Funding Medicines in New Zealand: Revision of the Medicines Waiting List

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Executive Summary

Earlier this year, Medicines New Zealand commissioned a paper showing that in December 2015, 81 medicines were awaiting decisions for funding and a Pharmaceutical Schedule listing by the Pharmaceutical Management Authority (PHARMAC) following positive recommendation from the Pharmacology and Therapeutics Advisory Committee (PTAC)[1].

This update shows that, 7 months later (by 31 July 2016) there were 91 medicines for 98 therapeutic indications awaiting listing on the Pharmaceutical Schedule after receiving positive PTAC recommendations. Delays to listing of these medicines range between 0.17 years and 10.25 years, and there is one medicine that is known to remain unfunded after more than 12 years.

This increase in numbers of unfunded medicines follows a significant budget increase of $39 million over 2016/17, which enabled funding of some new treatments for melanoma and hepatitis C. It would appear that, despite significant increases in funding for pharmaceuticals, the financial limitations of a capped medicines budget means that a range of medicines for patients with a variety of important diseases in New Zealand including cancer and diabetes must remain unfunded. PHARMAC has neither consulted on nor sought a Board decision for any of these products.

PHARMAC has recently (31 August 2016) amended the pictorial presentation of "How Medicines Are Funded" on its website to better reflect the prioritisation process it uses to "rank" applications following a PTAC recommendation. However, that process does not:

- show any specific process for applications PTAC has recommended for decline,
- give any indication of where the public might find information about its "high" and "low" ranked products (note PHARMAC's application tracker simply states "ranked" if this process is complete); or
- provide any way for the public to ascertain whether applications remain unfunded due to limitation in the Pharmaceutical Budget or whether PHARMAC does not regard them as worthy investments (although it does not explicitly indicate that no Board decision may be taken for those ranked as "low" priorities).

We argue that completion of the PHARMAC decision-making process for all applications would be in the interests of public good and transparency.

Limitations of the Current Study

[1] In New Zealand, the Pharmaceutical Management Agency (PHARMAC) decides which medicines will receive public funding, following advice from the Pharmacology and Therapeutics Advisory Committee (PTAC).

Given the stated timeframe of investigation ending on 31 July 2016, it is possible that medicines on the waiting list may have been funded after both PHARMAC Board and PTAC meetings after that date. There may also be some medicines for therapeutic indications that have been waiting before 2006.

Background

The Pharmacology and Therapeutics Advisory Committee (PTAC) is the primary expert clinical committee that reviews the clinical evidence around funding applications, and taking into account PHARMAC's nine decision criteria[2], makes recommendations to PHARMAC on which medicines to fund, and with what priority.

PHARMAC requires applicants to provide a health technology assessment (usually Cost Effectiveness Analyses) in their applications for funding. It also frequently performs a preliminary Health Assessment Reports (HAR) comparing the medicines in an application with a funded alternative. Both the application and PHARMAC's HAR are provided to PTAC to inform their decisions.

PTAC's recommendation, and a final HAR are then reviewed by PHARMAC staff, and an internal priority list of medicines is generated from which potential investment options are then chosen. This priority list is not published. It appears that PHARMAC then holds commercial negotiations with some applicants and, if an agreeable provisional contractual outcome can be reached, this is consulted and ultimately submitted to the PHARMAC Board for a final investment decision. Despite the expert status of PTAC, PHARMAC is not bound to accept its advice or follow its recommendations, and PHARMAC may attach a different listing priority to a medicine, make a decision that differs from PTAC's recommendation or, in many cases, make no decision at all.

While PHARMAC's Board minutes relating to funding decisions are not publicly available making any direct comparison between PTAC's recommendations and PHARMAC Board decisions impossible, , it is clear that not all products that have been recommended for funding by PTAC are the subject of a full decision-making process by the PHARMAC Board. Evidence of this can be found by cross checking published PTAC recommendations against Pharmaceutical Schedule listings, and also by referring to the "Application Tracker" on PHARMAC's website which lists a number of applications as "ranked" or "under assessment".

The intent of this report and analysis is to update the list of PTAC recommendations for new listings and recommendations for widened access to medicines that are already listed from that published earlier this year, to calculate how long patients have been waiting for these medicines, and to calculate how long the groups of medicines in each priority category (as allocated by PTAC) have been awaiting funding. This enables an expanded and accurate estimate of the list of medicines that have received a positive recommendation for funding by PTAC, but are yet to be funded.

