# Diabetes Subcommittee of PTAC meeting

# held 18 June 2008

# (minutes for web publishing)

Diabetes Subcommittee minutes are published in accordance with the *Terms of Reference for the Pharmacology and Therapeutics Advisory Committee (PTAC) and PTAC Subcommittees 2008*:

Note that this document is not necessarily a complete record of the Diabetes Subcommittee meeting; only the Minute relating to Diabetes Subcommittee discussions about an application that contain a recommendation in relation to an application are published.

The Diabetes Subcommittee may:

(a) recommend that a pharmaceutical be listed by PHARMAC on the Pharmaceutical Schedule and the priority it gives to such a listing;
(b) defer a final recommendation, and give reasons for the deferral (such as the supply of further information) and what is required before further review; or
(c) recommend that PHARMAC decline to list a pharmaceutical on the Pharmaceutical Schedule.

Some material has been withheld, in accordance with the Official Information Act 1982 (OIA) in order to protect the privacy of natural persons (section 9(2)(a)).

---

## Contents

# 1 Widening of Access to Pioglitazone

1.1 The Subcommittee considered an application from PHARMAC staff regarding widening of access to pioglitazone on the Pharmaceutical Schedule.

1.2 The Subcommittee considered that pioglitazone had a similar therapeutic effect to metformin; however, it was not the same effect.

1.3 The Subcommittee considered that, if access was widened, metformin would continue to be used first line because of its superior safety profile. Members noted that pioglitazone has associated cardiovascular and fracture risks (particularly of concern in the young given the potential for years of exposure).

1.4 The Subcommittee noted that the 2008 Type 2 Diabetes National Clinical Guideline for Management in Primary and Secondary Care recommended that pioglitazone only be used as monotherapy if patients cannot tolerate other oral hypoglycaemic agents.

1.5 The Subcommittee reviewed data provided by PHARMAC staff on the pharmaceuticals used in combination with pioglitazone. The Subcommittee noted that triple therapy (metformin, sulphonylurea, and pioglitazone) was not permitted under the current Special Authority; however, the data provided indicated that approximately 17% of patients were taking pioglitazone as triple therapy. Members noted that there was now evidence to show that the use of pioglitazone in triple therapy was clinically appropriate in some patients. Members noted that triple therapy was funded in Australia.

1.6 The Subcommittee considered that, if access was widened to include triple therapy, there would be a reduction in patients initiating insulin (or at least a delay in initiation). Members considered that patients might be trialed on triple therapy for up to 6 months prior to initiating insulin. Members considered that a significant proportion of this reduction would result from patients being permitted to trial triple therapy and a small number of patients whom are needle phobic or refuse to take insulin.

1.7 The Subcommittee considered that the Special Authority should use one consistent HbA1c threshold across the criteria and considered that this should be 7%.

1.8 The Subcommittee considered that because of the increased fracture risk associated with pioglitazone, widening of access by altering the Special Authority criteria (as above) would increase the number of bone scans (DEXA scans) undertaken and, therefore, the costs related to the increased use of pioglitazone. Members considered that there could also be an increase in brain-type natriuretic peptide (BNP) diagnostic testing and echocardiography.

1.9 The Subcommittee considered that, if access was widened to triple therapy, up to 30% more patients might access pioglitazone (primary care patients would be expected to show the biggest increase).

1.10 The Subcommittee considered that, if the Special Authority was removed completely, some prescribers may prescribe pioglitazone first line despite the latest guidelines advising against this. Members considered that there were sufficient safety concerns and financial risk to keep the Special Authority for pioglitazone in place.

1.11 The Subcommittee considered that there was no need to have renewal criteria because if patients did not derive benefit from pioglitazone treatment would be stopped and the patient changed to an alternative.

1.12 The Subcommittee **recommended** that the access to pioglitazone be widened to include triple therapy, that the HbA1c threshold is amended to 7% in all criteria options, and that the requirement for renewal be removed. The Subcommittee gave this recommendation a medium priority.

1.13 The Subcommittee noted that generic pioglitazone was likely to be available soon and considered that there would be no significant implementation issues if generic pioglitazone was the only funded preparation. Members considered that the savings likely to be generated by the introduction of a generic pioglitazone may cover the costs of wider access.

