lack of conversion. A drug which is an inhibitor of CYP2D6 (e.g. paroxetine) will, in effect, change a normal metaboliser to a poor metaboliser.
- A CYP2D6 poor metaboliser will have reduced capacity to metabolise some antidepressants (e.g. fluoxetine, paroxetine and amitriptyline) and be more sensitive to dose related adverse effects.
- Theophylline is a substrate for CYP3A4. Phenytoin induces CYP3A4 which increases the metabolism of theophylline and reduces plasma concentrations.

Many antidepressant and psychoactive drugs are metabolised by CYP2D6, and to a lesser extent, CYP2C19 which exhibit genetic polymorphism (see Table 1).

Table 1. Main metabolic pathways of commonly prescribed antidepressants

Drug	Main Metabolising enzyme	Notes
Fluoxetine	CYP2D6 Some other CYPS involved	Potent inhibitor of CYP2D6 Active metabolite (norfluoxetine) inhibits CYP3A4
Paroxetine	CYP2D6	Potent inhibitor of CYP2D6
Citalopram	CYP2C19 CYP2D6 only partly involved	Only inhibits CYP2D6 very weakly
Venlafaxine	CYP2D6	CYP2D6 inhibitors taken at same time will increase plasma concentrations of venlafaxine. Active metabolite is metabolised by CYP3A4
Most TCA's (e.g. amitriptyline)	CYP2D6 Some other CYPs involved	CYP2D6 inhibitors taken at same time will increase plasma concentrations of TCA

In general CYP2D6 poor metabolisers are likely to have poor tolerance to TCAs, venlafaxine and the SSRIs paroxetine or fluoxetine. A smaller dose may be required for therapeutic effect and to minimise adverse effects. Citalopram may be better tolerated by CYP2D6 poor metabolisers. Conversely, CYP2C19 poor metabolisers are likely to have poor tolerance of some TCAs and possibly citalopram.

Related reading and resources

De Leon J, Armstrong S, Cozza K. Clinical guidelines for psychiatrists for the use of pharmacogenetic testing for CYP450-2D6 and CYP450-2C19. Psychosomatics, 2006;47:75-85.

Drug Interactions; Defining genetic difference on pharmacologic responses. Available from; http://snipurl.com/xckc.

Martin J, Fay M. Cytochrome P450 drug interactions: are they clinically relevant? Aust Prescr, 2001;24:10-2. Available from; http://snipurl.com/xcka.

Changing to a Generic Drug

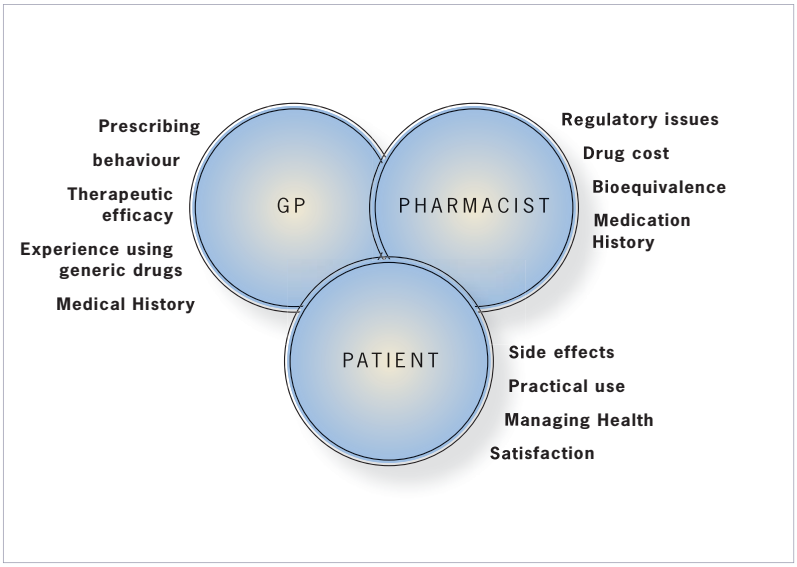
Over the past several years, the worldwide market for generic drugs has grown at a faster rate than the pharmaceutical industry as a whole. This is largely due to strong efforts to contain drug costs by government agencies, as well as growing confidence in generic quality by both health professionals and consumers.[1]

When an innovator product is replaced with a generic alternative, there are many issues that must be taken into consideration. Physician attitude towards generic substitution is most often related to their general prescribing behaviour, perception of therapeutic efficacy, beliefs about generic drugs and previous experience with using generic alternatives, including any negative effects.[2]

Pharmacists may consider regulatory issues, drug class, cost and bioequivalency information when dispensing generic products as well as a patient's medical and medication history and their comfort with a brand change.[1]

The main issues confronting patients undergoing a brand change to a generic substitute include overall satisfaction, changes in therapeutic effects, side effects, practical use (e.g. size, shape, appearance), willingness to take medication and concern about managing their health condition.[3] Increasing age is associated with less favourable attitude towards generic drugs and patients are often less accepting of using a generic drug to treat a serious disease.[4]

Figure 1: Components of the decision making process for accepting brand switching



Patients who received information from their physician or pharmacist about generic substitution were more likely to have switched from the branded product.

