9 April 2010

Committee Secretary
Senate Community Affairs References Committee
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Submission to the Inquiry into Consumer Access to Pharmaceutical Benefits

Dear Ms Bleeser

In 2005 Access Economics estimated that the allocated health costs nationally for people with MS were $117.1m. At $74.2m (62%), pharmaceutical costs were the largest component of this, with high care residential costs (19%) and inpatient costs (12%) the other two major health cost components.

In short, for people with MS, the PBS is a major aspect of ensuring that their health care needs are met. Consequently, MS Australia welcomes this inquiry and appreciates the opportunity to provide this submission to the Senate Community Affairs References Committee.

The PBS is a central part of Australia's health system and operates under the National Medicines Policy. The central objective of the Medicines Policy is "to meet medication and related service needs, so that both optimal health outcomes and economic objectives are achieved."[1] .

In relation to the Inquiry's terms of reference, our submission focuses primarily on this objective and the last term of reference of this Inquiry: 'any other related matters'.

If you require any further information, please contact:

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[1] Department of Health and Ageing, *National Medicines Policy, 2000* (Canberra: Commonwealth Department of Health and Ageing, 1999).

1. Multiple Sclerosis

Multiple sclerosis (MS) is a progressive, chronic disease of the central nervous system (brain and spinal cord). It is the most frequent neurological disease in young and middle-aged adults in developed countries and has a lifelong impact[2]. Because MS involves multiple areas of the central nervous system, it is characterised by a variable and complex range of symptoms, including visual disturbance, fatigue, pain, reduced mobility and coordination, cognitive impairment, and mood changes.[3]

Diagnosis usually occurs in a person's 20s or 30s, with a peak at 25-30 years. Thus, MS tends to strike people in their most productive years. It affects ability to fulfil expected life roles at a stage when careers, relationships, and adult life in the community are consolidating, with resulting impact on work, family, and social life.[4]. Consequently, MS may result in profound biographical disruption.[5]

The typical course of MS is initially relapsing-remitting, with symptoms partially or completely disappearing during remissions.

However, after about 10 years, the majority of people enter a secondary progressive phase and disability gradually accumulates. For a smaller group, the disease course is primary progressive, with ongoing worsening of the initial presentation.[6]

Importantly, the last decade has brought changes in medical management, with the introduction of disease-modifying drugs that reduce exacerbations in relapsing-remitting MS, resulting in less unpredictability in the early stages of the disease. [7]

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[2] Johnson, K.L., Yorkston, K. M., Klasner, E. R., Kuehn, C. M., Johnson, E., & Amtmann, D. (2004). The cost and benefits of employment: A qualitative study of experiences of persons with multiple sclerosis. *Archives of Physical Medicine and Rehabilitation*, *85*, 201-209.

[3] Polman, C. H., Thompson, A. J., Murray, T. J., & McDonald, W. I. (2001). *Multiple Sclerosis: The Guide to Treatment and Management* (5th ed.). New York: Demos

[4] Metz, L. (2003) The psychosocial consequences of multiple sclerosis. In W. I. McDonald & J. H. Nosworthy (Eds.), *Multiple Sclerosis 2* (pp. 329-339). Philadelphia, PA: Butterworth-Heinemann

[5] Reynolds, F, & Prior, S. (2003). "Sticking jewels in your life": Exploring women's strategies for negotiating an acceptable quality of life with multiple sclerosis. *Qualitative Health Research*, *13*, 1225-1251.

[6] Demetriou, M. (2005). Multiple sclerosis, genetics, and autoimmunity. In M. J. Olek (Ed.), *Multiple Sclerosis: Etiology, Diagnosis, and New Treatment Strategies* (pp. 103-112). Totowa, NJ: Humana Press.

[7] Calabresi, P. A. (2004). Diagnosis and management of multiple sclerosis. *American Family Physician*, *70*, 1935-1944.

2. Economic impact of MS

There are significant costs associated with having MS. Access Economics found that the average annual costs to people with MS and their families in Australia is $10,500 ($3,893 out-of-pocket and $6,593 for informal care). This is consistent with other cost data for chronic illness.[8]

Although 87% of people with MS are of working age, and most people with MS are employed when first diagnosed, 80% are not employed 10 years after diagnosis. Australian longitudinal data shows that there has been a 5.9% increase in the number of people with MS not in the paid workforce (up to 64.2%) between 2003 and 2007.[9]

Consequently, although many people with MS are employed initially, ultimately most end up on fixed incomes provided through part and full pensions. The combination of low incomes and the high economic costs of MS mean that the structure of Government programs (including co-payments, subsidy levels for medications, equipment and home modifications) are critical financial factor in their daily lives.

