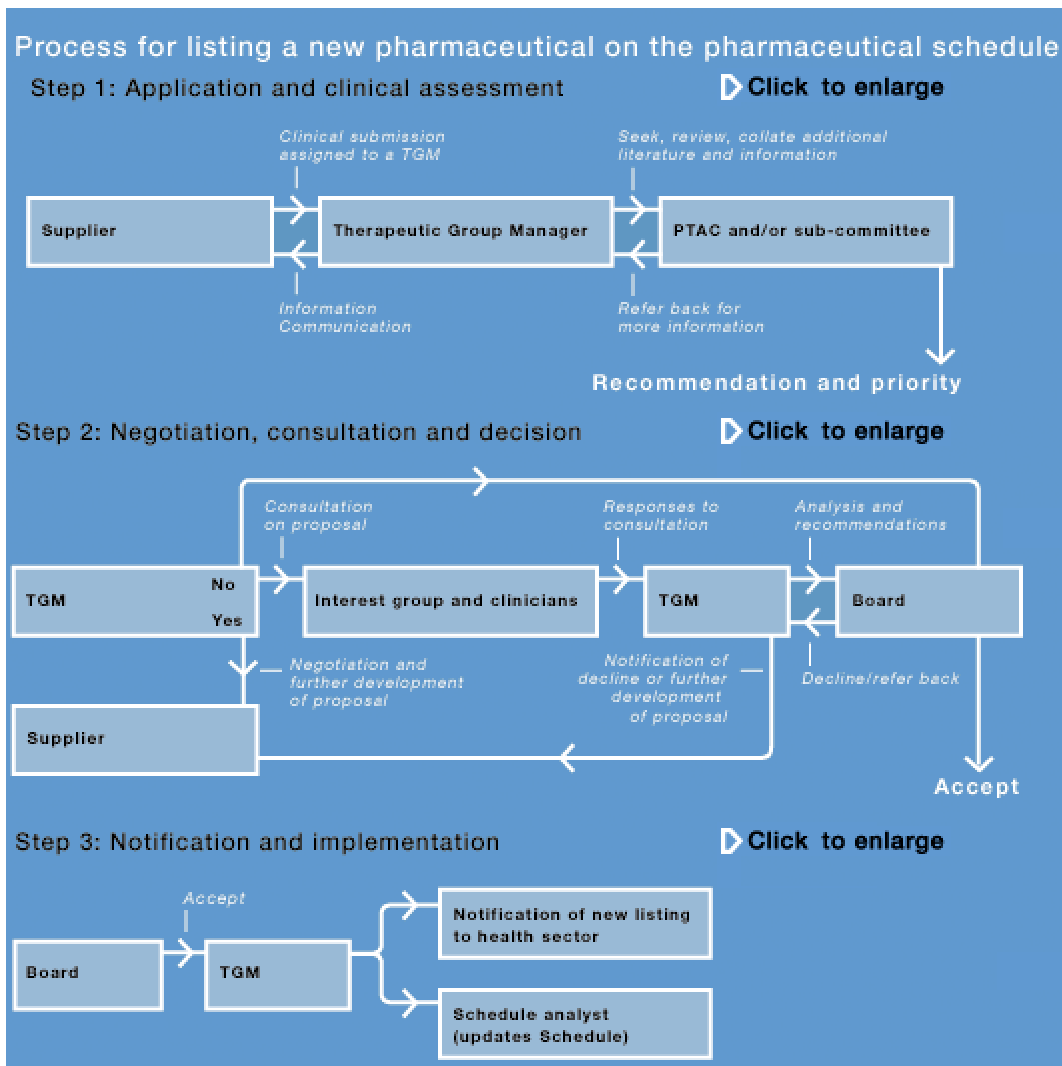


## **Attachment to ‘PHARMAC responds on long-acting insulin analogues’: further details**

### **1. PHARMAC’s processes**

PHARMAC’s process for assessing new pharmaceutical funding applications ([http://www.pharmac.govt.nz/funding\\_applications.asp](http://www.pharmac.govt.nz/funding_applications.asp)) is well established and involves both expert clinical review, negotiation with suppliers, consultation with the health sector, and then decision by PHARMAC’s Board:

- Once a new funding application has been received from a supplier, PHARMAC staff seek and collate more information for the application to be considered by the Pharmacology and Therapeutics Advisory Committee (PTAC);
- Following its consideration, PTAC either refers the application back to PHARMAC for further information or analysis, refers it on to one of its eleven expert subcommittees, or recommends whether PHARMAC funds the medicine and at what priority;
- If PTAC makes a recommendation for funding, PHARMAC then negotiates with the supplier to reach a provisional agreement on the terms and conditions of listing, including subsidy;
- PHARMAC then consults with the health sector on the proposal, takes this feedback into account, and submits the proposal (with any revisions) to the PHARMAC Board for a final decision.



## 2. PTAC

The volume of applications received by PHARMAC and considered by PTAC (<http://www.pharmac.govt.nz/ptac.asp>) is considerable. PTAC received 27 applications during 2004, and has received 25 this year so far. PTAC often reviews applications more than once (pending further information), usually reviewing at least ten applications each meeting. PTAC has eleven expert subcommittees that provide clinical evaluations in specialist areas.

PTAC meets four times each year, and during 2005 PTAC will have undertaken 51 reviews of new and revised applications etc. These numbers do not include applications sent directly to subcommittees and later ratified by PTAC – particularly many cancer drugs.

PTAC makes recommendations for moderate to high priority for funding in one quarter of cases, the rest being lower priority, declines, deferrals, or referrals to subcommittees.

PTAC agendas are full and submissions are extensive; agenda papers typically weigh 20 to 25 kg.

In turn, PHARMAC's budget has meant listing or extending access to 25 medicines in 2004/05, and decisions made since July 2005 affect 23 medicines costing an expected \$9.9 million this financial year (\$36 million by 2007/08).

### **3. Timelines with applications for long acting insulin analogues**

As part of obtaining satisfactory expert clinical advice, the application for insulin glargine was referred by PTAC to its Diabetes subcommittee. This is a normal process that aims to ensure objective decisions.

Timelines are as follows:

- Insulin glargine has been registered for use in New Zealand since June 2001, following first application for registration in May 1999 – some two years earlier.
- The supplier first applied to PHARMAC for funding in July 2004 – three years after registration.
- The application was considered by the PTAC in August 2004, which at that stage recommended a low priority for listing insulin glargine for the wider patient population proposed. PTAC considered that the evidence presented by the supplier demonstrated only modest improvements in HbA1c and hypoglycaemic episodes, and that insulin glargine would best benefit particular patient groups – particularly Type 1 diabetes with frequent hypoglycaemic episodes from existing insulin preparations.

PTAC requested PHARMAC undertake its own cost utility analysis (CUA) (PTAC had concerns with the CUA submitted by the supplier), and referred the application to its Diabetes subcommittee to develop appropriate targeting criteria; PTAC members considered the low priority recommendation might change if the Diabetes subcommittee could identify an appropriate target population and if there was a satisfactory CUA.

- PTAC's Diabetes subcommittee considered insulin glargine at its next meeting in May 2005. The subcommittee recommended a high priority for funding for certain patients with severe or nocturnal hypoglycaemia (described in Jeremy Krebs's article <http://www.nzma.org.nz/journal/118-1221/1641/>). PHARMAC's preliminary CUA for insulin glargine was part of the evidence considered by the subcommittee.
- In July 2005 an application from another supplier was received for another long-acting insulin analogue, insulin detemir, to be funded
- PTAC accepted the Diabetes subcommittee's May 2005 recommendation for insulin glargine when it next met in August 2005. At the same time PTAC considered insulin detemir, including PHARMAC's CUA for insulin glargine (where it was noted that cost/QALYs for insulin detemir may differ from insulin glargine). PTAC recommended

insulin detemir be listed for the same patient groups recommended for high priority for insulin glargine.

