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Submission to the Public Consultation on the draft revised Pharmaceutical Benefits Advisory Committee (PBAC) Guidelines (Draft Version 5.0)

Overview

Lundbeck is the only fully-integrated pharmaceutical company in the world solely devoted to the treatment of brain diseases. We dedicate our entire R&D investment to developing innovative medicines in areas of high clinical need for the treatment of a number of psychiatric and neurological diseases, including schizophrenia and Alzheimer's disease.

Lundbeck has been in Australia since 1997 and currently supply eight approved products to Australian patients living with mental illnesses including schizophrenia, major depression and bipolar disorder.

Lundbeck Australia welcomes the opportunity to make a submission to the review of Guidelines for preparing a submission to the PBAC Version 5.0.

The company is concerned that one new proposed change to these Guidelines is a cost cutting measure which, if implemented, has the potential to make it impossible for pharmaceutical companies to bring a vast number of new medicines to Australia. We do not believe this measure is in the best interest of patients, particularly those with mental illness, and will have serious long-term ramifications.

The proposed Guideline (Section 1.1) dealing with the selection of a comparator would demand that in order to be reimbursed, a new medicine must be compared to the cheapest-priced product currently on the market. This will apply across all therapeutic areas and take no account of clinical need. It will be unviable for innovator research companies to launch medicines in Australia at the same price as generic medicines, some of which are more than 10 years old. Psychiatry is particularly exposed by this measure due to the fact that the therapeutic area is so highly genericised.

There is already a drought in accessing new mental health medicines. Lundbeck believes this latest proposed instrument will be a further erosion of patient access to the Pharmaceutical Benefits Scheme (PBS) - a situation which has deteriorated alarmingly over recent years. This is evidenced by the fact that the most recent antidepressant to be PBS-listed was in 2009 and that all four PBAC submissions for new antidepressants in the last five years have been rejected.

Australian patients have recently missed out on reimbursed access to the following innovative Lundbeck therapies:

- Brintellix (vortioxetine): An antidepressant with a novel mechanism of action. Brintellix was rejected by the PBAC and is therefore only available to those Australians who can afford it on private script. The UK's National Institute for Health and Care Excellence (NICE) recently recommended Brintellix, enabling reimbursed access.
- Selincro (nalmefene): A novel treatment for alcohol dependence, unarguably an area of high clinical need in Australia. Subsidised access is available in multiple countries throughout Europe.

A market heavily dependent on generic medicines is exposed to shortages and stock-outs which presents a danger to patients. This situation is evident in New Zealand where the media reports increasing medicine shortages:

http://www.stuff.co.nz/national/health/76439113/patients-regularly-face-medicine-shortages-as-new-zealand-struggles-to-secure-supply

Incremental innovation in treatments is particularly important in mental health because relapse and treatment resistance are common so access to a wide range of the most modern therapies is essential. The current reimbursement environment gives little regard to incremental innovation, and the introduction of new guidance on choice of comparator will remove any recognition of the value of new advances.

Antipsychotics have different yet overlapping efficacy and safety profiles, as well as different delivery mechanisms such as long-acting injectable formulations, so there is a high clinical need for further therapies.

Despite the availability of many older **antidepressants** with established efficacy and safety, there is a high and increasing need for new antidepressants because more than a third of patients who tolerate treatment do not respond to first line therapy, and more than one third of patients develop treatment resistance.

In addition, the proposed change to the selection of comparator will damage the **future of clinical trials** as innovator companies will no longer design clinical trials with the intent of registering a medicine in Australia. This is already occurring for medicines entering phase III clinical trials. Overall, this situation fits awkwardly with the current government's public encouragement of innovation and clinical research and development.

Australia is falling behind other leading medical reimbursement systems in Europe, Canada and the UK despite the burgeoning incidence and prevalence of mental illness, which now ranks as one of the top three causes of burden of disease. In 2003, mental disorders accounted for 13% of the total disease burden in Australia. Recently released Australian Bureau of Statistics figures show Australia's suicide rate at a ten year high in 2014.

It should be noted that the medicines industry in Australia has been subjected to aggressive cost cutting over more than five years. This new measure is unnecessary given the magnitude of cost cuts made to the PBS over the last five years and the fact that expenditure has been flat since 2010.

Australians with mental illness and their treating doctors should have affordable access to the newest therapeutic advances and public policy should facilitate this. Otherwise Australia will no keep pace with other leading developed countries in patient access to innovative medicines.