Access Economics found that in 2005, over 50% of people with MS under the age of 65, and 84.1% of people with MS aged over 65 were receiving Government income support. This compares with the general population where 16.6% of those under 64 and 70.6% of those aged 65 and over received some form of income support payment.[10]

3. Access to pharmaceutical benefits for people with MS

The five existing MS immunomodulatory agents that are subsidised by the PBS are of great benefit to people with MS. The subsidised access to these treatments is an important part of the overall management of the disease in Australia. Without the PBS subsidy these treatments would be out of reach for most people.

There are, however, a number of general issues around access to pharmaceuticals that we want to raise in this brief submission. These issues are frequently raised with MS Australia by people with MS and their families.

While commercial and budget tensions are a necessary reality in the Australian system, the prominence and combination of these imperatives combined with the lack of structural involvement of consumers and consumer groups in the PBS processes can hinder the achievement of the objectives of the PBS in the delivery of timely access to effective medicines, quality of use of medicines and cost.

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[8] Access Economics, Acting Positively: Strategic Implications of the economic Cost of Multiple Sclerosis in Australia*, Canberra 2005*

[9] Simmons, RD, Tribe, KL, McDonald, EA: Living with multiple sclerosis: longitudinal changes in employment and the importance of symptom management. Journal of Neurology, in press 2010

[10] Access Economics 2005

In essence there are 3 elements to the broad question of improving access to pharmaceutical benefits for people with MS. These are:

3.1. Widening subsidised access to *existing agents* available on the PBS

Pharmaceutical therapies are the primary avenue of minimising the progression of MS. Currently the 5 PBS listed MS drugs are only available to those who have had two episodes/exacerbations in a two year period.

This is contrary to the best available evidence that makes it clear that the earliest possible intervention can have a significant long term impact on the progression of MS.

Based on the evidence currently available, neurologists strongly recommend that drug therapies are applied immediately when MS is first suspected through a clinically isolated syndrome (CIS), to help ensure progress of the disease is minimised

There have been four large-scale clinical trials have been conducted to determine whether early treatment following a CIS can delay the second clinical event, and therefore the diagnosis of clinically definite MS.

The results of these US trials and the Food and Dug Authority's subsequent approval of expanded labelling for Avonex, Betaferon, and Copaxone indicate earliest possible treatment for MS, in order to delay the development of permanent clinical disabilities.

The details of these trials are in Appendix 1.

It is essential that current PBS rules around access to drug therapies for diagnosed MS are modified so that consumers can access these immediately upon MS being a possible/likely diagnosis.

3.2 Widening subsidised access to *symptom treating agents* currently only available off-label

There are numerous drugs listed on the PBS and therefore accessible to consumers with particular conditioners that are also known to be effective for other conditions but not available through PBS.

This is a broad issue that needs to be addressed urgently. In relation to MS two of these drugs are Neurontin (Gabapentin) and Modafinil (provigil).

Gabapentin is available to help manage neurogenic pain and is used widely in inpatient cancer care and also by people with MS via private scripts. It is listed on the PBS for epilepsy and not for cancer or MS.

Neurogenic pain is a well recognised and commonly debilitating symptom of MS, and treatment options are limited.

Gabapentin is a proven and effective pharmacological treatment for people with MS, however the only option for people is to pay full price through private scripts at a cost of $62.60 (rrp) for 100 tablets.

Similarly, Modifanil is available to people with narcolepsy, but is not available to people with MS via PBS to help them manage their extreme and debilitating fatigue – one of the major and most common symptoms of MS. Modifanil costs $361(rrp) for 60 tablets.

This situation is only going to change if the manufacturers or licence holders initiate a submission for listing to the PBAC for these drugs for people with MS. Our current understanding is that it is up to the pharmaceutical companies to request these to be listed for MS, but the decision to invest in a listing submission in Australia is a commercial one.

The case of erectile dysfunction drugs is in this class of symptom relieving agents but the situation is slightly different in that several efficacious drugs were available through PBS (two forms of alprostadil) until 2001. These were removed from the PBS at the same time that the PBAC's recommendation for a limited listing of sildenafil citrate (Viagra) was declined by the Health Minister.

