The Government's Administration of the Pharmaceutical Benefits Scheme (PBS)

Mundipharma Pty Limited Supplementary Submission to the Senate Inquiry:

August 2011

Senate Finance and Public Administration References Committee Inquiry

SUPPLEMENTARY SUBMISSION

Senate Finance and Public Administration References Committee inquiry into:

'The Government's Administration of the Pharmaceutical Benefits Scheme (PBS)'

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Senate Finance and Public Administration References Committee inquiry into: The Government's Administration of the Pharmaceutical Benefits Scheme (PBS)

Executive Summary

Please find below, Mundipharma's responses to questions that were received on notice, during our appearance at the Senate Finance and Public Administration References Inquiry into the administration of the Pharmaceutical Benefits Scheme (PBS) on Thursday, 21st July 2011.

Additionally, Mundipharma takes this opportunity to provide supplementary submission information. The purpose of this additional information is to clarify for the Committee certain matters that have been raised by other witnesses during the course of the Inquiry.

(A) Finance & Public Administration References Committee: Questions taken on notice

1. ***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.*

As stated in our original submission to the Committee, Mundipharma is disappointed at the lack of consultation with the Company prior, or indeed subsequent, to this important adverse Government decision being taken. Importantly, Mundipharma was only advised of this decision by telephone from DoHA late on Thursday 24th February 2011, the day prior to the Minister's Media Release statement on this matter on Friday 25th February 2011.

Until that time, Mundipharma was given every reason to believe the process for the listing of Targin® tablets was proceeding on track according to normal Departmental processes. Had earlier advice been received, issues around the importation from the UK of stock of considerable value and consequent associated financial loss to Mundipharma could obviously have been avoided.

We are pleased to provide more detailed information, as requested by the Committee. Below, is a chronology of interactions Mundipharma has had with both DoHA and the Minister for Health & Ageing's office since notice was received that the PBS listing of Targin® tablets was to be *deferred indefinitely*.

Mundipharma would also take this opportunity to express its disappointment that neither the Government nor the Department has taken any initiative to proactively contact Mundipharma to discuss this important decision. That is, apart from the initial phone call late on 24th February 2011 (the day prior to the Minister's announcement). Other than that, all interactions with both the Government and the Department of Health & Ageing have been initiated by Mundipharma.

Date	Action
24th February 2011 (pm)	Phone call from advising that the PBS listing of Targin® tablets is to be *deferred indefinitely*. Listing would be considered when *fiscal circumstances permit*.
25th February 2011	Media release from the Hon Nicola Roxon MP confirming the *indefinite deferral*.