[2] PHARMAC's nine decision criteria are to be replaced by 12 Factors for Consideration in mid-2016.

Method

Minutes from quarterly PTAC meetings were assessed from February 2006 (the first year that these were reliably published online) to July 2016. Generation of a tabulated list of therapeutic agents, including vaccines (the latter of which came under PHARMAC responsibility from 2013 onwards) was then undertaken using the following metrics:

- PTAC meeting date for first positive recommendation
- Intended Indication/indications
- PTAC first recommendation (decline, list, referral to subcommittee etc.) and priority status (positive recommendations only and any changes in priority status).

PTAC's recommendations were reviewed from publicly available minutes (those published on the PHARMAC Website as of July 2016) and these were compared with the list of medicines (including vaccines) funded by PHARMAC as published in its Pharmaceutical Schedule (including more recently, the Hospital Medicines List (HML)) – again as at July 2016.

We have included PTAC recommendations for widened access to medicines that already have a listing on the Pharmaceutical Schedule (i.e. to fund medicines with less restrictive special authority criteria, for wider population coverage or new indications).

Results

Minutes for over 400 individual therapeutic agents/medicines or indications were considered in the quarterly meetings of PTAC from February 2006 through to July 2016. Of those around 60% were given a positive recommendation from PTAC (to list on the HML or Pharmaceutical Schedule with a positive priority (usually a high, medium, moderate, or low priority) or only if cost-neutral).

However, 118 (around half) of those positive recommendations were still awaiting a final PHARMAC funding decision on inclusion in the Pharmaceutical Schedule as at July 2016 (See Table 1).

The longest waiting time for a medicine was 10.25 years for telmisartan (although adrenalin auto injector for anaphylaxis which first received a medium priority in November 2005 but remains unfunded in fact has the longest known waiting time of more than 12 years). The second longest waiting period was 9.75 years for fluvestrant for post-menopausal locally advanced or metastatic breast cancer. The shortest waiting time is 0.17 years to fund for nivolumab (non-small cell lung cancer), PAH treatments including selexipag, taurolidine and citrate solution, denosumab and saproterin.

Table 1. The positive recommendations of PTAC since 2006 that have yet to be listed on the New Zealand Pharmaceutical Schedule as of 31 July 2016

Product	Indication	New listing or wider access	Date of Positive Rec	Date of Positive Recommendation	Waiting Period (Years)
	GREATER THAN 5 YEARS WAIT				
Telmisartan	Hypertension	New	May-06	Only if cost-neutral	10.25
Fluvestrant	Locally advanced metastatic breast cancer	New	Nov-06	Low	9.75
Desogestrel	Contraception	New	Aug-07	Low	9.00
Dornase Alfa	Cystic fibrosis under 6 years	Widen Access	Feb-16	Medium	9.00
Ketotifen fumarate	Occular allergy	New	May-08	Only if cost-neutral	8.25
Oxybutinin patches	Urinary incontinence	New	Jul-08	Low	8.08
Pemetrexed	First line treatment of non-squamous non-small cell lung carcinoma	New	Jul-08	Only if cost-neutral	8.08
Bimatoprost and timolol Eye Drops	Glaucoma	New	Feb-09	Only if cost-neutral	7.50
Rosuvastatin	3rd line hypercholesterolemia	New	Feb-09	Medium	7.50
Travoprost and timolol Eye Drops	Glaucoma	New	Feb-09	Only if cost-neutral	7.50
Buprenorphine transdermal patch	Moderate to severe pain	New	May-09	Low	7.25
Duloxetine hydrochloride	Treatment of major depressive disorder that is not responsive to other antidepressants	New	Jul-09	Only if cost-neutral	7.08
Sitaglipten	Type 2 diabetes	New	Aug-09	Low	7.00
Bevacizumab	Metastatic Colorectal Cancer	New	Feb-10	Low	6.50

