



## **Access by patients in New Zealand to new medicines (2000-2006)**

**How have they been faring in recent times in relation to their trans-Tasman counterparts?**

Michael Wonder, Global Pricing & Market Access

Wellington, 18 February 2010



# Disclaimer

---

- Any views presented verbally or in writing are those of the presenter and are not necessarily those of his employer, Novartis Pharmaceuticals

# Objective

---

- To compare the level & timeliness of the access of patients to innovative new prescription-only medicines in Australia and New Zealand for the period 2000 – 2006

## Context and motivation

---

- Recent acceptance for publication of a paper on timely access to new medicines in Australia

Wonder MJ, Munro AM, Parsons R. Are Australians able to access new medicines on the PBS in a more or less timely manner? An analysis of PBAC recommendations, 1999-2003. *Value in Health* 2006; 9 (3): 205-12.

- Early discussions on the scope/direction of the PBS reform package

# Study design

---

- There is no widely accepted (i.e. gold standard) analytical framework
  
- Retrospective longitudinal design
  - Best possible/most appropriate design is very much dependent on the research objective/s and key question/s
  - Given its objective, the study had to be retrospective
  - Studies of this design are prone to certain biases (i.e. selection bias, recall bias, time lag bias, etc)
  
- Study period - Jan 2000 to Jun 2006
  - A long period will increase sample size
  - Period should be contemporary
  - Increased transparency on reimbursement submissions and/or decisions in Australia from Dec 1999

# Study design

---

- Control/reference = Australia, test = New Zealand. A fair comparison?
  - Both countries are members of the OECD
  - Both countries have tax payer funded, centralised medicine reimbursement systems
  - Both use the results of economic evaluations to inform their decision-making on which medicines should be funded

# Study design

---

- Both publish which medicines are reimbursed in a Schedule which was issued during the study period on a frequent basis
  - Schedule of Pharmaceutical Benefits
  - New Zealand Pharmaceutical Schedule
- Both schedules also include medicines used primarily in hospitals
  - Section 100 (Australia)
  - Section H (New Zealand)
- One needs access to a serial collection of the respective Schedules to be able to conduct a meaningful analysis

## Study definition of access

---

- The general public was deemed to have access to a new prescription-only medicine if it was publicly reimbursed in the respective country (i.e. if it was listed in the Schedule of Pharmaceutical Benefits in Australia or in the New Zealand Pharmaceutical Schedule in New Zealand)
  - Many new prescription-only medicines are costly and unaffordable for many patients. Universal access is not possible without (public) subsidy.

# Study sample

---

## ■ Medicines

- The Pharmaceutical Schedules of both countries also include a limited range of medicinal preparations (i.e. blood glucose test strips, medicinal foods, etc). These were excluded.

## ■ Registered medicines

- In Australia, a medicine needs to be registered by the Therapeutic Goods Administration (TGA) before it can be listed in the Schedule and a medicine can only be listed in the Schedule in accordance with its registered indication/s
- In New Zealand, a medicine to be listed in the Schedule before it is registered by the New Zealand Medicines and Medical Devices Safety Authority (Medsafe)
- For the comparison to be balanced, medicines were included in the sample only if they were registered (in Australia)

# Study sample

---

- Prescription-only medicines
  - Australian and New Zealand have comparable medicine scheduling systems
  - The schedules in both countries include (a limited number of) non-prescription medicines. New non-prescription medicines were excluded. This was justified insofar as they are invariably used to treat less serious diseases/conditions and are generally available at a reasonable cost in both countries.

## Study sample

---

- New (single) chemical entities (NCEs)
  - The focus was on NCEs (i.e. pharmacological innovation) rather than new brands, formulations or strengths of existing medicines (i.e. pharmaceutical innovation). This was justified given the greater concern in both countries for access to those in the former category.
  
- New combination products were excluded
  - I assumed that patients should be able to access the component medicines separately; issues of having to make two or more patient contributions notwithstanding
  
- New vaccines were also excluded
  - In Australia, the use of vaccines is subsidised under a separate program

# Relevant sections within the Schedules

---

- **Schedule of Pharmaceutical Benefits**
  - Section 2: Ready-Prepared Pharmaceutical Benefits
    - General Pharmaceutical Benefits (Section 85)
    - Items Available Under Special Arrangements (Section 100)
  
- **New Zealand Pharmaceutical Schedule**
  - Section B (Community Pharmaceuticals)
  - Section H (Hospital Pharmaceuticals)
    - Part II (National Contract Pharmaceuticals)
  - Medicines in Part IV were excluded because universal access is not assured.