2nd March 2011	Mundipharma encounters Minister Roxon at Medicines Australia Parliamentary Dinner (Canberra). Minister Roxon verbally agreed to meet with Mundipharma.
3rd March 2011	Letter Mundipharma to Minister Roxon requesting advice on a suitable time to meet with the Minister (refer above). Brief explanation provided to the Minister of the reasons why laxatives are a less than effective substitute for addressing OIC in opioid treated severe pain patients.
7th April 2011	Letter from Pharmaceutical Evaluation Branch (to Mundipharma, received on 11th April, replying to Mundipharma's letter of 3rd March on behalf of Minister Roxon. re-stated the Government's position and added that: i. "The Government is therefore concentrating on listing drugs at this time for more serious conditions and where alternate (sic) treatment options are not available. ii. "Those listings that have been deferred in the prevailing fiscal environment remain eligible for future consideration when fiscal circumstances permit." iii. "Deferred listings will not need to be reconsidered by PBAC or the PBPA unless the sponsoring company wishes to present further clinical evidence to support a price increase or cut." iv. "The PBAC considered that use of Targin may reduce misuse of oxycodone, which was taken into consideration when PBAC accepted a higher price for this medicine in comparison with oxycodone alone." v. "The resultant cost of Targin was similar to oxycodone plus an over the counter laxative." vi. "Minister Roxon's office will contact you separately if a meeting is to be arranged with the Minister or her office."
18th April 2011	Letter Mundipharma to Minister Roxon responding to the Ministers letter dated 7th April. Mundipharma: i. Expressed dismay that, some seven (7) weeks since the deferral was announced, the company is no closer to receiving any commitment from Government as to when the PBS listing of Targin tablets will proceed. ii. Again, requested an urgent meeting with the Minister. iii. Provided expanded advice on the negative impact this decision is having on the health and well-being of chronic severe pain patients iv. Noted the financial cost to Mundipharma of holding stock of considerable value and that "Conservatively, we estimate the local regulatory submissions ('user pay') costs to date of bringing this novel, new medicine to Australian patients to be well in excess of $1 million." This letter and attachments was copied to all current members of Cabinet.
9th May 2011	Email from (Office Manager, Office of the Hon Nicola Roxon MP) advising "Unfortunately, Minister Roxon is unable to meet, however, Policy Adviser, from her office would be happy to meet and discuss this matter further." Meeting arranged with for Wednesday, 8th June 2011.
8th June 2011	Meeting with Policy Adviser to the Hon Nicola Roxon MP.
20th June 2011	Follow-up email Mundipharma to responding to his request for information on current stock holdings of Targin® tablets and providing details on expiry dating and comprehensive reasons why Mundipharma will need to commence stock destruction of the 5/2.5mg tablet strength around the end of 1Q12.

2. ***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?*

It is unclear to Mundipharma, precisely the information that Senator Fierravanti-Wells is seeking. The Department of Health & Ageing (DoHA), in its letter to Mundipharma dated 7th April 2011, has advised that;

"Those listings that have been deferred in the prevailing fiscal environment remain eligible for future consideration when fiscal circumstances permit. ***Deferred listings will not need to be reconsidered by PBAC or the PBPA, unless the sponsoring company wishes to present further clinical evidence to support a price increase or cut."*** (Mundipharma emphasis).

Consequently, as DoHA has provided their assurance that Targin® tablets will not be required to be reconsidered by either PBAC or the PBPA (again confirmed in the DoHA submission to the Inquiry, dated 11th July 2011), no further costs relating to Government evaluation fees and charges (cost recovery) will be incurred by Mundipharma.

Mundipharma is not withdrawing Targin® tablets from future consideration by Cabinet.

Finally, the most important potential cost, and Mundipharma's primary consideration resulting from this PBS listing *indefinite deferral*, is that to patients. Targin® tablets are now only available to chronic severe pain patients with a capacity to afford this innovative and beneficial medicine. The costs to poorer patients, is denial of access to improved treatment of their pain and associated iatrogenic comorbidities.

3. ***Senator POLLEY:*** *Yes. 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.*

In response to this question on notice, Mundipharma would refer the Committee to its original submission commencing on page 17, addressing the Committee's term of reference *'(C) Any*

consequences for the pharmaceutical sector of such deferrals'. Mundipharma provided to the Committee, the basis for its commercial decision to import a quantity of Targin® tablets stock from the UK, of considerable value, in order to meet its obligations under guarantee of supply upon the listing of Targin® tablets on the Pharmaceutical Benefits Scheme (PBS). We make reference to the statement in the Department of Health & Ageing submission to the Inquiry, that:

"Decisions about whether to obtain stock, ahead of formal advice from the Department one month prior to the actual date that the listing will proceed, are commercial decisions made by individual companies. Companies are not required to pre-stock, in anticipation of a positive listing outcome. They are only required to assure the Department, that, when listing does proceed, they will be able to make stock available on the PBS. Once approval to list on the PBS is known, companies are able to proceed with their projected listing date or defer listing if they are unable to supply by that date.

It is not for the Department to speculate on each individual company's capacity to supply prior to advising of the approval to list."