Clinical Need

Lundbeck contends that mental health is a therapeutic area of high clinical need because of the severity and heterogeneity of conditions such as schizophrenia, bipolar disorder and major depression which necessitates the availability of a broad range of medicines. For example antipsychotics differ in side-effect profiles, yet have only small differences in efficacy (Leucht et al 2013). Publically available information shows that in Australia orally administered second generation antipsychotics have been cost minimised to one another, showing that it has not been possible to demonstrate to PBAC's satisfaction superiority of one medicine over another. There is currently no recognition of the value of incremental innovation in medicines which offer **differing** efficacy and

side effect profiles- something which is of particular importance in treating psychiatric illnesses. For example increased adherence in schizophrenia delivers better patient outcomes. A new antipsychotic may achieve better patient adherence if it has fewer side effects such as weight gain. However the PBAC process is not geared for consideration of this fact.

People with long-standing psychotic illnesses, especially those requiring depot medication, are amongst the most vulnerable in our society. Many of these patients are unable to work and the cost of obtaining a script privately would be prohibitive. (Ilchef 2011). This includes those living in rural, remote and indigenous communities where governments are striving to close the health gap. It is therefore imperative that the pathway to new PBS listings in mental illness is not further impeded.

PBAC Guidelines v 5.0 Review

Lundbeck wishes to comment in particular on two matters:

1) The opportunity to introduce systematic clinician and consumer input

2) The selection of the comparator

An opportunity to include systematic clinician and consumer input

The current review provides an opportunity to update the PBAC Guidelines to incorporate more meaningful systematic consumer and clinician input into the PBAC process. Such perspectives are neither adequately nor systematically captured by the current process. This introduces significant uncertainty, and can lead to PBAC rejecting submissions on the basis of unclear clinical place in therapy and unclear clinical relevance of a new medicine's effect. Formal consumer and clinician input via a panel would be invaluable for clarifying factors such as place in therapy, clinical need, clinical relevance of outcomes, and whether there are specific patient groups which would benefit most from the new medicine. This process would also capture other patient and carer-relevant factors which are not routinely factored into randomised clinical trials evidence. Ultimately this would also assist PBAC by reducing uncertainty. Such a process ("PACE"- Patient and Clinician Engagement) has recently been introduced by the Scottish Medicines Consortium for end of life and very rare conditions in recognition of the fact that existing cost-effectiveness thresholds are not always appropriate for these conditions.

Lundbeck requests PBAC incorporates a PACE-style process before it makes recommendations on new mental health medicines.

The selection of the comparator

An introduction of the recommendation to use the cheapest comparator at PBAC level would move comparator selection from a clinical consideration to an economic one. That this is problematic may be illustrated by way of an example of a forthcoming Lundbeck product. Brexpiprazole, a new atypical antipsychotic for the treatment of schizophrenia may be forced to be compared to a very old antipsychotic medicine, many of which are still relied upon by a small number of patients today- for example chlorpromazine or haloperidol. Such a comparison would be problematic for two reasons.

Firstly, from a clinical perspective, the comparison would be indirect due to an absence of head-to-head evidence. Although indirect comparisons are commonly conducted for PBAC submissions, indirect comparison of a very old with a very new medicine is inevitably uninformative due to differences in the conduct of clinical trials over the decades, meaning there would be very little, if any, exchangeability of trials data. This in turn only provides uncertainty in drawing a clinical conclusion and is not informative in determining the cost-effectiveness of the new medicine. This scenario has already occurred with Lundbeck's Selincro (nalmefene) having been rejected by PBAC in November 2015 on the basis (among other things) that the PBAC believed differences in outcomes between the naltrexone and nalmefene trials meant that any comparison between the two was unlikely to give a reliable estimate of their comparative efficacy. Under the proposed Guidelines, this scenario will be repeated on a regular basis, delaying or even preventing affordable patient access.

Secondly, from an economic perspective, it will simply not be viable for a new medicine to be listed on a cost-minimisation basis to an old medicine which was PBS-listed decades ago and/or has undergone significant price erosion. This may suit the health budget and consumers in some therapeutic areas where in clinical practice there are no differences in effectiveness and safety between the new and the old medicine. However, in an area of significant clinical need such as mental health, flexibility in choice of comparator is required to ensure Australian patients attain equitable access to new medicines.

The wider implication of the proposed "comparator" Guideline is that globally available new medicines will never be registered in Australia. This is already evident for some antipsychotic medicines entering Phase III clinical trials where the Australian market has been excluded in decision making about clinical trial design. This is a symptom of the already challenging reimbursement environment in Australia, one which will only become more difficult should Guideline v 5.0 be implemented.

Lundbeck therefore requests that any reference to comparator price be removed from the proposed Guidelines in order to retain flexibility and deliver equitable access for patients in areas of high clinical need.

References:

Ilchef R. PBS delising. Aust NZ J Psychiatry 2011;45:501.

Leucht S, Cipriani A, Spineli L, Mavridis D, Öray D, Richter F *et al*. Comparative efficacy and tolerability of 15 antipsychotic drugs in schizophrenia: a multiple-treatments meta-analysis. Lancet 2013; 382: 951-62.