SSRI antidepressants and brand changing

The issues surrounding brand changing may become more complex when the drug in question is used to treat a serious medical condition such as depression.

Consideration must be given to the perceptions and attitudes of a patient receiving antidepressant therapy and how this may affect the way they accept a change to their drug therapy, both physiologically and psychologically.

Patients are often concerned that a change in their antidepressant medication may result in reduced clinical effect and/or increased side effects.

The generic form of paroxetine due to be released in New Zealand (Loxamine) has met Medsafe's bioequivalence standards, in accordance with international guidelines (see bioequivalence article, page 17). This means that the risk of a reduced response, increased side effects or the appearance of discontinuation syndrome due to a significant change in the dose received is very unlikely. It is probable that perceptions and attitudes to the change may be stronger determinants of response and acceptance of change than bioequivalence issues.

Brand changing with other SSRIs has occurred in New Zealand. In the case of citalopram the generic was associated with a significant number of reports to MARC. Most of these related to a perceived loss or change in therapeutic effect but it has not been determined if this was due to reduced drug content or attitudes and perceptions.

The change to Loxamine will involve a large number of people using a drug which has not been used before in New Zealand. This drug is however, already widely available throughout Europe, with sales for 2005 and 2006 in excess of 150 million tablets.* No patterns of adverse effects have been reported with Loxamine, indicating that problems in New Zealand will be unlikely. However pharmacists are in an ideal position to monitor patient feedback, response, side effects and attitudes to the change.

To report any suspected adverse reactions, contact

Centre for Adverse Reactions Monitoring - CARM

Phone 03 479-7247, www.carm.otago.ac.nz

PHARMAC help line 0800 66 00 50

Although therapeutic problems were sometimes the most important adversity, more commonly it was a failure of communication which contributed largely to the lack of satisfaction.

Due to the nature of mental illness and/or previous experiences, there may be some groups of people that are less accepting of a change to a generic drug. These people may require extra information or counselling through the process and include;

- People with recurring episodes of depression who responded well when previously treated with the innovator product
- People who have been stabilised on an innovator product for a long time
- Subgroups of people with OCD, anxiety disorders or co-morbid psychiatric disorders
- People who have been poorly informed about a previous brand change
- People who had a negative experience with a previous brand change

Satisfaction with the communication received was closely correlated with satisfaction about the change to the generic drug itself.

**Personal communication - Regulatory Affairs Manager, Pacific Pharmaceuticals*

How do patients perceive the risk of changing to a generic drug?

One of the main barriers in changing brands of medication is the patient's perception of risk.

A study conducted among American consumers of health care services found that between 14% and 54% believed that generic prescription drugs are both less safe and less effective than the innovator product. Perception of risk was dependent on the severity of the medical condition being treated, with patients with a heart condition perceiving the highest risk.[5] Another study found significant differences in acceptability rates of generic substitution according to pharmacological class of drug – generic substitution was less accepted for drugs acting on the CNS (including antidepressants).[6]

Although generic drugs are clinically equivalent to their innovator counterparts, there will always remain a population of people who believe they are receiving an inferior product and therefore will be dissatisfied with the change. A recent study conducted in Norway assessed patient attitudes towards generic drug substitution.

- 36% reported one or more negative experiences in relation to the substitution
- 21% reported an overall negative experience after the change
- 12% reported experiencing side effects
- 18% felt that the generic drug had a weaker effect than the innovator medication
- 41% would not change if they had no economic incentive to do so
- 27% said that they would never accept substitution

There were no actual reports of clinical failure of the generic drugs. Negative experiences with generic drug substitution were not related to polypharmacy, patient age or gender.[3]

At the time of brand changing, generic drug substitution for many patients is not considered an equal alternative to innovator drugs. However, over time most patients do accept the change and the generic drug attains the status of the branded version. A study in the United States has found that since 1979, 94 to 97% of patients in the state of New Jersey have agreed to use a generic substitute.[1]

Differences in appearance and brand loyalty

Generic drugs often differ in appearance and packaging from the innovator product which may cause anxiety and confusion in patients. Those receiving drug treatment for psychological disorders may be especially vulnerable to this.[5] Changing the colour, taste or form of a drug can result in non-compliance.