## Definition of new medicine

---

- A medicine was considered to be new if its first listing in the Schedule of Pharmaceutical Benefits occurred during the study period and this occurred no more than 10 years after its initial registration by the TGA
  - This was done to exclude any medicine that was likely to be out of patent in Australia when it was first listed
  - A medicine that been registered and deregistered only to be re-registered and subsequently listed in the study period was considered for inclusion
  - A medicine that was listed and subsequently delisted in the study period was excluded

## Definition of innovative new medicine

---

- Some NCEs were excluded on the basis that they were considered to be innovative new formulations of existing medicines (pharmaceutical innovation) rather than innovative new medicines (pharmacological innovation)
  - A new pharmacological analogue of an existing medicine, including an analogue of an existing (recombinant) biological medicine, was considered to be a new medicine
  - A new formulation of an existing medicine (i.e. salt, ester, pegylated form, glycosylated form) was considered to be a new formulation rather than a new medicine
  - A new presentation of an existing medicine that is to be administered by the *same* route (i.e. tablet versus capsule, cream versus ointment, etc) and thus be used by the same patient population was considered to be a new formulation

# Definition of innovative new medicine

---

- A new presentation of an existing medicine that is to be administered by a *different* route (i.e. injection versus tablet) *and* be used by a different patient population was considered to be a controversial new medicine
- A new enantiomer of an existing medicine was considered to be a controversial new formulation
- A new medicine that is the pro-drug of an existing medicine was considered to be a controversial new formulation
- A new structural form of an existing biological medicine (i.e.  $\beta$  versus  $\alpha$  form) was considered to be a controversial new formulation

# Data collection on innovative new medicines

---

## ■ Date of reimbursement

- Initial reimbursement = date of first listing in the respective Schedule
- Australian source – serial issues of the Schedule of Pharmaceutical Benefits (Department of Health and Ageing website)
- New Zealand source – serial issues of the New Zealand Pharmaceutical Schedule (PHARMAC website)

## ■ Date of registration

- Australian source – Australian Prescription Products Guide (APPGuide), MIMS Annual and related appendices, relevant sponsors
- New Zealand source – Medsafe website (New Zealand Gazette), relevant sponsors

# Data collection on innovative new medicines

---

## ■ Therapeutic area

- WHO ATC classification system was used as a proxy; strictly speaking it is not a therapeutic classification system
- Coded only to the first (main group) level
- Source – WHO Collaborating Centre for Drug Statistics Methodology website

## ■ Medicine schedule

- Australian source – Australian Prescription Products Guide (APPGuide) and the MIMS Annual and related appendices
- New Zealand source – Medsafe website (Classification of Medicines)

# Samples

---

- Core data set

- Innovative new medicines listed in the Schedule of Pharmaceutical Benefits in the study period

- Common data set

- Innovative new medicines listed in the Schedule of Pharmaceutical Benefits and the New Zealand Pharmaceutical Schedule in the study period

- Unique data set

- Innovative new medicines listed only in the Schedule of Pharmaceutical Benefits in the study period (i.e. Core data set – common data set)

## Access was assessed in 3 ways

---

### ■ Breadth

- Assessed by counting the number of medicines, their classification by therapeutic area (WHO ATC main group) and their initial and subsequent use (across indication)

### ■ Depth

- Assessed by examining the restrictions (if applicable) of the medicines on their initial and subsequent use (within indication)

## Access was assessed in 3 ways

---

### ■ Timeliness

- Assessed by comparing the dates of the initial reimbursement of the medicines in both countries
- The time period between these dates was calculated (in days) for each medicine, a positive value signified that the medicine was first reimbursed in Australia, a negative value signified that it was first reimbursed in New Zealand. The results were expressed as the total and average time periods.

## Additional analyses on timeliness

---

- A similar analysis was conducted for the respective dates of their initial registration
- The time period from the date of registration to the date of reimbursement was also calculated. A check was made to ensure that a medicine's first registered indication coincided with its first reimbursed indication.