1.14 The Decision Criteria relevant to this recommendation are: *(i) The health needs of all eligible people within New Zealand; (iii) The availability and suitability of existing medicines, therapeutic medical devices and related products and related things; (iv) The clinical benefits and risks of pharmaceuticals; (vi) The budgetary impact (in terms of the pharmaceutical budget and the Government's overall health budget) of any changes to the Pharmaceutical Schedule; (viii) The Government's priorities for health funding, as set out in any objectives notified by the Crown to PHARMAC, or in PHARMAC's Funding Agreement, or elsewhere.*

## 2 Insulin aspart (NovoMix 30)

2.1 The Subcommittee reviewed an application from Novo Nordisk for the listing of 30% insulin aspart and 70% insulin aspart protamine suspension (NovoMix 30) on the Pharmaceutical Schedule for the treatment of diabetes mellitus. The Subcommittee noted that this was the first application received for funding NovoMix 30 and that it had not been previously considered by PTAC.

2.2 The Subcommittee considered that the strength and quality of the evidence was poor to moderate. The Subcommittee noted that there were 9 trials provided which compared NovoMix 30 with human insulin 30/70, of which only one provided long-term data (Trial 1353 – 48 weeks).

2.3 The Subcommittee noted that four of the trials were randomised double blind studies (Trial 1234, Trial 1466, Trial 3002, and Trial 3006) and four trials included patients with type 1 diabetes although the majority of patients had type 2 diabetes.

2.4 The Subcommittee considered that a meta-analysis of the studies suggested that NovoMix 30, when compared with human insulin 30/70:

- lowered postprandial glucose increments after breakfast and dinner;
- was associated with higher fasting plasma glucose levels;
- did not affect HbA1c levels;
- did not affect the occurrence of minor hypoglycaemic episodes; and
- reduced the rate of major and nocturnal hypoglycaemic episodes.

However, the Subcommittee noted that the event rates for hypoglycaemia, in particular for nocturnal and major hypoglycaemia, were low.

2.5 The Subcommittee considered that, if listed, NovoMix 30 would be used preferentially over human insulin 30/70 (Humulin 30/70 and PenMix 30) and that a number of patients may switch from these products to NovoMix 30. Members also considered that short-acting insulin prescriptions may be reduced.

2.6 The Subcommittee considered that NovoMix 30 would be used mainly in type 2 diabetes, as a twice-daily premixture is very commonly used as initial treatment when insulin is required. The Subcommittee considered that NovoMix 30 would be used for initiation of treatment in such patients and that there would also be patients who would transfer from current premixes. Members considered that NovoMix 30 may also be used in some type 2 patients presently on combinations of rapid-acting and intermediate-acting insulin.

2.7 The Subcommittee noted that there are also a significant number of type 1 diabetes patients on twice daily mixtures who may transfer to NovoMix 30. The Subcommittee considered that some patients using separate injections of rapid-acting and intermediate-acting insulin may replace some of their separated injections with NovoMix 30 and that this may result in increased compliance.

2.8 The Subcommittee also considered that, while there was no evidence regarding the use of NovoMix 30 in children, the use of NovoMix 30 would appeal to this patient group, as it would reduce the number of injections required. The Subcommittee therefore considered that if NovoMix 30 was listed on the Pharmaceutical Schedule the overall market would increase.

2.9 The Subcommittee considered that NovoMix 30 has the same or similar therapeutic effect as Humulin 30/70 and Penmix 30 and that the dose equivalency was approximately the same. The Subcommittee considered the supplier's estimate of an average daily dose of 56.34U to be accurate.

2.10 The Subcommittee noted that funding of another biphasic analogue mix preparation Humalog Mix 25 (25% insulin lispro and 75% insulin lispro protamine suspension) had been recently considered by PTAC. Members considered that, if both NovoMix 30 and Humalog Mix 25 were listed on the Pharmaceutical Schedule, reference pricing could occur between these products. However, Members considered it was desirable that both products be fully funded. The Subcommittee considered that it was not appropriate to run a sole supply process between these products due to their different delivery devices and patient's preferences for different delivery devices (e.g. spring loaded pens) in this

market. Members noted that Novo Nordisk and Eli Lilly used different delivery devices that had different advantages and convenience factors.