This is a significant omission from the PBS. There is now no PBS subsidy available to men with MS and other illnesses for products to treat erectile dysfunction.

The fact that there were two subsidised products and a recommendation for a third means that the clinical and cost-benefit arguments has been settled for the target groups, so these products need to be listed on the PBS.

3.3. Gaining rapid access to *new agents* coming to market

Currently a number of oral treatments are under evaluation by the TGA that are eagerly awaited by the MS community. As an alternative to regular injections, they provide additional, less onerous treatment options. A number of other MS specific drugs are in the pipeline and are also keenly anticipated.

It is important that access to these treatments is timely, safe and cost effective.

4. Employment, Productivity and management of MS

In recent Australian research, management of symptoms was cited as a significant issue in employment longevity. Fatigue was the most common reason given for loss of employment. Other symptoms such as pain, heat stress and physical problems are also major factors influencing decisions to leave employment[11].

These, combined with behavioural and workplace accommodation issues combine to lower the participation of people with MS in the Australian workforce.

[11] Simmons et al.

Figure 1: Symptom related reasons cited for leaving employment:[12]

	Self-reported reason for leaving employment	% of respondents indicating had left employment due to MS, 2007 (n = 619)
Impact of MS symptoms	Fatigue	69.5
	Physical problems with legs or feet	43.8
	Physical problems with arms or hands	39.4
	Difficulty with memory, concentration or thinking	36.7
	Balance or dizziness	31.2
	Heat sensitivity	30.0
	Pain	23.3
	Bladder or bowel problems	23.1
	Poor vision	17.1
	Tremor	14.9
	Non-pain sensation symptoms	13.1
	Speaking difficulties	9.7

(Source: Simmons et al 2010)

Affordable access to symptom managing agents to manage fatigue and neurogenic pain mentioned above would have beneficial effects on productivity and continuity of employment for people with MS.

However they are only available off-label and so are not widely used. It is also important to note that these issues are frequently raised by people with MS in numerous forums regularly, particularly in requesting ways to solve what is for many of them, a significant barrier to staying at work.

4.1 Workplace Modification Scheme

If ways cannot be quickly found to get Gabapentin and Modafinil listed on PBS, the Australian Government's Workplace Modification Scheme may be able to provide a partial access solution for people with MS in the workforce.