Mundipharma notes that only those new PBS listings with an anticipated incremental cost to the PBS greater than $10 million in any of the first four years of listing were, at that time, required to be considered by Cabinet. As Targin® tablets do not fall into this definition; we respectfully suggest that the company was entitled to anticipate a PBS listing date, as planned, of 1st April 2011. In the event, Mundipharma was confounded by the non-communicated change to the process whereby all recommended PBS listings with a potential cost to the PBS are now referred to Cabinet for a decision. We repeat that if we had received advanced notice of this critical change to the PBS listing process Mundipharma would not have imported stock into Australia at that time.

As explained in our submission to the Inquiry, it is not possible to return this stock to the manufacturer in the UK for reprocessing. Because of the PBS listing *indefinite deferral*, and in order to minimise the financial loss to the Company, Mundipharma is now seeking advice whether it is possible to conduct stability testing on the Targin® tablets batches currently held in Australia, with a view to requesting an increase of the shelf life. This may or may not be possible and, in any event, is another significant cost to the company including, of course, application for approval to proceed with such a course of action from the TGA.

Currently, Mundipharma holds the following volume of stock in its warehouse:

Description	Batch	Expiry Date	Qty On Hand (Units)	Qty to be written off in Q2 2012
Targin 5/2.5mg Tablets 28's	159505	31/12/2012	17,279	14,279
Targin 10/5mg Tablets 28's	159506	30/11/2013	17,279	
Targin 20/10mg Tablets 28's	159507	30/11/2013	11,519	
Targin 40/20mg Tablets 28's	159503	30/11/2013	11,519	

As can be seen, at the current rate of distribution Mundipharma anticipates that over 14,000 units of Targin® 5/2.5mg tablets will be required to be destroyed at the beginning of second quarter (2Q) 2011. No comment is provided on the three higher strengths as it is sincerely hoped, given the Government's commitment to Australians to bring the budget into surplus in 2012/13, that these higher strengths of Targin® tablets will be PBS listed during this time without the need to destroy this stock.

SUPPLEMENTARY COMMENTS

A. Submission of the Australian Government Department of Health & Ageing dated 11th July 2011

We refer to comments contained in the Department's submission:

"With respect to oxycodone with naloxone (Targin®), the PBAC considered that it could provide an alternative pain management therapy to opioids alone or in conjunction with prophylactic laxatives. This was reflected in the cost of this medicine which was similar to oxycodone plus an over-the-counter laxative. The potential for reduction in illicit drug use claimed in the submission to the PBAC was not based on evidence."

Some statistics of interest - the PBAC's decision to list Targin® tablets was based on:

- Approx. 1,400 pages of evidence;
- With over 135 references; and
- Involving data on 9,187 patients.

After considering all of this evidence, the PBAC concluded that:

*".....it was appropriate to list oxycodone with naloxone (Targin) on the PBS as the availability of this product is **likely to increase prophylactic management of OIC (Opioid Induced Constipation)**, the cost of the product is*

*similar to oxycodone plus an over-the-counter laxative, the product may prevent constipation and not cause diarrhoea, **and it may also reduce diversion**."* (PBAC's Public Summary Document) (Mundipharma emphasis).

In other words, PBAC determined that Targin® tablets should be listed - at least partly - due to its reduced potential for diversion. Although this is an important aspect, it is accepted that it is only one element of many complex considerations by PBAC, leading to their positive recommendation for the PBS listing of Targin® tablets. The primary PBAC rationale was based on Targin® tablets being able to prevent opioid induced constipation.

B. Oral Evidence to the Committee by the Department of Health & Ageing on 25th July 2011 (Canberra)

In oral evidence from the Deputy Secretary of DoHA to the Senate Inquiry on 25th July 2011 (Canberra), stated:

"In 2010, 63 per cent of all first-time, cost-effective submissions were rejected by the PBAC. This is not a one-off statistic but a consistent marker of the rigour of the assessment process undertaken. It is this assessment process which I would suggest is the main decision point for companies in determining whether to bring a drug to the subsidised market in Australia."

