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Senate Finance and Public Administration References Committee:
Inquiry regarding *Administration of the Pharmaceutical Benefits Scheme (PBS)*

Additional Information for the Record
&
Response to questions taken on notice by Mr Bruce Goodwin, Managing Director, Janssen Australia, on 21 July 2011

Additional Information for the Record

(1) Response to evidence presented by Mr David Learmonth, Deputy Secretary, Department of Health and Ageing, 25 July 2011, as follows:

"Most of these drugs (deferred in February) were cost-minimised or 'me too' drugs, with no added efficacy or health outcome and no less toxicity than existing treatments but with a net cost to the government. For example, paliperidone long acting, known as Invega Sustenna, which is a treatment for schizophrenia, was recommended by the PBAC on the grounds that it is of similar efficacy and toxicity to the existing long-acting therapy, Risperdal Consta, but it has a net cost to government. Both of these long-acting injections are made by the same company, Janssen-Cilag. In fact paliperidone, or Invega Sustenna, is a metabolite of risperidone. This simply means that paliperidone is the substance that the body converts risperidone into when that drug is taken".

Contrary to Mr Learmonth's statement, there are clear pharmacokinetic differences between paliperidone and risperidone long-acting injections (LAIs).

Paliperidone palmitate is formulated as a water soluble suspension with a particle size distribution that has sustained release properties designed for once-monthly (4 weekly) intramuscular injections, with a rapid uptake to therapeutic plasma levels. In contrast, due to its extremely low water solubility, risperidone long-acting dissolves slowly, taking 21 days from the first injection to release risperidone.

After absorption, paliperidone palmitate is hydrolysed to paliperidone (9-hydroxyrisperidone). Although 9-hyroxyrisperidone is an active metabolite of risperidone, paliperidone palmitate and risperidone long-acting injections are not interchangeable due to substantial differences in their pharmacokinetic profiles.

Firstly, the differing pharmacokinetic profile of risperidone LAI results in a two-weekly injection interval, with an eight week delay to attaining therapeutic drug levels. To accommodate this delay to efficacy, six weeks (or more) of daily administration of oral antipsychotics (risperidone) is required. In contrast, the rapid and sustained pharmacokinetic release profile of paliperidone palmitate ensures early symptom improvement (by day 4 after initiation) and attainment of therapeutic plasma levels within 1 week of initiation, with efficacy maintained during a longer, 4-weekly injection interval.

In clinical practice, this means paliperidone palmitate can be used in the acute patient setting, where clinicians are required to release patients back into the community within 8-10 days where possible.

Secondly, paliperidone palmitate is primarily excreted by the kidneys whereas risperidone long-acting injection relies mostly on liver metabolism for elimination. A lack of reliance on liver metabolism is an important pharmacokinetic difference, minimising the risk of inter-patient variability in the ability to metabolise and/or eliminate paliperidone palmitate as follows:

- enables use of paliperidone palmitate in patients with mild to moderate liver impairment without dose adjustment or concern for drug accumulation due to abnormal hepatic function;
- ensures no impact on the metabolism of paliperidone palmitate due to smoking, which can induce liver metabolism of some long-acting antipsychotics, resulting in the requirement for higher doses; and,
- ensures no impact that genetic polymorphisms may have on an individual variation in the ability to metabolise antipsychotics; for example, there can be 'fast' or 'slow' hepatic metabolisers of risperidone.

Therefore, unlike risperidone LAI, the pharmacokinetic features of paliperidone palmitate LAI result in rapid attainment of therapeutic plasma levels and efficacy, maintenance of therapeutic concentrations allowing for 4-weekly dosing, with minimal inter-patient variability due to a lack of liver metabolism.

(2) Response to the claim that alternative treatments are already available on the PBS

Janssen understands the Government deferred the PBS listing of Invega Sustenna® (paliperidone palmitate) because alternative medicines are listed on the PBS, including Janssen's Risperdal Consta® and olanzapine long-acting injections.

Long-acting atypical antipsychotic injections are used by patients with a history of non-adherence to medication. Non-adherence (particularly with oral medication) is a key driver of relapse and re-hospitalisation. Every relapse (acute episode) in schizophrenia causes permanent brain damage and increases treatment resistance.