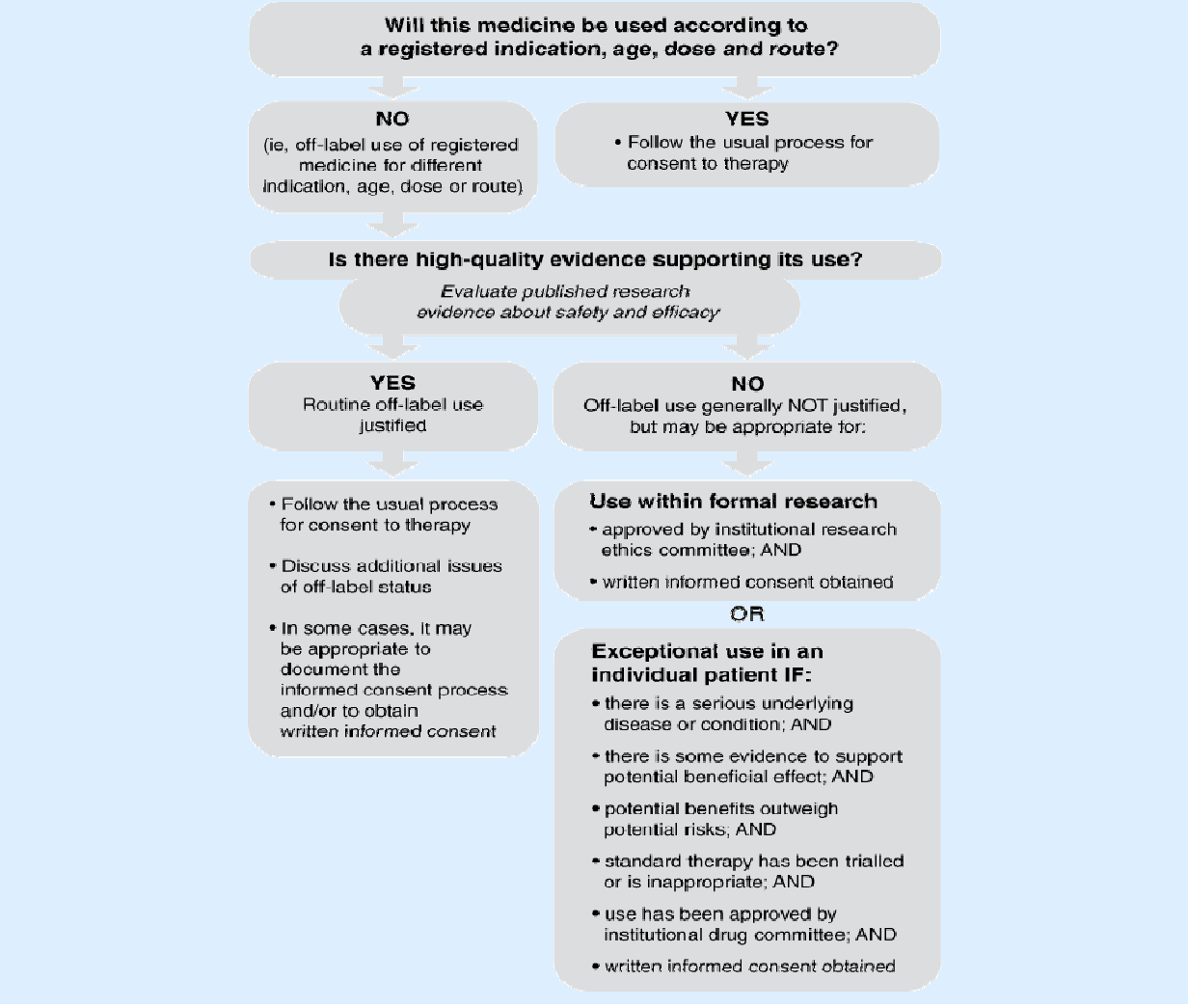
[12] Simmons et.al

This program sits within the Department of Education, Employment and Workplace Relations (DEEWR), and is designed to provide equipment and modifications that are essential for a person with a disability gaining or maintaining employment.

A range of modifications are available through this scheme including specialised technology, mobility aids and access modifications. Drugs to minimise fatigue and neurogenic pain are legitimate aids to work performance, however, they do not currently fund off-label medications.

Off-label medications such as these are regularly funded by compensation schemes and private funders after carefully assessing the clinical and functional appropriateness of medications on an individual basis. One particularly useful decision making model that would be suitable for the Workplace Modifications Scheme is described in Gazarian et.al.[13] and depicted below.

Figure 2 Assessing appropriateness of off-label medicines use



[13] Madlen Gazarian, Maria Kelly, John R McPhee, Linda V Graudins, Robyn L Ward and Terence J Campbell: Off-label use of medicines: consensus recommendations for evaluating appropriateness, Medical Journal of Australia 2006; 185 (10): 544-548

As a short term measure the PBAC administrators could work with the DEEWR Workplace Modification Scheme to design and implement a model that would provide off-label symptom managing agents to eligible people with chronic disease through the Workplace Modifications Scheme.

While this is not a long term equitable solution to achieving affordable access to these products, it would address access to those people for whom it is an urgently needed and reasonable workplace modification.

5. Recognition of productivity in listing evaluations

The cost effectiveness of new therapeutic groups being evaluated and their impact on new drugs should include a requirement for a robust analysis of the impact on productivity. This is pertinent in MS due to the chronic and cumulative disability and disease costs, and the impact of disease symptoms on employment participation.

While productivity is difficult to measure within patient groups, it is something that is becoming important in the wider health reform debate in Australia, with the Prime Minister recently describing health reform as a key economic policy issue.

6. Role of Consumer Groups in PBAC listing evaluation

The Government has improved the transparency and opportunities for participation by consumers and consumer groups in recent years which is very welcome and provides useful information to the PBAC. However this is a fundamentally a reactive, not proactive, role.

The examples above indicate that there is a need for other mechanisms to be available to seek the listing of pharmaceutical that fall into this situation. Other avenues for consumers or their organisations to seek listings may be one vital option to ensure adequate and appropriate access is achieved.

7. Costs of Generics

Pharmaceuticals are a major cost for people with MS, and other chronic illnesses. The 12.5% reduction for the use of generics is helpful, but a move to a 25% discount for using generics would provide a larger incentive for their use, and would have more impact on reducing the cost of chronic illness borne by these individuals and families.