Mundipharma agrees with DoHA that the statistic presented is '*a consistent marker of the rigour of the assessment process undertaken*'. However, we would contend that it is precisely because of the undisputed rigour of this process, together with the low chance of success and requirement for multiple submissions, that a company submitting a cost-effectiveness submission to PBAC and successfully overcoming these substantial hurdles to achieve a recommendation for PBS listing from the PBAC should reasonably expect the listing to proceed.

Targin is oxycodone…with naloxone which has a laxative effect

It was reported in Hansard that on the 31st May 2011, the Deputy Secretary of DoHA advised the Senate Community Affairs Legislation Committee that:

"Targin is oxycodone, which is regularly prescribed for that indication, with naloxone which has a laxative effect. It is equivalent to taking oxycodone in its usual form and a laxative."

Targin® tablets are not a strong opioid analgesic combined with a laxative. Targin® tablets are unique in being the only strong opioid analgesic proven to prevent OIC. That is, it prevents an opioid (in this case, oxycodone) from causing constipation in the first place rather than attempting to induce a bowel movement symptomatically once constipation has become a problem.

In oral evidence from the Deputy Secretary of DoHA to the Senate Inquiry on 25th July 2011 (Canberra), stated:

"Secondly, Targin is an alternative pain management therapy to opioids alone or in conjunction with prophylactic laxatives. ***Naloxone, which is the drug it is in combination with, is an opioid antagonist which helps prevent constipation. I said during the May Senate estimates that Naloxone has a laxative effect.*** *I did not say that Naloxone is a laxative; it is not. However, patients who take opioids and have constipation can manage this by taking a laxative. The PBAC noted that many people purchase over-the-counter laxatives, and the company itself did not claim that Targin was superior to oxycodone plus prophylactic over-the-counter laxatives."* (Mundipharma emphasis).

Mundipharma is not asserting that the Deputy Secretary said that naloxone is a laxative but, nonetheless, feels it is necessary to clarify this matter further for the Committee. As the Deputy Secretary agrees that naloxone helps prevent (opioid-induced) constipation, the two sentences highlighted above are inconsistent and potentially ambiguous. If a product is able to prevent opioid-induced constipation, then the issue of constipation (and attempted treatment with a laxative to force a bowel movement) for patients does not arise.

Forward Estimates (Cost Savings)

In oral evidence from the Deputy Secretary of DoHA to the Senate Inquiry on 25th July 2011 (Canberra), stated:

"Thirdly, in its submission Mundipharma claims that the forward estimates savings were agreed. This is simply not true. Only the Department of Finance and Deregulation can agree costings, and no such savings were agreed."

Mundipharma made no representation in its submission to the Inquiry that costings were agreed with DF&D. At the time that the costings were being agreed with the DoHA (via DUSC), in December 2010, there was - and still is - no process in place for the DF&D to interact with companies, including Mundipharma. At the time, DUSC staff indicated to the Sponsor that once

the estimates had been *agreed* upon it would then be a matter for the DoHA to present these estimates to the Department of Finance & Deregulation. Mundipharma's health economics consultants did offer to assist in that presentation of the estimates (in order to ensure clarity and accuracy) but was verbally informed that this would neither be possible nor appropriate.

The Deputy Secretary also stated:

"Finally, in its submission Mundipharma claims that the Department of Health and Ageing agreed that there will be a saving from a reduction in the abuse of OxyContin tablets. My statement during the May Senate estimates that the government would not have figures showing savings from reduction in abuse and diversion stands. It is based on the PBAC's public summary document of July 2010, which states:

…the potential for reduction in illicit drug use was not based on evidence and…estimated savings to the PBS were…uncertain."