Although there is no evidence that generic drugs are inferior to innovator products patients may often resist changing from a brand they know well to a generic equivalent which may look different.[6] Patients prefer to stick to a brand name drug if they have already been familiarised with it.[1] The longer a generic brand has been available, the more likely it is used by pharmacists and prescribers. Prescriber and pharmacist habits and preferences may be influenced by informational constraints, loyalties to drug companies and desire to satisfy patients.[4]

Individual educational intervention that lasted less than five minutes in most cases, resulted in a high rate of generic acceptability.

1. Suh D. Trends of generic substitution in community pharmacies. Pharm World Sci 1999;21(6):260-65.
2. Banahan B, Kolassa E. A physician survey on generic drugs and substitution of critical dose medications. Arch Intern Med 1997;157(18):2080-88.
3. Kjoenniksen I, Lindbaek M, Granas A. Patients' attitudes towards and experiences of generic drug substitution in Norway. Pharm World Sci 2006;28:284 - 289.
4. Mott D, Cline R. Exploring generic drug use behaviour: The role of prescribers and pharmacists in the opportunity for generic drug use and generic substitution. Med Care 2002;40(8):662-74.

Patient information programmes make brand changing easier

The Norwegian study found that patients who received information from their physician or pharmacist about generic substitution were more likely to have changed from the innovator product.

Over half of the patients (54%) remembered receiving information from their pharmacist on generic substitution and 24% remembered receiving this information from their doctor.[3]

A recent study based in Spain assessed acceptance of substitution of innovator drugs for generic drugs for chronic conditions in primary care. Of the patients who received verbal information and written material on generic drugs, 98.9% agreed to receive a generic formulation. The reasons for refusal in the remaining patients included the influence of physicians other than the general practitioner, patients' satisfaction with the innovator product and adverse effects.

There was no statistically significant difference between patients that agreed and those that didn't agree with substitution based on age, gender or educational level. There were however, significant differences in acceptability rates according to individual primary care centres, suggesting differences in quality of information provided. It was concluded that individual educational intervention (that lasted less than five minutes in most cases) in patients with repeat prescriptions resulted in a high rate of generic acceptability. All patients accepted the intervention. The intervention also helped to stimulate health practitioner's knowledge of generic drugs.[6]

In a study that assessed the impact of introducing generic substitutes to patients in a general practice clinic in Scotland, 70% accepted the generics and were satisfied. Of the remaining patients, 20% were still taking the branded drug, 4% were on other prescribed treatment, 4% had stopped treatment and 3% were purchasing their own alternative. Patients were either sent an explanatory letter detailing the change or were informed when first collecting their repeat prescription. Reasons for dissatisfaction were largely due to the quality of information provided to the patient rather than problems with the generic drug itself. Almost three quarters of patients (73%) could recall being informed of the change in at least one way. Satisfaction with the communication received was closely correlated with satisfaction about the change to the generic drug itself. After four months, generic prescribing increased from 37% to 58%.[7]

The results of these studies suggest that appropriate care must be taken to inform patients properly. Interviews with patients highlighted the aspects of the experience which caused most dissatisfaction. Although therapeutic problems were sometimes the most important adversity, more commonly it was a failure of communication which contributed largely to the lack of satisfaction. Patients were much more likely to be willing to try the new treatment if they thought they understood the reason for the change. Almost all patients were aware that saving money was at least part of the reason for the brand change and they all felt that a trial of a cheaper alternative was reasonable.[7]

Dissatisfaction usually centres around two main issues:

Power; patients feel weak or not in control of their health management if they perceive a change has been forced upon them.[7]

Communication; patients require empathy from their healthcare provider in order to feel satisfied, so they will accept major change if it is delivered in a manner which makes them feel valued. This also helps to avoid much of the negative feeling generated by the change itself and enhances the patient/healthcare provider relationship which can easily be damaged by these changes.[7]

5. Ganther J, Kreling D. Consumer perceptions of risk and required cost savings for generic prescription drugs. J Am Pharm Assoc 2000;40:378-83.
6. Valles J, Barreiro M, Cereza G, Ferro J, Martinez M, Escriba J, et al. A prospective multicenter study of the effect of patient education on acceptibility of generic prescribing in general practice. Health Policy 2003;65:269-75.
7. Dowell J, Snadden D, Dunbar J. Changing to generic formulary: how one fundholding practice reduced prescribing costs. BMJ 1995;310:505-508.