## Supplementary analysis

---

- To examine the effect of the selection of Australia as the reference country
  - A determination was made of all new, prescription-only medicines that were first listed in the New Zealand Pharmaceutical Schedule in the study period

# Results

---

- 79 innovative new, prescription-only medicines (core data set) were listed in the Schedule of Pharmaceutical Benefits in the study period
  - 6 (8%) were controversial inclusions
  - 18 (23%) medicines were first listed as Section 100 items

## Common data set

---

- 23 (29%) of the medicines in the core data set were listed in the New Zealand Pharmaceutical Schedule in the study period (common data set)
  - 2 of the 23 were considered to be controversial inclusions
- 19 (83%) of the 23 medicines in the common data set were reimbursed first in the Schedule of Pharmaceutical Benefits

## Timeliness – common data set

Medicine	Disease/Condition	Listing Date (Australia)	Listing Date (New Zealand)
Entacapone	Parkinson's Disease	1/02/2000	1/11/2005
Leflunomide	Rheumatoid arthritis	1/02/2000	1/05/2002
Temozolamide	Cancer	1/02/2000	1/05/2006
Irinotecan	Cancer	1/05/2000	1/12/2002*
Naltrexone	Opiate addiction	1/02/2000	1/06/2004
Insulin aspart**	Diabetes mellitus	1/08/2000	1/11/2002
Quetiapine	Schizophrenia	1/11/2000	1/05/2001
Tramadol	Pain	1/11/2000	1/06/2003
Ursodeoxycholic acid**	Biliary cirrhosis	1/11/2000	1/02/1999
Brinzolamide	Glaucoma	1/02/2001	1/06/2004
Dorzolamide	Glaucoma	1/02/2001	1/07/1998
Oxaliplatin	Cancer	1/12/2001	5/02/2004*

\*Date of registration as its first listing in the Schedule preceded its registration

\*\* Controversial inclusion

## Timeliness – common data set

Medicine	Disease/Condition	Listing Date (Australia)	Listing Date (New Zealand)
Imatinib	Leukemia	<b>1/12/2001</b>	1/12/2002
Pioglitazone	Diabetes mellitus	<b>1/11/2003</b>	1/09/2004
Zoledronic acid	Cancer	<b>1/05/2002</b>	1/12/2002
Tiotropium	COPD	<b>1/02/2003</b>	1/02/2005
Travoprost	Glaucoma	<b>1/08/2002</b>	1/06/2004
Bimatoprost	Glaucoma	<b>1/02/2003</b>	1/08/2005
Etanercept	Rheumatoid arthritis	<b>1/07/2003</b>	1/02/2004
Ezetimibe	High cholesterol	1/08/2004	<b>1/07/2004</b>
Adalimumab	Rheumatoid arthritis	<b>1/05/2004</b>	1/01/2005
Adefovir	Hepatitis B	<b>1/12/2004</b>	1/05/2006
Thalidomide	Multiple myeloma	1/02/2006	<b>18/12/2003*</b>

\*Date of registration as its first listing in the Schedule preceded its registration

## Timeliness – registration (common data set)

---

- 15 (65%) of the medicines were registered first in Australia
- The overall between-group difference was 2,703 days (mean 114 days) in favour of Australia. This difference was not significant (one sample t test  $p = 0.24$ , 95% CI -82 to 307 days using a hypothetical mean = 0).

## Timeliness – reimbursement (common data set)

---

- The overall between-group difference was 16,183 days (mean 704 days/23 months) in favour of Australia. This difference was highly statistically significant (one sample t test  $p = 0.0004$ , 95% CI 335 to 1051 days using a hypothetical mean = 0).

## Timeliness – registration to reimbursement

---

- The time period from registration to reimbursement was shorter in Australia for 18 (79%) of the 23 medicines in the common data set
  - The earlier registration of ursodeoxycholic acid, dorzolamide and ezetimibe in New Zealand may have facilitated their earlier reimbursement

## Timeliness – registration to reimbursement

---

<b>Parameter</b>	<b>Registration – reimbursement (Australia)</b>	<b>Registration – reimbursement (New Zealand)</b>	<b>Difference</b>
Total (days)	12,055	25,648	13,593*
Mean (days)	524	1115	591 (253 – 928)
Mean (months)	17.2	36.7	19.4

