

Diabetes Subcommittee of PTAC
Meeting held 11 December 2013

(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 relevant portions of the minutes relating to Diabetes Subcommittee discussions about an Application or PHARMAC staff proposal that contain a recommendation are generally 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.

These Subcommittee minutes were reviewed by PTAC at its meeting 8 & 9 May 2014, the record of which will be available in July 2014.

Record of the Diabetes Subcommittee of the Pharmacology and Therapeutics Committee (PTAC) meeting held at PHARMAC on 11 December 2013

GLP-1 and DPP4 Special Authority Funding Criteria

- 1.1 The Subcommittee noted PTACs recommendation for the Diabetes Subcommittee to provide further definitions for targeting patients with occupational risk of hypoglycaemia prior to funding.
- 1.2 The Subcommittee considered both criteria for GLP-1s and DPP4s as suggested by PTAC. With regards to the suggested criteria for the GLP-1s, the Subcommittee considered the requirement for maximum tolerated doses of a thiazolidinedione to be not clinically appropriate due to the clinical concerns associated with this drug class. The Subcommittee considered that due to the method of administration, patients may prefer an oral agent and therefore the risk of overuse with the GLP-1s would be minimal if both agents had the same restrictions. Members considered that the same Special Authority criteria could therefore apply to both GLP-1s and DPP4s.
- 1.3 The Subcommittee considered that in practice defining occupational risk of hypoglycaemia is difficult.
- 1.4 The Subcommittee **recommended** that the GLP-1s and DPP4s not be funded if co-prescribed with insulin.
- 1.5 The Subcommittee **recommended** the following Special Authority criteria for GLP-1s and DPP4s:

Initial application from any medical practitioner. Approvals valid for six months for applications meeting the following criteria:

1. Either:
 - 1.1. Patient is not achieving effective control of HbA1c despite treatment with maximum tolerated doses of metformin and sulphonylurea for at least 6 months; or
 - 1.2. Patient is not achieving target HbA1c despite treatment with maximum tolerated doses of sulphonylurea and metformin is contraindicated; or
 - 1.3. Patient is not achieving target HbA1c on maximum tolerated doses of metformin for the previous 6 months and is unable to use insulin or sulphonylurea therapy due to occupational risk; **as the risk of severe symptomatic hypoglycaemia is unacceptable in the opinion of the treating physician**
2. **Patient is not prescribed insulin**
3. It is anticipated that a reduction in HbA1c of 5 mmol/mol would achieve the HbA1c target **for that patient**

Renewal from any medical practitioner. Approvals valid for two years for applications meeting the following criteria:

1. Patient has achieved an HbA1c reduction of at least 5 mmol/mol from baseline and;
2. **Patient is not prescribed insulin**

Insulin needles/syringes

- 1.6 The Subcommittee noted there was a problem with access to insulin pen needles/syringes due to the current restriction of 100 needles/syringes per prescription. Members considered that most patients should use a new needle/syringe each day.
- 1.7 The Subcommittee **recommended** increasing the maximum quantity allowed on a prescription to 200 needles/syringes. Members considered that this would have no significant budgetary impact, as patients can currently access more needles/syringes by getting extra prescriptions, but would be more convenient to patients and prescribers.

Long Acting Insulin

- 1.8 The Subcommittee noted the high use of insulin glargine and considered that this may be being driven by intensive marketing. The Subcommittee discussed anecdotal evidence that some patients were being switched for no clinical reason. The Subcommittee **recommended** that PHARMAC consider this as a possible activity for the Best Practice Advocacy Centre (BPAC).

2 Insulin Pumps and Cystic Fibrosis Related Diabetes

Application

- 2.1 The Subcommittee reviewed a PHARMAC generated proposal to fund insulin pumps for cystic fibrosis related diabetes (CFRD)

Recommendation

- 2.2 The Subcommittee **recommended** that insulin pumps and consumables for patients with cystic fibrosis related insulin dependence be funded with a high priority with the same funding criteria as for Type 1 Diabetes

The Decision Criteria particularly 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*

Discussion

- 2.3 The Subcommittee considered the evidence for insulin pumps in CFRD to be poor. Members noted that there were no head to head trials comparing MDI (multiple daily injections) to pumps for this patient population. From the

evidence currently available Members considered that insulin pumps do not provide any additional health benefit compared with MDI unless the Special Authority criteria are met. The Subcommittee considered that further research with long term randomised controlled trials would be required to demonstrate any additional benefit.