Counselling patients through a brand change

Accentuate the positive...

The pharmacist is in an ideal position to counsel patients through a brand change. A good understanding of the likely reasons behind any objections and a positive reinforcement of the facts during the first interaction with the patient will ensure greater acceptance of change.

It is important to realise that in both clinical trials and in practice there is a significant placebo effect. This applies to most medical conditions including depression. This means that the actual taking of a "medicine" whether it contains an active ingredient or not can elicit a measured clinical response. It can therefore be logically argued that even if a generic drug was 100% identical, with respect to drug content and the rate of release, a person's actual perception or acceptance of receiving something different may influence therapeutic effect.

3 key questions and possible answers

Why the change?

The rationale for change is outlined in the patient information leaflet produced by PHARMAC. Giving this pamphlet to the patient and working through the key points with them should provide the patient with sufficient understanding of the reasons for the change.

Is it the same medicine, and will it do the same job?

A confident response can be supported with the professional knowledge and data the pharmacist has on bioequivalence (see related article) and other information in this journal.

From the patient information leaflet...

'The medicine itself is not changing, only the brand. Medsafe, the agency that approves medication for use in New Zealand, approved Loxamine after carefully considering clinical study data. To gain this approval, the new supplier had to show that Loxamine delivers the same amount of the same medicine at the same rate as Aropax. This means you should have the same clinical effect from taking Loxamine as you would from Aropax. If you notice any change you should discuss this with your doctor.'

Will there be any side effects?

Understanding the potential for "new" side effects is key to an effective response to this question, and will require a considered approach from the pharmacist. Some side effects are related to the dose of medicine and are increased if the amount of medicine received is increased – others can occur when the dose of medicine received is suddenly reduced.

At the extremes of compliance with international standards of bioequivalence testing it is possible that content could vary (0.8–1.25) compared with the reference product. At these extremes the appearance of discontinuation effects are unlikely

but there is a possibility of some dose related side effects. However, information received from Pacific Pharmaceuticals shows that the results of the studies on Loxamine are well within the bioequivalence acceptance limits and that any variations in the dose received compared with Aropax are very unlikely to be clinically significant. (For more information on bioequivalence refer to page 12).

Consider the following.....

The government agency Medsafe requires that Loxamine is tested to ensure that it is equivalent to Aropax and will give the same therapeutic effect without increasing the chance of side effects.

However, equivalent does not mean identical and there will always be slight variations in the amount of medicine in tablets due to manufacturing processes. This means that there are even slight variations in the amount of medicine between individual tablets and different batches of the same brand. The testing that Medsafe requires on Loxamine means that any variation in the amount of medicine between Loxamine and Aropax is very unlikely to be any different from variations between different batches of Aropax.

It is very unlikely patients will experience any change in side effects with Loxamine but if they are concerned they should be encouraged to discuss this with their pharmacist and doctor.

Other side effects may be due to fillers and colouring used to make the tablet rather than the active medicine. A comparison of the excipients contained in Aropax and Loxamine can be found on page 17.

Patient information

Order now

Brand change notification:

Paroxetine 20 mg tablet Aropax changing to Loxamine

You are currently taking a medicine called paroxetine which is known by the brand Aropax. Other companies also make paroxetine and PHARMAC is changing the brand the government pays for (the subsidy) to Loxamine.

Why is the brand changing?

PHARMAC has reached an agreement with a new supplier of paroxetine. This provides opportunity for considerable health gains, because savings from this agreement will allow PHARMAC more funds for other medicines.

Will the medicine work the same?

Yes.

The medicine itself is not changing, only the brand. Medsafe, the agency that approves medication for use in New Zealand, approved Loxamine after carefully considering clinical study data.

This means you should have the same effect from taking Loxamine as you would from Aropax. If you notice any change don't hesitate to discuss this with your doctor.

Will the new tablets or pack look different?

Yes.

The Loxamine tablets look different as they are made by a different manufacturer, but they contain the same medicine. The size and colour of the pack will also look different, although the tablets will still come in blister packs. The tablets have a break line which makes it easier to adjust doses if needed.

If you need to break the tablet in half, place it on a dry, clean, flat surface with the break line facing up. Place your thumbs on either side of the break line and apply pressure. If you have trouble breaking the tablets please contact PHARMAC on **0800 11 22 37** to request a tablet cutter.