8. Copayments

People with MS and other chronic conditions cannot afford any increase in co-payments for PBS medications. Even the smallest increase in copayments can have a significant impact on people with such a large reliance on PBS, and many of whom are living on low incomes as a consequence of their illness.

Appendix 1: Clinically Isolated Syndrome trial outcomes

The **CHAMPS** (Controlled High-Risk Subjects Avonex® MS Prevention Study) study was designed to determine whether

1) using interferon beta-1a (Avonex) early in demyelinating disease could delay the second episode of demyelination (which would signal clinically definite MS), and:

2) treatment would have an impact on MRI-detected brain lesions. The subjects in the study had each experienced a single, isolated neurological event suggesting demyelination and had multiple, clinically "silent" (without symptoms) MRI lesions, making them at high risk for a second neurological event and therefore a diagnosis of clinically definite MS.

The results indicated that interferon beta-1a significantly delayed the onset of clinically definite MS, as indicated by a delay in a second clinical attack. In addition, MRI findings showed that the patients receiving interferon beta-1a had a significantly smaller increase in the volume of brain lesions, as well as fewer new lesions.[14]

Based on the results of this study, the Food and Drug Administration (FDA) extended the labelling of Avonex) to include individuals who experience their first clinical episode and have MRI-detected brain lesions consistent with multiple sclerosis.

The **ETOMS** (Early Treatment of MS) study was designed to determine whether very low dose interferon beta-1a (Rebif®) would delay the onset of clinically definite MS in people who had experienced one clinical event and had multiple MRI-detected lesions consistent with MS.

Results indicated that fewer people on interferon beta-1a (Rebif) developed clinically definite MS (34%) than in the placebo group (45%) during the study time. In addition, the number of new lesions and the increase in the total accumulation of areas of myelin damage were significantly lower in the treatment group. The dose of Rebif used in the study was 1/6 of that generally used in the United States to treat relapsing-remitting MS.[15]

To date, the FDA has not reviewed the data from this study.

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[14] Jacobs LD, Beck RW, Simon JH, Kinkel RP, Brownscheidle CM, Murray TJ, et al. Intramuscular interferon beta-1a therapy initiated during a first demyelinating event in multiple sclerosis. CHAMPS Study Group. *New England Journal of Medicine* 2000; 343:898–904.

[15] Kappos L, Polman CH, Freedman MS, et al: Treatment with interferon beta-1b delays conversion to clinically definite and McDonald MS in patients with clinically isolated syndromes. Neurology 2006;67:1242-1249.

The **BENEFIT** (Betaferon® in Newly Emerging MS For Initial Treatment) study was designed to determine whether interferon beta-1b can delay the onset of clinically definite MS in people with CIS who are at high risk for developing MS.

Results indicated that treatment may significantly delay the development of clinically definite MS: At day 255 of the study, one-quarter of patients in the placebo group had developed CDMS while it took 618 days for a comparable number of patients in the treatment group to develop CDMS. At the end of the two-year study, 28 percent of patients in the treatment group had developed CDMS compared to 45 percent of the placebo group.[16]

Based on the results of the BENEFIT trial, the FDA has expanded the indication of Betaferon® (interferon beta-1b) to include individuals who have experienced a first clinical episode and have MRI features consistent with MS.

The **PreCISe** study was designed to determine how long it would take individuals with CIS who were taking glatiramer acetate (Copaxone®) to experience a second attack that would confirm the diagnosis of definite MS. An interim analysis of data was performed as initially planned at the outset of the trial.

The investigators have reported that compared to the group taking a placebo, the risk of developing clinically definite MS in the group taking glatiramer acetate was significantly reduced.[17]

Based on the results of the PreCISe trial, the FDA has expanded the indication of Copaxone® (glatiramer acetate) to include individuals who have experienced a first clinical episode and have MRI features consistent with MS.

[16] Kappos L, Freedman MS, Polman CH, et al: Effect of early versus delayed interferon beta-1b treatment on disability after a first clinical event suggestive of multiple sclerosis: A 3 year follow-up analysis of the BENEFIT study. Lancet 2007;370:389-397.

[17] Kinkel RP, Kollman C, O'Connor P, et al: IM Interferon beta-1a delays definite multiple sclerosis 5 years after first demyelinating event. Neurology 2006;66:678-684