\* Two tailed p value = 0.0015

## Unique data set

---

- There were 56 new, prescription-only medicines that were reimbursed only in Australia in the study period, an average of about 10 additional new listings per year
  - 15 (26%) of these medicines were first listed as Section 100 items

## Unique data set by ATC main group

---

<b>ATC Main Group</b>	<b>Number</b>	<b>Percentage</b>
N (Nervous system)	12	15
L (Anti-neoplastic)	10	13
C (Cardiovascular)	6	8
J (Anti-infective)	6	8

## Unique data set

---

Category	Disease/condition	Pharmacological class	Medicine
No listed treatment	Alzheimer's Disease	Cholinesterase inhibitor	donepezil, rivastigmine, galantamine
	Pulmonary arterial hypertension	Prostacyclin analogue	iloprost
		Endothelin receptor antagonist	bosentan
	Motor neurone disease	Glutamate antagonist	riluzole

## Unique data set

Category	Disease/condition	Pharmacological class	Medicine
New pharmacological class	Osteoarthritis	Coxib	celecoxib
	Non-urgent percutaneous intervention with intracoronary stenting	RGD mimetic	eptifibatide
	Prevention of thromboembolic events following surgery	Direct thrombin inhibitor	bivalirudin
	Atopic dermatitis	Calcineurin inhibitor	pimecrolimus
	Plaque psoriasis	Monoclonal antibody to CD11	efalizumab
	HIV infection	HIV-1 fusion inhibitor	enfuvirtide
	Non-small cell lung cancer	Epidermal growth factor receptor antagonist	gefitinib

## Unique data set

Category	Disease/condition	Pharmacological class	Medicine
New pharmacological class	Sepsis	Recombinant human activated protein C	drotrecogin
	Prevention of venous thromboembolic events	Factor Xa inhibitor	fondaparinux
	Rheumatoid arthritis	Interleukin-1 antagonist	anakinra**
	Kidney transplantation	mTOR inhibitor	sirolimus, everolimus
	Asthma	Leukotriene receptor antagonist	monteleukast
	Smoking cessation	Serotonin-noradrenaline reuptake inhibitor	bupropion
	Narcolepsy	Wakefulness promoting agent	modafinil
	Chemotherapy induced nausea	Substance P neurokinin-1 receptor antagonist	aprepitant

\*\* Not registered in New Zealand

## Unique data set

Category	Disease/condition	Pharmacological class	Medicine
New additions to existing pharmacological class	Hypertension and heart failure	Angiotensin II receptor antagonist	eprosartan
	Hypertension	Calcium channel blocker	lercanidipine
	Diabetes mellitus	Sulphonylurea	glimepiride
		Thiazolidinedione (PPAR agonist)	rosiglitazone
	Peptic ulceration and gastro-oesophageal reflux disease	Proton pump inhibitor	rabeprazole
	Acute myocardial infarction	Recombinant form of tissue plasminogen activator (fibrinolytic)	tenecteplase

## Unique data set

Category	Disease/condition	Pharmacological class	Medicine
New additions to existing pharmacological class	Heart failure	Aldosterone antagonist	eplerenone
		Beta blocker	bisoprolol
	HIV infection	Protease inhibitor	amprenavir, atazanavir
		HIV-1 reverse transcriptase inhibitor	tenofovir, emtricitabine
	Community acquired pneumonia	Fluoroquinolone	moxifloxacin
	Dyslipidemia	Fibrate	fenofibrate**
	Malignant melanoma	Alkylating agent	fotemustine
	Acromegaly	Somatostatin analogue	lanreotide
Rheumatoid arthritis and ankylosing spondylitis	TNF $\alpha$ inhibitor	infliximab	

\*\* Not registered in New Zealand

## Unique data set

Category	Disease/condition	Pharmacological class	Medicine
New additions to existing pharmacological class	Depression	Serotonin-noradrenaline reuptake inhibitor	reboxetine
	Iron overload	Iron chelator	deferiprone**
	Epilepsy	Pyrrolidine derivative	levetiracetam
	Schizophrenia	Benzamide	amisulpride
		Serotonin (5HT2) antagonist	aripiprazole
	Nausea and vomiting following cytotoxic chemotherapy or radiotherapy	Serotonin (5HT3) antagonist	granisetron
	Breast cancer	Aromatase inhibitor	exemestane