PHARMAC
Pharmaceutical Management Agency

Independent testing indicates that Aropax and Loxamine are very similar in taste.

There is no evidence that Loxamine is more likely to cause indigestion or is difficult to swallow. Some patients (even adults) crush tablets to make them easier to swallow. In this case, point out that any difference in taste or texture is likely to be due to different fillers which hold the tablet together and not a difference in the active medicine.

Is it made by a reputable company?

People may be interested in where Loxamine is made and the extent to which it has been used in other countries.
Loxamine tablets are manufactured in Australia. It is widely used in about 20 European countries including the UK and sales for 2005 and 2006 exceeded 150 million tablets.

Do I have a choice?

From the patient information leaflet..

'Loxamine will become available (fully subsidised) from 1 April 2007. The subsidy for Aropax will decrease from 1 June 2007, and be removed altogether from 1 September 2007. Your pharmacist will explain your options during this transition.'

There will be an expectation from the patient that the pharmacist will be fully informed of the options available to them, so pharmacists will need to be prepared for this. Explaining the change has been initiated by PHARMAC, and clearly outlining the cost implications should they choose to remain on Aropax will help the decision making process for the patient.
Patients can contact PHARMAC on 0800 66 00 50

People with mental illness experience a range of stigma and discrimination based on the attitudes and perceptions of society. The lack of understanding with regard to mental illness and the resulting stigma attached to mental illness is still evident in our communities despite of programmes such as the 'Like Minds Like Mine' campaign.

"The stigma associated with taking medication is pretty hard, at the chemist we might wait till it is empty before we get our script and asking questions is too much if there are other people in the chemist."

Culture and communication

When communicating with patients it is helpful to see things through the patient's eyes. This includes understanding cultural influences on their health and taking the time to understand what is important to your patient.

In this article we suggest an approach to cross cultural communication. While this may feel uncomfortable at first, this 'Pause, Ask and Act' approach can lead to an improvement in health care providers interactions with their patients and their families.

Pause Be aware of how your own cultural outlook impacts on the communication.

Ask Don't be afraid to ask - you're not expected to be an expert on everything.

Act Give the patient and the family the information and support they need to actively participate in the management of their own health.

'Pause'

Be aware of how your own cultural outlook might impact on the interaction with the patient

The cultural backgrounds of health care providers and patients strongly influence their values and beliefs.
These can become so entrenched that they feel intrinsically 'right'. Differences in viewpoint across the clinician-patient relationship can lead to misunderstanding, discomfort, non-cooperation and a lack of trust.

Core issues which have potential for cross-cultural misunderstandings include those relating to:

- authority
- spirituality
- physical contact
- communication styles
- gender, sexuality, and family

'Ask'

Don't be afraid to ask – you're not expected to be an expert on everything

Seeing the health issue through the patient's eyes is the key to patient-centred medicine. It is especially important in cross-cultural consultations as there are increased opportunities for misconceptions and misunderstandings.
The best way to gain an understanding of the way each individual patient sees the situation is to ask open questions. It is very unlikely that a patient would be offended if you were to ask them to give you more information on specific cultural conventions.

Issues to be explored include:

- patient's beliefs about their illness and expectations for the future
- spiritual, social, emotional and physical effects of their illness
- patient's usual social and health supports

'Act'

Create the opportunity for patients to actively participate in the management of their own health

Enabling people to participate in the management of their own or their family's health issues does not necessarily mean passing over decision making. It is more likely to include encouraging and supporting people to:

- Ask questions
- Formulate the problem
- Set goals
- Choose between management options
- Exercise control over various interventions

The degree to which people want to participate in the management of their health issues varies from person to person. People may prefer a family member to take on this active role. In some cultures this is a close male family member, in others an elder female. For example, in Māori culture with its tradition of collective responsibility and decision making the whole whānau may be involved. This concept is often referred to as a 'Whānau-centered approach'.

Pharmacists can actively encourage patients and their families to be involved in all aspects of health care and decision-making. The patient may nominate a person to speak on their behalf.

Questions that enable involvement are:

- Is there anything you want to ask?
- This is my understanding so far - is there anything you would like to add?
- What would you like to see happen from here?
- These are the options as I see them. What do you think?
- How would you like us to go about that?

Paroxetine Change Resources

- ‘Brand Change Notification for paroxetine’ patient information
- ‘My Medicine Looks Different’ patient Information leaflet
- Pill cutters

order online from www.bpac.org.nz

or phone PHARMAC on 0800 66 00 50

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Paroxetine switch home

- Quiz
- bpac depression resources
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