Figures 'showing savings from abuse and diversion' are available, and these savings were estimated and agreed with DUSC (DoHA), but as the Deputy Secretary states, not DF&D. As with all health economics modelling, there is a degree of uncertainty around forward estimates, and both Mundipharma and the Department of Health and Ageing acknowledged this. Because of the nature of addicts and addiction, and as expected, there is somewhat of a knowledge gap when it comes to quantifying the abuse and diversion of prescription medicines in Australia. However, all statistics presented to the PBAC were estimates based on surveys; **but these are also the same sources of data used by policy makers developing anti-abuse programs**.

Notwithstanding, the potential abuse deterrence characteristic of Targin® tablets was accepted by PBAC as an important consideration in the PBS listing approval recommendation. The PBAC did accept that there would be a reduction in abuse. The Public Summary Document states:

"The PBAC considered that it was appropriate to list oxycodone with naloxone on the PBS as the availability of this product is likely to increase prophylactic management of OIC, the cost of the product is similar to oxycodone plus an over-the-counter laxative, the product may prevent constipation and not cause diarrhoea, ***and it may also reduce diversion****."* (Mundipharma emphasis).

Availability of laxatives on the PBS for chronic severe pain patients

In oral evidence from the Deputy Secretary of DoHA to the Senate Inquiry on 25th July 2011 (Canberra), stated:

"Clinicians can either direct a patient to purchase that over the counter or they can prescribe one of the laxatives on the PBS. There are numerous laxatives listed on the PBS and 44 different items on the palliative care schedules."

Whilst Mundipharma does not accept that an opioid with a simple laxative is a clinically effective alternative for Targin® tablets, it is true that laxatives are available on the PBS - but for a very specific and restricted group of patients only. Most patients who could access 'General' PBS reimbursed laxatives are unlikely to be patients being prescribed opioid analgesics. For example, bisacodyl on the PBS is restricted to the following groups of patients:

a) Paraplegic and quadriplegic patients and others with severe neurogenic impairment of bowel function;
b) Patients who are receiving long-term nursing care on account of age, infirmity or other condition in hospitals, nursing homes or residential facilities;
c) For use by a patient who is receiving long-term nursing care and in respect of whom a Carer Allowance is payable as a disabled adult;
d) Patients receiving palliative care;
e) Terminal malignant neoplasia;
f) Anorectal congenital abnormalities;
g) Megacolon.

Mundipharma would also take this opportunity to clarify for the Committee, the nature of the '44 different items on the palliative care schedules'. In fact, there are just 26 separate and distinct Item Numbers listed in the Palliative Care schedule due to different brands of the same item. Moreover, this reduces to 13 when every listing comprises an Item Number for initial treatment and a second Item Number for 'Continuing treatment for a palliative care patient where constipation is a problem. Written or telephone applications for increased repeats may be approved where consultation with a palliative care specialist or service has occurred'. The number of items reduces again to 11 items when methylnaltrexone is excluded. Methylnaltrexone, is an opioid antagonist injection restricted to use 'in combination with oral laxatives, for a palliative care patient with opioid induced constipation who has failed to respond to oral laxatives.'

Moreover, "For the purpose of prescribing under the Palliative Care Section of the PBS, a patient receiving palliative care is defined as: *A patient with an active, progressive, far-advanced disease for whom the prognosis is limited and the focus of care is the quality of life. This makes these medicines available for any person with a life-limiting condition, regardless of the disease they suffer."*

All palliative care listings are "Authority Required". All prescribers can request an initial authority to provide a maximum of 4 months therapy for palliative care patients. Where a subsequent authority is requested for continuing treatment, the provision of repeats is subject to confirmation by the prescriber that a palliative care physician or palliative care service has been consulted regarding the care of the patient.

Clearly, given the severe restrictions to the prescribing of laxatives in the 'General' section of the PBS, and the fact that laxatives can only be prescribed for patients with 'life-limiting i.e. terminal conditions in the Palliative Care section, laxatives simply cannot be prescribed on the PBS to the majority of chronic severe pain patients in the primary care (GP) setting.