- Given the application for another long-acting insulin antagonist (insulin detemir), advice was sought from the Diabetes subcommittee comparing the two products. The Diabetes subcommittee met again in October 2005, considering (amongst other material) adaptations to PHARMAC's CUA for insulin glargine specific to patients with previous severe hypoglycaemia, and a CUA for insulin detemir for those patients.

PHARMAC is now negotiating with the suppliers of both insulin glargine and insulin detemir for a commercial arrangement to list one or both long acting insulin analogues; any agreed proposal(s) would then be considered by PHARMAC's Board. Any proposals for the listing of any long-acting insulin analogues would then be subject to the standard decision criteria that all proposals are weighed against, alongside competing investment opportunities at the time.

#### 4. Relevant portions of PTAC and Diabetes subcommittee minutes

**Record of the Pharmacology and Therapeutics Advisory Committee Meeting held on 19 August 2004**  
([http://www.pharmac.govt.nz/latest\\_PTAC\\_minutes.asp](http://www.pharmac.govt.nz/latest_PTAC_minutes.asp))

##### **Insulin glargine (Lantus)**

The Committee reviewed an application from Aventis to list insulin glargine on the Pharmaceutical Schedule.

The Committee reviewed the studies that had been provided in the submission for the use of this product in patients with type I and type II diabetes. Members noted that the trials were predominantly open-label in design due to the difficulty in blinding participants to the clarity difference between isophane insulin and insulin glargine. They considered that the majority of the trials had adequate sample sizes and treatment duration.

The Committee considered that, to represent a significant advance in insulin treatment, evidence of improved control (measured by HbA1c) and reduced hypoglycaemic episodes (particularly severe hypoglycaemia), as well as simplification in treatment schedules, would be required. Members noted that insulin glargine should provide physiological benefits over existing insulin preparations; however, they considered that the evidence demonstrated only a modest improvement in HbA1c and hypoglycaemic episodes.

The Committee considered that insulin glargine would be of most benefit in particular patient groups, including patients with type-I diabetes who have frequent hypoglycaemic episodes with existing insulin preparations.

The Committee reviewed the cost-effectiveness study provided by the supplier and considered that the modelling used was not appropriate for standard clinical practice. The Committee therefore disagreed with some of the assumptions in the analysis and recommended that PHARMAC conduct its own cost-utility analysis.

Members considered that the Diabetes Sub-committee of PTAC should review the application and that the Sub-committee be asked to recommend appropriate targeting criteria.

The Committee **recommended** that insulin glargine be listed on the Pharmaceutical Schedule, but should also be referred to the Diabetes Sub-committee of PTAC. In view of the high price and modest clinical benefit of insulin glargine compared with currently available insulins the Committee gave a low priority to

listing. However, members considered that this recommendation might change if the Diabetes Sub-committee could identify an appropriate target population and if there were a satisfactory CUA.

The decision criteria relevant to the assessment of this application include: (i) the health needs of all eligible people within New Zealand, as diabetes is a major health problem in New Zealand; (ii) the particular health needs of Maori and Pacific peoples, due to the higher prevalence of diabetes in these populations; (iii) the availability and suitability of existing medicines, therapeutic medical devices and related products and related things, as current insulin regimes are far from ideal; (iv) the clinical benefits and risks of pharmaceuticals, as insulin glargine has some clinical advantages over currently available insulins; (v) the budgetary impact (in terms of the pharmaceutical budget and the Government's overall health budget) of any changes to the Pharmaceutical Schedule in view of the high price of insulin glargine; 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, as diabetes is a priority for health funding.

Minutes of the Diabetes subcommittee's 17 May 2005 and PTAC's 17-18 August 2005 meetings have yet to undergo full public release. Draft minutes of the Diabetes subcommittee's 10 October 2005 meeting await ratification by the subcommittee.