\*\* Not registered in New Zealand

## Unique data set

---

<b>Category</b>	<b>Disease/condition</b>	<b>Pharmacological class</b>	<b>Medicine</b>
New additions to existing pharmacological class	Non-small cell lung cancer	Antifolate antimetabolite	pemetrexed
	Pain	Opioid receptor agonist	hydromorphone
	Osteoarthritis	Oxicam	meloxicam
	Osteoporosis	Bisphosphonate	risedronate
	Contraception	Progestogen	etonogestrel
	Asthma	Glucocorticoid	ciclesonide

## Unique data set

Category	Disease/condition	Pharmacological class	Medicine
New formulation for new patient population (Controversial inclusion)	Spasticity of spinal and cerebral origin	Gamma amino-butyric acid (GABA) analogue	baclofen (intrathecal)**
	Opiate dependence	Opioid receptor agonist	buprenorphine**
	Glioblastome multiforme	Alkylating agent	carmustine
	Luteal phase support in IVF	Progestogen	progesterone

\*\* Not registered in New Zealand

## New Zealand as the reference country

---

- 33 innovative new medicines were listed in the New Zealand Pharmaceutical Schedule in the study period
  - 21 of these medicines are in the common data set
  - 8 medicines were first listed in the Schedule of Pharmaceutical Benefits before the study period
  - 1 medicine was first listed in the Schedule of Pharmaceutical Benefits after the study period
    - trastuzumab (early breast cancer) -1 Oct 2006
  - 3 medicines remain unlisted
    - anagrelide was rejected by the PBAC in Jun 2003
    - ropinirole was rejected by the PBAC in Mar 2006
    - pentostatin was designated as an orphan drug by the TGA on 15 May 2009

## Updated analysis

---

- Additional analysis should be undertaken because the reimbursement systems are dynamic
- Same study period for Australia but extended for New Zealand
  - Australia – listed in Schedule between Jan 2000 and Jun 2006
  - New Zealand – listed in Schedule before Feb 2010
- Same extended study period for both
  - Australia – listed in Schedule between Jan 2000 and Dec 2009
  - New Zealand – listed in Schedule before Dec 2009

## Updated analysis

---

- Of the 56 medicines in the unique data set, 53 are currently listed in the Schedule of Pharmaceutical Benefits
  - amprenavir was delisted on 1 Apr 2007
  - moxifloxacin was delisted on 1 Jan 2007
  - efaluzumab was delisted on 1 Jun 2009
- Of the remaining 53 medicines in the unique data set, only 4 remain unregistered in New Zealand
  - anakinra
  - moxonidine
  - fenofibrate
  - buprenorphine

## Updated analysis

---

Of the 49 medicines in the unique data set that are currently registered in New Zealand, 13 have since been listed in Section B of the New Zealand Pharmaceutical Schedule

- aprepitant (nausea)
- iloprost (PAH)
- bosentan (PAH)
- tenofovir (HIV infection)
- atazanavir (HIV infection)
- enfuvirtide (HIV infection)
- emtricitabine (HIV infection)
- exemestane (breast cancer)
- sirolimus (organ transplantation)
- levetiracetam (epilepsy)
- amisulpride (schizophrenia)
- aripiprazole (schizophrenia)
- bupropion (smoking cessation)

## Updated analysis

---

- Another 3 have since been listed in Section H of the New Zealand Pharmaceutical Schedule
  - eptifibatide – acute coronary syndrome
  - infliximab – rheumatoid arthritis
  - (sirolimus)
  - baclofen (intrathecal) – spasticity
  - (bupropion)

**The net effect is that there are 33 innovative new medicines that were reimbursed in Australia in 2000-2006 that are not reimbursed in New Zealand as at Feb 2010**

# Conclusions

---

- More innovative new medicines are reimbursed in Australia than in New Zealand
  - The difference is about 10 medicines per year
- Innovative new medicines are reimbursed sooner in Australia
  - The average difference is just under 2 years
- The reason for these differences is not because innovative new medicines are not registered in New Zealand or that the time that that it takes to register them is longer

# Conclusions

---

- The opportunity cost of New Zealanders not being able to access 33 innovative new medicines and having delayed access to another 32 innovative new medicines is unclear
  - It may be possible to estimate this in monetary terms
  - It is not so easy to estimate this in benefit (health) terms. The magnitude of the net benefit (to New Zealand) is unlikely to be zero.