Medicare Australia data reveals that less than 1 percent of long-acting atypical antipsychotic prescriptions are for olanzapine. In other words, the actual uptake of olanzapine in the clinical setting is very low. Thus, for patients at risk of relapse who do not respond to Consta, Sustenna is the only viable alternative.

Therefore, the PBS listing of Sustenna is crucial to improving treatment for some of Australia's most socially isolated, disadvantaged and stigmatised people.

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(1)

Senator POLLEY: Mr Goodman, could you run through with the methodology used by Deloitte's in their report, which I understand took into account direct and indirect cost to the community, not to hospitals and not to government? I do not think these have been very clearly explained. Can you run through the methodology used?

Response:
Deloitte Access Economics was commissioned by Janssen Australia to estimate the economic cost of a relapse among people living with schizophrenia, and to estimate potential savings to the health care system and the economy through greater utilisation of atypical long-acting antipsychotic injections (LAIs) rather than atypical oral antipsychotics. Cost savings are expected to be derived from an increased adherence to medication associated with the use of long-acting antipsychotic injections.

Deloitte Access Economics undertook a thorough and systematic review of published literature and publically available health and hospital data to estimate the cost of schizophrenia relapse and the potential savings to the health care system and the economy through greater utilisation of atypical long-acting injections. The Report contains an inventory of over 100 references (sources) used to calculate and support key findings.

Please find following a summary of the methodology used to determine Report's key findings. For further information, please refer to Deloitte Access Economics' Cost of Relapse in Schizophrenia Report (attached).

Methodology of Key Findings

i. *The number of relapses in people living with schizophrenia in Australia was estimated to be 25,571 over a 12 month period in 2009-10.*

Methodology: For the purposes of this study, relapse in schizophrenia was defined as an admitted episode of hospital care that resulted in at least one overnight stay (i.e., a non-same day separation).This is a narrower definition compared to other studies.

ii. *The total cost of relapse in people with schizophrenia was estimated to be $698.6 million over a 12 month period in 2009-10, while the average cost per relapse was estimated to be $27,320.*

Methodology: As people living with schizophrenia who do not relapse already use health care and other economic resources, the cost of a relapse is represented by the additional resources used (or resources lost in terms of productivity) due to relapse.

A summary of estimated relapse costs is presented in the table below. Contrary to Senator Polley's question, the estimated direct costs of schizophrenia relapse include hospitalisation, emergency services and pharmaceutical costs (amongst others). Thus, the report estimates the potential costs to government.

Table ii: Summary of estimated relapse costs, 2009-10

Type of cost	Total cost	Average cost per relapse
	$ (million)	*$*
Direct costs		
Hospitalisation	463.1	18,110
Emergency department services	2.2	86
Ambulance care	0.7	27
Outpatient care	20.1	786
Pharmaceutical treatment	1.8	70
Total – Direct costs	487.9	19,080
Indirect costs		
Lost productivity due to unemployment	24.5	958
Lost productivity due to premature mortality	5.2	203
Prison costs	32.0	1,251
Legal costs	1.5	59
Deadweight loss	147.5	5,768
Total – Indirect costs	210.7	8,240
Total – Direct and indirect costs	698.6	27,320

Note: Based on an estimated 25,571 relapse episodes in 2009-10. The cost of residential mental health care and informal care associated with relapse in people living with schizophrenia could not be estimated due to insufficient data.
Source: Access Economics calculations.

The direct health care system cost due to relapse in people living with schizophrenia was estimated to be $487.9 million in 2009-10. Hospitalisation was the greatest cost factor, accounting for $463.1 million, equating to 66.3% of the total relapse cost. Other costs include emergency department services ($2.2 million), ambulance services ($0.7 million), outpatient services ($20.1 million), and pharmaceuticals ($1.8 million).

Relapse in schizophrenia also generates a range of indirect costs to people living with schizophrenia, family and friends and the economy. Total indirect cost was estimated to be $210.7 million over a 12 month period in 2009-10. There were an estimated 6,340 people not employed due to relapse and an estimated 1,661 people not employed at any one time, resulting in lost productivity of $24.5 million. There was also lost productivity due to premature mortality associated with suicide, estimated at $6.4 million. People with schizophrenia, in particular those experiencing a relapse; also have an elevated risk of criminal activity. Around 70.7% of imprisonment cost for people with schizophrenia was attributed to relapse, amounting to $32.0 million, with an associated legal cost of $1.5 million.