- 2.4 The Subcommittee considered that there was no evidence to suggest that insulin pumps extend the life expectancy for patients with CFRD over that of MDI.
- 2.5 The Subcommittee considered that only a minority of patients with CFRD have full insulin requirements (cystic fibrosis with insulin dependence) with the majority needing a small amount of insulin.
- 2.6 The Subcommittee considered the population that would receive the greatest benefit would be those patients with cystic fibrosis related insulin dependence. Cystic fibrosis related insulin dependence is similar in presentation to patients who have had a pancreatectomy and have similar disease characteristics to Type 1 diabetes.
- 2.7 The Subcommittee agreed with PHARMAC's estimates around patient numbers. The Subcommittee estimated that approximately 50% of CF (cystic fibrosis) patients have no diabetes, approximately 25% have dysglycaemia and the remainder have insulin dependence. The Subcommittee estimated that approximately 5% of CF patients would seek funding for a pump.
- 2.8 The Subcommittee considered that CFRD patients receive similar health outcomes to patients with type 1 diabetes; however due to the shortened life expectancy of this group, these patients do not live as long, and therefore depending on the age of the patient, CFRD patients may not get the long term benefits expected for patients with type 1 diabetes.
- 2.9 The Subcommittee considered that there are other reasons that make glycaemic control more difficult with CF that may be better managed by insulin pumps, and theoretically could reduce hospitalisations. This group of patients are more susceptible to infections and better clearance of infections may be achieved with tighter glycaemic control. In addition CF patients often require steroids which can make tight glycaemic control difficult to achieve. The Subcommittee also considered that due to the higher frequency of meals that need to be eaten, glycaemic control is often difficult with MDI and pumps could lead to better nutritional outcomes.
- 2.10 The Subcommittee noted the CF has a significant impact on quality of life and that insulin pumps may help to improve this for patients with CFRD.
- 2.11 The Subcommittee considered that the Special Authority criteria could be amended as follows to allow widened access to insulin pumps for CF patients with insulin dependence:

Patient has type 1 diabetes or has undergone a pancreatectomy **or has cystic fibrosis related insulin dependence**;

3 Insulin pumps and pregnancy

Application

- 3.1 The Subcommittee reviewed a PHARMAC generated proposal to fund insulin pumps for pregnancy and diabetes

Recommendation

- 3.2 The Subcommittee **recommended** PHARMAC staff investigate other potential ways that funding of insulin pumps for pregnancy and diabetes could be considered in a cost effective manner.

Discussion

- 3.3 The Subcommittee considered the results from a study published by Bell and colleagues (Bell et al. Diabetologia. 2012;55:936-47) and noted that the benefits of low blood sugar levels (HbA1c <7%) were most important pre-pregnancy for decreasing the risk of congenital anomalies.
- 3.4 The Subcommittee considered that patients with gestational diabetes would have no need for an insulin pump. A Member noted that insulin pumps had been used in various centres for insulin dependent patients planning a pregnancy and in some places in type 2 patients with poor glycaemic control.
- 3.5 Members noted that women who were pregnant may have marked glycaemic variability during pregnancy.
- 3.6 Members considered that an insulin pump may allow tighter glycaemic control without risking hypoglycaemia. Members considered that there was a higher risk of diabetic ketoacidosis with an insulin pump, due to pump failure, than with multiple daily injections (MDI).
- 3.7 The Subcommittee considered the evidence for insulin pumps for pregnant people with Type 1 diabetes to be poor. Members noted that there were no head to head trials comparing multiple daily injections (MDI) to pumps for this patient population. Members considered that from the evidence currently available insulin pumps did not show any additional health benefit compared with MDI unless the current Special Authority criteria were met. The Subcommittee considered that further research with long term randomised controlled trials would be required to demonstrate any additional benefit.
- 3.8 The Subcommittee noted that HbA1c is a poor measure of blood glucose control during pregnancy due to the physiological changes that occur during pregnancy with an influx of new red blood cells and that post-prandial blood glucose levels better predicted adverse effects on fetal growth.