2.11 The Subcommittee considered that patients who would benefit the most from NovoMix 30 were those unsuccessfully treated with oral agents and those using twice-daily insulin regimes who have inadequate glycaemic control. Members considered that, if listed, NovoMix 30 should not have any clinical restrictions applied.

2.12 The Subcommittee **recommended** that 30% insulin aspart and 70% insulin aspart protamine suspension be listed on the Pharmaceutical Schedule with a low priority.

2.13 The Subcommittee noted that the supplier had a registered NovoMix 70 and considered that there would be a small niche use for this in addition to NovoMix 30. The Subcommittee considered that it would be desirable to have a range of mixtures of this biphasic analogue mix to allow for tailoring of doses.

2.14 The Decision Criteria relevant to this recommendation are: *(iii) The availability and suitability of existing medicines, therapeutic medical devices and related products and related things; (iv) The clinical benefits and risks of pharmaceuticals; (vi) The budgetary impact (in terms of the pharmaceutical budget and the Government's overall health budget) of any changes to the Pharmaceutical Schedule; and (viii) The Government's priorities for health funding, as set out in any objectives notified by the Crown to PHARMAC, or in PHARMAC's Funding Agreement, or elsewhere.*

# 3 Sitagliptin

3.1 The Subcommittee noted that PTAC had considered, and declined an application from Merck Sharpe and Dohme for sitagliptin (Januvia), a dipeptidyl peptidase (DPP-4) inhibitor used in the treatment of patients with type 2 diabetes, to be listed on the Pharmaceutical Schedule. Members noted that PTAC had requested the application and minute be considered by the Diabetes Subcommittee.

3.2 The Subcommittee noted that in the key trials provided, sitagliptin showed modest efficacy and was generally associated with a lack of weight gain. The Subcommittee noted that sitagliptin appeared to be associated with fewer hypoglycaemic episodes than sulphonylureas.

3.3 The Subcommittee considered strength and quality of the evidence provided was moderate. Members considered that the data was short term and based on surrogate markers.

3.4 The Subcommittee considered that sitagliptin had a similar therapeutic effect to metformin but had a novel mode of action.

3.5 The Subcommittee considered that sitagliptin would be used in combination with metformin, sulphonylureas, pioglitazone, and insulin. The Subcommittee considered that sitagliptin may be used as an alternative to pioglitazone given the safety issues

associated with pioglitazone. Members considered that sitagliptin may delay the onset of insulin use and considered that, if listed, it would be used in second or third line therapy.

3.6 The Subcommittee considered that the additional health benefits from sitagliptin were its weight neutrality and low risk of hypoglycaemia. The Subcommittee considered that as sitagliptin was an oral and single daily dose it may be associated with improved compliance.

3.7 The Subcommittee considered that the risks of sitagliptin were undefined at this time due to the short-term, limited experience with this new class of drug. Members reiterated PTAC's concerns regarding the interpretation of limited long-term safety data and the safety issues that have emerged with longer-term data for the glitazones.

3.8 The Subcommittee considered that sitagliptin would be used by type 2 diabetes patients who were failing to benefit from other oral hypoglycaemic agents. The Subcommittee considered that prescribers would be likely to be initially cautious with prescribing sitagliptin and considered that the patient population estimated by the supplier was accurate.

3.9 The Subcommittee considered that Maori would benefit from the listing of sitagliptin because of the high rate of diabetes amongst this subset of the population.

3.10 The Subcommittee noted the cost-utility analysis provided by the supplier and amended by PHARMAC staff and the potential costs to the Pharmaceutical Budget should sitagliptin be listed.

3.11 The Subcommittee **recommended** that the application to list sitagliptin on the Pharmaceutical Schedule be declined until longer-term data was available.

3.12 The Subcommittee noted that other DPP-4 inhibitors were being registered by suppliers and that applications for funding were likely. Members considered that these pharmaceuticals would also need to show long-term data.

## 4 Insulin glargine (Lantus SoloStar) for diabetes mellitus

4.1 The Subcommittee noted that PTAC had considered, and referred to the Subcommittee for consideration, an application from Sanofi-Aventis for a new pre-filled disposable insulin delivery device (Lantus SoloStar) for insulin glargine to be listed on the Pharmaceutical Schedule as a replacement for the currently funded insulin glargine 3 ml cartridges and Owen Mumford disposable insulin delivery device. The Subcommittee noted the response that the supplier had made to PHARMAC regarding the PTAC minute. Members noted that the Lantus SoloStar device was cost neutral compared with currently funded cartridges and Owen Mumford devices.