Golimumab	Second-line TNF-inhibitor treatment of rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis	New	May-10	Low	6.25
Ibrutinib	Relapsed or refractory mantle cell lymphoma (MCL) that has progressed within 24 months of allograft or chemotherapy or chemo-immunotherapy	New	Nov-15	Low	6.25
Levofloxacin	Treatment for helicobacter infection	New	May-10	Other	6.25
Methoxyflurane	PSO	Widen Access	Feb-16	Low	6.25
Metronidazole vaginal gel	Vaginal infections	New	May-10	Only if cost-neutral	6.25
Sildenafil	Fontan patients	Widen access	May-10	High	6.25
Sildenafil	Neonatal/infantile PAH secondary to CLD	Widen access	May-10	Medium	6.25
Quetiapine modified-release tablets	Schizophrenia and other psychoses	New	Jun-10	Low	6.17
Pipobroman	Polycythemia rubra vera and essential thrombocythemia	New	Aug-10	Medium	6.08
Deferiprone	Iron Overload secondary to acquired anaemia	Widen access	Nov-10	Medium	5.75
Miglustat	Mild to moderate Type 1 Gaucher's disease	New	Nov-10	Low	5.75
Nab-paclitaxel	Advanced breast cancer	New	Nov-10	Only if cost-neutral	5.75
Trastuzumab	HER2 positive metastatic gastric cancer	Widen access	Feb-11	Low	5.50
	3-5 YEARS WAIT				
Cevimeline	Dry Mouth	New	Aug-11	Low	5.00
Pregabalin	Neuropathic pain	New	Aug-11	Low	5.00

Rituximab	Relapsed/Refractory follicular non-Hodgkins lymphoma	Widen access	Aug-11	Low	5.00
Ustekinumab	Psoriasis	New	Aug-11	Only if cost neutral	5.00
Saxagliptin	Type II diabetes	New	Nov-11	Low	4.75
Dutasteride	BPH	New	Feb-12	Only if cost-neutral	4.50
Eplerenone	Heart failure patients intolerant to optimal dosing of spironolactone	New	Nov-15	Low	4.50
Asenapine	Schizophrenia and Bipolar 1 Disorder	New	Aug-12	Only if cost neutral	4.00
Linagliptin	Type 2 diabetes.	New	Aug-12	Low	4.00
Liraglutide	Type 2 diabetes.	New	Aug-12	Low	4.00
Telaprevir	Genotype 1 chronic hepatitis C	New	Aug-12	High	4.00
TNF Inhibitors	Behçet's Disease	Widen access	Aug-12	Medium	4.00
Tocilizumab	Rheumatoid arthritis	Widen Access	Nov-15	Only if cost neutral	4.00
Melatonin	Psychiatric comorbidities and secondary insomnia associated with dementia	New	Nov-12	Low	3.75
Sildenafil	Cardiac Surgery	Widen access	Nov-12	Hosp only	3.75
Carbetocin	Uterine atony and excessive bleeding following elective caesarean	New	Feb-13	Only if cost neutral	3.50
Rilpivirine	HIV	New	Feb-13	Only if cost neutral	3.50
Nab-paclitaxel	Metastatic breast cancer	New	Aug-13	Low	3.00
Rotavirus vaccine	Universal childhood vaccine	New	Aug-13	Medium	3.00

Vitamin D	Admin to pregnant women for prophylaxis of rickets in infants at high risk	New	Aug-13	Only if cost neutral	3.00
Vitamin D	Admin to infants at high risk of rickets	New	Aug-13	Only if cost neutral	3.00
Vitamin D	Treatment of infants with rickets	New	Aug-13	Low	3.00
	1-3 YEARS WAIT				
Adalimumab	Weekly dose rescue therapy for Crohn's Disease	Widen Access	Nov-13	Low	2.75
Ciprofloxacin eye drops	Chronic suppurative otitis media	Widen access	Nov-13	High	2.75
Dapaglifozin	Type 2 diabetes	New	Nov-13	Low	2.75
Melatonin	Secondary insomnia in children and adolescents with neurodevelopmental or psychiatric comorbidities	New	Feb-14	Low	2.58
Nab-Paclitaxel	Previously experienced hypersensitivity reactions to paclitaxel or docetaxel	New	Feb-14	Only if cost neutral	2.58
Pertuzumab	First line patients with HER-2-positive metastatic breast cancer in combo with trastuzumab and docetaxel	New	Feb-14	Low	2.58
TNF alpha inhibitors	Inflammatory bowel disease associated arthritis (IBD-A)	Widen Access	Feb-14	Low	2.58
Acitretin	Relax SA	Widen Access	May-14	None	2.25
Adrenlaline auto injector	Patients that have experienced anaphylactic reaction to venom or food	New	May-14	Medium	2.25
Apixaban	Prophylaxis of venous thromboembolism following major orthopaedic surgery	New	May-14	Only if cost neutral	2.25
Apixaban	Stroke prevention in non-valvular atrial fibrillation	New	May-14	Low	2.25
Aripiprazole depot injection	Schizophrenia	New	Nov-15	Only if cost neutral	2.25