- 3.9 The Subcommittee considered that PHARMAC should consider an alternative approach for potentially funding insulin pumps in pregnancy such as a pool of insulin pumps.

4 Dapagliflozin

Application

- 4.1 The Subcommittee considered PTACs request for clinical advice for a treatment algorithm for the available anti-diabetic agents, including unfunded agents and the request for advice as to whether there were any specific class of unfunded hypoglycaemic agent that had a clinical advantage that would give one class a higher priority.

Recommendation

- 4.2 The Subcommittee **recommended** PHARMAC staff investigate possible treatment algorithms, for the available anti-diabetic agents, including unfunded agents and the costs that would be associated, for review at the next Subcommittee meeting.

Discussion

- 4.3 The Subcommittee noted PTAC's minutes on the application for dapagliflozin for Type 2 diabetes and the low priority given by the Committee.
- 4.4 The Subcommittee noted that dapagliflozin had a unique mechanism of action that was independent of beta cell function. Members considered that dapagliflozin had an impact in reducing HbA1c similar to the DPP4s and GLP-1s.
- 4.5 The Subcommittee considered that from the available evidence the SGLT-2 class appeared to have the least potential for harm from a side effect profile however this class has the shortest duration of available safety data.
- 4.6 The Subcommittee considered that the efficacy of dapagliflozin was dependent on renal function and therefore this agent would not be suitable for patients with renal impairment.
- 4.7 The Subcommittee considered that all unfunded hypoglycaemic agents (GLP-1, SGLT-2, DPP-4) had similar effects to metformin and sulphonylureas in that they all reduce HbAa1c by approximately 0.5 to 1%.
- 4.8 The Subcommittee did not consider one specific class of unfunded hypoglycaemic agent (GLP-1, SGLT-2, DPP-4) to have a clear clinical advantage over another.

- 4.9 The Subcommittee noted that the dipeptidyl peptidase-4 inhibitor (DPP-4) linagliptin has a point of difference compared with other DPP-4's in that it is not renally excreted and does not require dosage adjustment in renal impairment.
- 4.10 The Subcommittee considered that patients who had failed on treatment with sulphonylureas and metformin would most benefit from treatment with dapagliflozin. Members considered that restrictions would need to be placed on the use of dapagliflozin to target this population and that the same Special Authority as described earlier in the meeting (DPP-4s and GLPs) could be used.
- 4.11 The Subcommittee made reference to the NICE treatment algorithm for type 2 diabetes and considered that a similar approach could be developed by the committee. The Subcommittee considered that another meeting in the next six months would be required to review possible algorithms.

5 Diabetes Default dispensing review

Application

- 5.1 The Subcommittee considered the paper provided by PHARMAC staff including suggested reasons for restrictions to monthly default dispensing (e.g. potential for side effects, potential for overdose, stability, and minimising wastage). Members noted suggested reasons for more all-at-once dispensing (e.g. assisting adherence, consistency with similar medicines, and low cost for the additional medicine dispensed in comparison to pharmacist time).

Recommendation

- 5.2 The Subcommittee **recommended** that insulin be changed to all-at-once-default dispensing to reduce the risk of patients running out of supply.

Discussion

- 5.3 The Subcommittee noted that the decision on default dispensing changes, if any, would be subject to financial analysis of the affordability for DHBs/PHARMAC (e.g. due to the potential for increased medicines wastage with greater all-at-once dispensing) and a PHARMAC Board or delegated authority decision.
- 5.4 The Subcommittee had no clinical concerns with default all-at-once dispensing for any of the medicines listed in the 'Diabetes' and 'Diabetes Management' level 2 therapeutic groups as at December 2013. Members supported greater use of all-at-once default dispensing to assist adherence, increase convenience for patients, and reduce workload for pharmacists and doctors. The Subcommittee noted that, where appropriate (e.g. trial periods, safety concerns), the default dispensing can be overridden by doctors and pharmacists allowing shorter periods of supply.

- 5.5 In particular, the Subcommittee noted that insulin was currently month-default-optional-all-at-once (Section F Part II of the Pharmaceutical Schedule). Due to the life-saving and chronic nature of insulin treatment, the Subcommittee **recommended** that insulin be changed to all-at-once-default to reduce the risk of patients running out of supply.