4.2 Members noted the supplier's claims that the new delivery device incorporated a number of new and improved features compared with existing insulin pen devices. These included simplicity of use, reduced force required to deliver the injection, easy-to-read dose display, the strength and robustness of the device, and a maximum deliverable

dose of 80u (compared with 60u for FlexPen (Levemir) and 21u or 42u for Autopen 24 used for Lantus currently.

4.3 The Subcommittee considered the evidence in the application that considered patient acceptance, usability and preference of comparable insulin delivery devices. Members noted that the results were positive in these areas for the SoloStar device.

4.4 The Subcommittee noted that SoloStar could be wound back if users over-dialled their insulin dose and considered that this was a useful function. Members noted that the Owen Munford device could not be wound back and considered that currently this may result in some wastage.

4.5 The Subcommittee noted that the supplier proposed to introduce SoloStar gradually; however, the Subcommittee considered that the uptake of the new device is likely to be fast. Members considered that there would need to be a transition period of at least 6 months during which cartridges for the Owen Munford device remained available.

4.6 The Subcommittee noted the comments made by Sanofi-Aventis in relation to the PTAC minute. Members noted that using SoloStar without a needle (or with a blocked needle) can result in permanent damage to the device; however, this is common to all insulin delivery devices.

4.7 The Committee **recommended** that because the Lantus SoloStar device offered some advantages and there would be no cost associated with listing the device, the Lantus SoloStar device should listed on the Pharmaceutical Schedule with a high priority.

4.8 The Decision Criteria relevant to this recommendation are: *(i) The health needs of all eligible people within New Zealand;*; *(iii) The availability and suitability of existing medicines, therapeutic medical devices and related products and related things; (iv) The clinical benefits and risks of pharmaceuticals; (vi) The budgetary impact (in terms of the pharmaceutical budget and the Government's overall health budget) of any changes to the Pharmaceutical Schedule; and (vii) The direct cost to health service users.*

## 5 5-second Optium Blood Glucose Test Strip

5.1 The Subcommittee noted that PTAC had considered, and referred to the Subcommittee for consideration, an application from Medica Pacifica for a new generation (5-second) of Optium blood glucose test strips to be listed on the Pharmaceutical Schedule at the same price, and under the same restrictions, as the current Optium blood glucose test strips.

5.2 The Subcommittee noted that the supplier had submitted an application for the 3- second strip in November 2007 and that the Subcommittee at its November 2007 meeting had recommended it be listed on the Pharmaceutical Schedule. Members noted that to ensure continuity of supply the supplier now considered it preferable to align supply with the same test strip as that used in Australia, i.e. the 5-second strip rather than the 3-second strip.

5.3 The Subcommittee noted that the new test strip was compatible with the Optium Xceed blood glucose meters currently funded on the Pharmaceutical Schedule; therefore, patients would not be required to change meters with the introduction of the new generation Optium blood glucose test strips.

5.4 The Subcommittee noted that the new generation Optium test strip appeared to have some advantages over the existing Optium test strip; namely, it requires less blood (0.6uL rather than 1.5uL) and gives quicker results (5 seconds rather than 10 seconds).

5.5 The Subcommittee noted the test results for the new generation of Optium blood glucose test strips from the Clinical Pathology Department of Auckland City Hospital. The Subcommittee considered that the average imprecision of 7.7% was acceptable. The Subcommittee considered that the average bias of +13.1% was acceptable and was lower than the 3-second test strip and comparable with the re-calibrated Accu-chek Performa test strip (13.7%).

5.6 The Subcommittee **recommended** that the new generation 5-second Optium test strips be listed on the Pharmaceutical Schedule, subject to acceptable field-testing results to be conducted by [withheld under s9(2)(a) of the OIA ].

5.7 The Decision Criteria relevant to this recommendation are: *(i) The health needs of all eligible people within New Zealand*; *(iii) The availability and suitability of existing medicines, therapeutic medical devices and related products and related things; (iv) The clinical benefits and risks of pharmaceuticals; (vi) The budgetary impact (in terms of the pharmaceutical budget and the Government's overall health budget) of any changes to the Pharmaceutical Schedule; and (vii) The direct cost to health service users.*