Gabapentin	Remove SA	Widen Access	May-14	None	2.25
Intracavernosal alprostadil	Erectile dysfunction related to spinal cord injury	New	May-14	Medium	2.25
Ipilibumab	Previously treated and unresectable stage III or IV melanoma	New	Feb-16	Low	2.25
Isotretinoin	Relax SA	Widen Access	May-14	None	2.25
Lixisenatide	Adults with Type II diabetes	New	May-14	Low	2.25
Midodrine	Relax SA	Widen Access	May-14	None	2.25
Minoxidil	Remove SA	Widen Access	May-14	None	2.25
Phosphodieraterase V inhibitors (PDE5 inhibitors	Erectile dysfunction related to spinal cord injury	New	May-14	Medium	2.25
Rivaroxaban	Venous thromboembolism	New	May-14	Only if cost neutral	2.25
Rivaroxaban	Secondary prohylaxis of venous thromboembolism	New	May-14	Only if cost neutral	2.25
Rivaroxaban	Stroke prevention in non-valvular atrial fibrillation	New	May-14	Only if cost neutral	2.25
Stribild	HIV-1	New	May-14	Only if cost neutral	2.25
COX-2 inhibitors	Arthritis	New	Aug-14	Only if cost neutral	2.00
Ingenol mebutate 0.015%	Facial and scalp solar keratosis	New	Aug-14	Only if cost neutral	2.00
Nicotine inhaler and oral spray	Smoking cessation	New	Aug-14	Only if cost neutral	2.00
Nicotine replacement therapy sample packs	Smoking cessation	New	Aug-14	Only if cost neutral	2.00
Sofosbuvir	Hep C - all	New	Aug-14	Low	2.00

Aminolevulinic acid	Visulisation of glioma	New	Nov-14	High	1.75
Epoprostenol	PAH	New	Nov-14	High	1.75
Rotigotine transdermal patch	Parkinsons disease	New	Nov-14	Only if cost neutral	1.75
Sub-cutaneous trastuzumab	HER 2 positive breast cancer	New	Nov-14	Only if cost neutral	1.75
Obinutuzumab	First line treatment of Chronic Lymphocytic Leukaemia	New	Feb-15	Medium	1.42
Omalizumab	Chronic sponteneous urticaria	Widen Access	Nov-15	Low	1.42
TNF alpha inhibitors	Undifferentiated spondyloarthritis	Widen Access	Feb-15	High	1.42
Denosumab	Osteoporosis	New	May-15	Medium	1.17
Indacterol maleate/glycopyrronium	Chronic obstructive pulmonary disease	New	May-15	Low	1.17
Macitentan	Pulmonary arterial hypertension	New	May-15	Low	1.17
Pertuzumab	Metastatic HER2 positive breast cancer	New	May-15	Low	1.17
Plerixafor	Stem cell mobilisation - HML	New	May-15	High	1.17
Pomalidomide	Relapsed or refractory multiple myeloma	New	Feb-16	Low	1.17
Sofosbuvir with ledipasvir	Hepatitis C - all other sub-populations	New	May-15	Low	1.17
Topical NSAID	Osteoarthritis	New	May-15	Low	1.17
Ustekinumab	Severe chronic plaque psoriasis	New	May-15	Only if cost neutral	1.17
Varenicline	Smoking cessation - reduce re-treatment interval	Widen Access	Feb-16	Low	1.17