Much of the expenditure on direct health care system costs and social security (transfer) payments associated with relapse is funded by government. This requires government to effectively increase tax revenue to achieve a budget neutral position. The total public cost of relapse in people living with schizophrenia was estimated at $517.1 million (including $10.8 million in social security payments) with an associated deadweight loss of $147.5 million.

iii. *If long-acting injectable antipsychotic utilisation was increased to 30% in Australia (as in the UK and US), there would be an additional 12,791 people prescribed a LAI. Assuming all people switched were non-adherent to oral antipsychotics, the avoided cost of relapse through improved adherence to medication would be approximately $52.5 million per year. The reduction in the number of relapses would also improve health outcomes and avoid 310 DALYs per year.*

Methodology: Poor adherence with medication to treat schizophrenia has been associated with a substantial increase in the risk of a relapse. For example, 40% of people are likely to suffer a relapse within two years if they persist with medication treatment, whereas around 80% of people are expected to experience a relapse if they have poor adherence (NIMH 2010).

Long-acting injectable (LAI) antipsychotic therapies provide the potential to improve adherence compared with oral medications because they are administered less frequently. Furthermore, non-adherence is easier to detect because LAIs are administered by medical professionals.

In Australia, approximately 17% of people with schizophrenia are prescribed LAIs (Monshat et al 2010). It is generally accepted that adherence for oral antipsychotics (both typical and atypical) is low. For example, Dolder et al (2001) found that adherence for oral atypical and typical antipsychotics were similarly poor at 12 months, with 54.9% and 50.1% respectively. At two years adherence may be as low as 25% (Chue 2010).

It was assumed that patients stabilised on oral antipsychotic treatment and who are adherent would not be switched to a LAI. Therefore, in order to assess the benefits of LAIs, the potential avoided costs from switching a non-adherent person on an oral antipsychotic to a LAI was estimated.

The annual probability of relapse from switching a non-adherent person on an oral antipsychotic to a LAI was estimated to decrease from 36.9% to 21.9%. Thus the likelihood of relapse is decreased by 15.0 percentage points or 40.7%. On average, the annual avoided cost was estimated to be $4,103 (per expected relapse).

Refer to the attached *Deloitte Access Economics: The Cost of Relapse in Schizophrenia* for full references.

(2)

CHAIR: Would you provide to the secretariat on notice what, if any, consultation you had with the government before the announcement was made and what you have had since so that we can get an idea when we look at how this was brought about and where it is heading.

Response:
If we were to refer to the literal meaning of 'consultation', the response would have to be that Janssen had no consultation with Government prior to the announcement. The Pharmaceutical Evaluations Branch of the Department of Health and Ageing phoned Janssen's Managing Director in the afternoon of 25 February 2011 to inform him of the deferral of the PBS listing of Sustenna, approximately one month prior to the expected PBS listing date.

Since the announcement, Janssen Australia has met with the offices of several Cabinet Ministers, Members and Senators, in an attempt to clarify the rationale for the deferrals and explain why Australians living with schizophrenia, their treating clinicians and carers need access to this medication.

(3)

Senator FIERRAVANTI-WELLS: I have a question for all the companies to take on notice, please. In relation to costs associated with reconsideration, it has been deferred, we do not know till when. There obviously will be potential costs. Are there costs in relation to any reconsideration or will there be costs in relation to withdrawal of your product for consideration?

Response:
The Government has not provided advice or guidance on the process of reconsideration. Therefore, we do not have an understanding of what the costs will be. If further applications to the Pharmaceutical Benefits Advisory Committee (PBAC) are required, the cost will be approximately $150,000 per major PBAC evaluation.

Janssen has invested significant and important resources in the introduction of Sustenna. The costs associated with the deferral will increase over time as we continue to maintain patients enrolled in clinical trials and other access programs.

(4)

Senator POLLEY: Could you take on notice to give us the quantities of stock that will expire in December 2012 and 2013 and whether there is going to be a wholesale destruction of those medicines? If you could provide that to us on notice, that would be most useful.

Response:

The value of Janssen's Sustenna inventory at the time of deferral (approximately one month prior to the expected PBS listing date) was $2.2million. This stock will expire in December 2012. Whilst the Government's decision has significantly impacted the Janssen business, we are using our best endeavours to minimise stock write-off by using this inventory to maintain patients enrolled in clinical trials and other access programs.