	LESS THAN 1 YEARS WAIT				
Bendamustine	Chronic Lymphocytic Leukaemia Non-Hodgkin's Lymphoma - unable to tolerate fludarabine, cyclophosphamide and rituximab (FCR)	New	Aug-15	Medium	0.92
Bendamustine	Chronic Lymphocytic Leukaemia Non-Hodgkin's Lymphoma - first line	New	Aug-15	Low	0.92
Bevacizumab	First line treatment of recurrent, persistent or metastatic cervical cancer	New	Aug-15	Low	0.92
Insulin Pumps	Type I diabetes in Pregnancy	New	Aug-15	Low	0.92
Lidocaine 4% with Adrenlaline 0.1% and tetracaine 0.5%	Wound repair - children	New	Aug-15	Medium	0.92
Lidocaine 4% with Adrenlaline 0.1% and tetracaine 0.5%	Wound repair - unrestricted	New	Aug-15	Low	0.92
Pemetrexed	Advanced non-squamous non-small cell lung carcinoma - maintenance	New	Aug-15	Low	0.92
Pemetrexed	Advanced non-squamous non-small cell lung carcinoma - second line	New	Aug-15	Only if cost neutral	0.92
Rituximab	Resistant nephrotic syndrome	Widen Access	Aug-15	Medium	0.92
Sodium chloride prefilled syringe	Sterile procedures	New	Aug-15	High	0.92
Subcutaneous tocilizumab	Adult rheumatoid arthritis - last line	New	Aug-15	Low	0.92
Tolcilizumab	Polyarticular juvenile idiopathic arthritis	New	Aug-15	Medium	0.92
Zoster vaccine	65 years and older	New	Aug-15	Medium	0.92
Zoster vaccine	People aged 65 with a 2 year catch up (65-80 years)	New	Feb-16	Low	0.92
Idarucizumab	Dabigatran reversal	New	Nov-15	Medium	0.42

Varenicline	Smoking cessation - 2 week starter and follow-on packs	Widen Access	Feb-16	Only if cost neutral	0.42
Nivolumab	Locally advanced or metastatic non-small cell lung cancer	Widen Access	May-16	Low	0.17
PAH treatments	Dual Therapy for patients with PAH in NYHA/WHO functional class III and IV following 3-6 month monotherapy with sildenafil	Widen Access	May-16	High	0.17
PAH treatments	Dual Therapy for patients with PAH in NYHA/WHO functional classes II	Widen Access	May-16	Low	0.17
Pembrolizumab	Metastatic or unresectable melanoma stage III or IV	New	Nov-15	Low	0.17
Sapropterin	Phenylkenouria and hyperphenylalaninaemia for women pregnant or planning a pregnancy	New	May-16	High	0.17
Selexipag	Pulmonary Arterial Hypertension	New	May-16	Low	0.17
Taurolidine and citrate solution	Section H - locking of central venous access devices in those at high risk of developing central line-associated bacteraemia	New	May-16	OICN	0.17

From a summary of the PTAC priority categories (Table 2), there appears to be a reasonable level of correlation between the priority of the PTAC recommendation and the length of waiting times (i.e. mean waiting time for high priority medicines seems to be lower than that for medium and low).

Table 2. Waiting times by priority category to July 2016

PTAC priority category	Number of recommendations	New Listings	Widened access	Mean waiting time (years)	Range of waiting times
High	10	6	4	2.03	0.17-6.25
Medium	18	13	5	3.11	0.42-9.00
Low	50	41	9	3.29	0.17-9.75
Only If Cost Neutral	33	31	2	3.68	0.17-10.25
None/Other	7	1	6	3.04	2.25-6.25
TOTAL	118	92	26	3.25	0.17 -10.25

The mean waiting times for all medicines on this list has increased from that in December 2015 to 3.25 years, with the same significant range in waiting times (0.17 to 10.25 years). Most interestingly, the majority (78%) of the outstanding recommendations appear to be for new listings (i.e. recommendations for a range of new medicines rather than widened access to existing funded medicines).

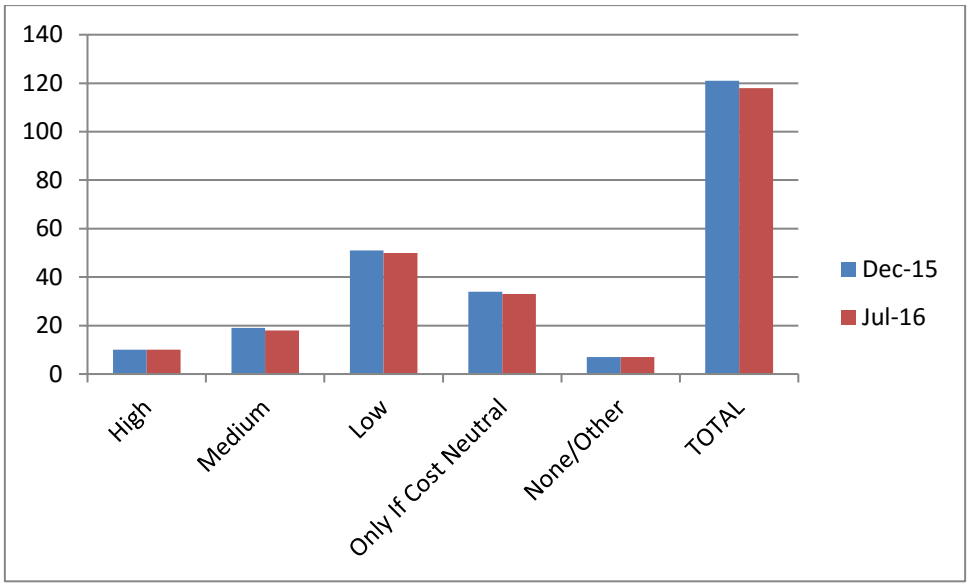
Table 3. Change in Mean Waiting Time and Range of Waiting Time

PTAC priority category	Mean waiting time (years) Dec 2015	Mean waiting time (years) Jul 2016	Range of waiting times to Dec 2015	Range of waiting times to Jul 16
High	2.03	2.03	0.17-6.25	0.17-6.25
Medium	2.50	3.11	0.17-7.5	0.42-9.00
Low	2.89	3.29	0.17-9.75	0.17-9.75
Only If Cost Neutral	3.45	3.68	0.17-10.25	0.17-10.25
None/Other	3.04	3.04	2.25-6.25	2.25-6.25
TOTAL	2.78	3.25	0.17 -10.25	0.17 -10.25

Discussion

The last 6 months, and the Governments' recent $39 injection into PHARMAC's annual budget, have seen a slight reduction in the number of pharmaceuticals waiting to be listed on the Pharmaceutical Schedule (see **Graph 1**).

Graph 1. Change in waiting times by priority category July 2016 compared to December 2015



However, the overall increase in the number of unfunded pharmaceuticals that have received a positive recommendation from PTAC, and with overall waiting times growing despite significant additional investment, it is clear that some further action is required. We suggest that it is time PHARMAC reduced the list of potential investments by completing the decision-making process for those pharmaceuticals on the list that it has no intention of funding. Some of those recommendations date back 10 years or more. Almost half of them have been on the list for 3 years or more.

It is clear that, over time PHARMAC changed its original policy and practice of processing all applications to a decision by the PHARMAC Board. The diagram of the Decision Making Process available on PHARMAC's website, which until recently remained largely unchanged since PHARMAC's inception in 1993, indicated that *all* applications to list pharmaceuticals in the Pharmaceutical Schedule, once reviewed by PTAC, then undergo a process of prioritisation, negotiation with the supplier, consultation and a Board Decision. The diagram did not indicate that this process is followed only for those pharmaceuticals that ultimately gain a listing. However, that is predominantly the case nowadays. PHARMAC recently (31 August 2016) replaced that diagram with a pictorial presentation showing more clearly how it prioritises applications. However, it is not clear whether it prioritises those application PTAC recommends to decline and clearly shows that those assigned a "low" ranking (as opposed to PTAC recommendation) may still simply be left unresolved.

Data presented in PHARMAC's Annual Reviews until 2003 suggest that the full processing of all applications to a Board decision was once followed. Until then, PHARMAC published a list of "Applications Declined by the PHARMAC Board". These tables also provided a reconciliation of applications received, listed and declined and reported the percentage "success" rate. It should be noted that in 1994 and 1995, twenty (20) applications were considered and declined by the

PHARMAC Board.[3] Those numbers were down to between two and four per year by the year 2000[4]. Annual Reviews since 2004 have omitted to publish this information.

Indeed, since 2003, PHARMAC has consulted on just a few proposals to decline to list pharmaceuticals on the Pharmaceutical Schedule – e.g. acetylcholinesterase inhibitors (2003), trastuzumab (2008), budesonide capsules, memantine (2010) and eculizumab (2013). The rest of the applications received, reviewed and given a positive recommendation by PTAC now remain unresolved.

Are we really to believe that the single or biggest factor holding back funded access to these drugs is lack of money? Or are there among them, a number of products that PHARMAC has no intention of funding for other reasons? If so, surely consulting on declining these applications and taking them to the PHARMAC Board for a decision would result in greater transparency around all applications, in particular those that PHARMAC considered to be priority for funding, and around any remaining funding shortfalls.

[3] "Applications considered and decided" table Page 17, Annual Review, 1996
[4] Applications declined by the PHARMAC Board" table Page 26, Annual Review, 2003