

February 2004: PTAC minutes for web publishing

PTAC minutes are published in accordance with the following definitions from the PTAC Guidelines 2002:

“**Minute**” means that part of the record of a PTAC or Sub-committee meeting (including meetings by teleconference and recommendations made by other means of communication) that contains a recommendation to accept or decline an application for a new investment or a clinical proposal to widen access and related discussion.”

Note that this is not necessarily a complete record of the PTAC meeting; some material may be withheld for reasons such as protection of supplier commercial information that has been supplied in confidence.

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Letrozole (Femara)

The Committee reviewed correspondence from Novartis regarding the minutes of PTAC's November 2003 meeting.

Members acknowledged that the ASCO recommendations regarding the first-line use of aromatase inhibitors related to adjuvant treatment of breast cancer. They considered that the evidence presented by Novartis predominantly related to patients with metastatic disease, and that these patients had a short life expectancy. The intent of treatment in these patients was to extend life, whereas in the adjuvant setting the intention was to prevent disease recurrence.

The Committee considered that its recommendation that tamoxifen should be used first-line in the adjuvant setting should remain unchanged, and that this should include patients with locally advanced disease until further data becomes available. Members also considered that PTAC's previous recommendation regarding letrozole should remain unchanged, and that Novartis' application to widen its funding to advanced breast cancer should remain a low priority due to the small overall survival benefit. The Committee considered that the priority could be increased to medium if a suitable commercial agreement could be reached.

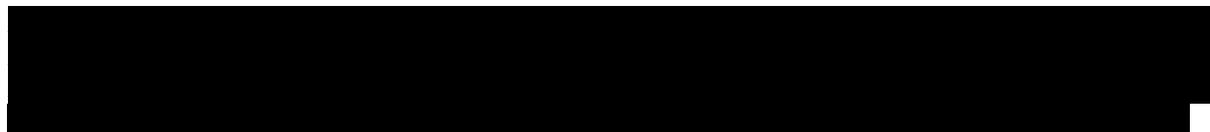
The Committee considered that, in the context of Novartis' application, the term "advanced breast cancer" was open to some ambiguity since locally advanced breast cancer could fall under this term, whereas PTAC's recommendation related to metastatic breast cancer, and those patients who have a recurrence following completion of tamoxifen therapy. The Committee recommended that CaTSOP develop some Special Authority criteria to reduce this ambiguity.

Risperidone microspheres (Risperdal Consta) depot injection

The Committee noted the 15 January 2004 record of the Mental Health Sub-committee of PTAC in relation to risperidone microspheres (Risperdal Consta). Members noted that the sub-committee made some changes to the criteria that PTAC had recommended in May 2003, resulting in the following proposed Special Authority criteria:

Risperidone microspheres (Risperdal Consta) is subsidised for patients with schizophrenia or related psychoses who:

- (i) have a documented history of adverse effects with standard depot antipsychotics; OR
- (ii) have a documented history of non-adherence to oral atypical antipsychotics, where the risk of a conventional depot trial is considered to be unacceptable.



The Committee noted that there was some evidence that in many cases the current clinical practice in terms of treatment of newly diagnosed patients with schizophrenia or related psychoses was to start them on atypical antipsychotics. Members also noted, however, that atypical antipsychotics were in many cases no more effective than conventional antipsychotics but they had a better side effect profile. The Committee considered that adverse effects of conventional depot antipsychotics could be significant, and

in some cases this was the main reason why patients refused injections. The Committee noted that such patients would be negotiating with their prescribers on an on-going basis to switch to oral medications at the earliest opportunity. Members considered that the benefit of risperidone microspheres could be in the early stages of treatment as it might be easier for clinicians to convince patients to take it given its better tolerability. The Committee considered that once the treatment was initiated patients might stay on it for years.

The Committee recommended the listing of risperidone microspheres on the Pharmaceutical Schedule and gave a high priority to its recommendation. One member considered that the recommendation should be given a moderate priority instead of high. Members recommended the following Special Authority criteria (changes to the version proposed by the Mental Health Sub-committee are in bold and strikethrough):

Risperidone microspheres (Risperdal Consta) is subsidised for patients with schizophrenia or related psychoses who:

- (i) have a documented history of **clinically significant and intolerable** adverse effects with standard depot antipsychotics; **AND**
- (ii) have a documented history of non-adherence to oral atypical antipsychotics. ~~where the risk of conventional depot trial is considered to be unacceptable.~~

The relevant decision criteria are: (i) the health needs of all eligible people within New Zealand; (the Committee considered that patients with schizophrenia at a high risk of non-compliance are at high need for health services) (ii) the particular health needs of Maori and Pacific peoples; (the Committee noted that schizophrenia accounts for a higher proportion of admissions for Maori compared with Pakeha; the Committee further considered that Maori would be more likely to experience repeated hospital admissions; research shows Maori are more likely to be prescribed depot antipsychotic medication than people of other ethnicity) (iii) the availability and suitability of existing medicines, therapeutic medical devices and related products and related things (the Committee noted that there was no long-acting injectable intramuscular atypical antipsychotic available on the Pharmaceutical Schedule); (iv) the clinical benefits and risks of pharmaceuticals (the Committee considered that risperidone microspheres offered significant clinical benefits over the existing subsidised treatments (both conventional and atypical antipsychotics); the Committee considered however that a longer duration of action could be associated with greater risk of side effects); (v) the budgetary impact (in terms of the pharmaceutical budget and the Government's overall health budget) of any changes to the Pharmaceutical Schedule (the Committee considered that the listing of risperidone microspheres would be likely to be associated with extra expenditure to the pharmaceutical budget); (vi) the direct cost to health service users; 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 (the Committee noted that one of the government's population health objectives was to "improve the health status of people with severe mental illness" and that risperidone microspheres could contribute to this objective).

Verteporfin (Visudyne) – photodynamic therapy

The Committee considered the further application from Novartis for the funding of verteporfin for the treatment of small ($< \text{MPS DA} = 10.2\text{mm}^2$) subfoveal choroidal neovascularisation (CNV) lesions. Members noted that this indication was different from the indications listed in the Medsafe data sheet, which were for the treatment of patients with predominantly classic or occult subfoveal choroidal neovascularisation due to age-related macular degeneration (AMD), or with subfoveal choroidal neovascularisation caused by other macular diseases.

The Committee considered that photodynamic therapy using verteporfin was a highly specialised procedure, which would be provided only by some hospitals for outpatients and by a small group of private ophthalmologists. Members questioned the appropriateness of funding verteporfin through the

community section of the Pharmaceutical Schedule. They noted that Medsafe had registered verteporfin as a medicine and therefore the supplier had applied to PHARMAC for funding. The Committee maintained its previous view that the evidence of efficacy of this treatment in the indication proposed by the Novartis was based on the data from a subgroup of patients, which was obtained through an exploratory post-hoc analysis of the results of three clinical trials. Committee members understand that there appears to be long waiting lists for publicly funded ophthalmological services across the country, particularly for procedures such as cataract surgery, which is known to reduce visual disability in the community. They considered that funding for a new medicine such as verteporfin needs to be considered in the context of access to ophthalmological services in total, as delayed diagnosis of subfoveal choroidal neovascularisation could significantly reduce the effects of the medication. Visual impairment is associated with falls in the elderly but the Committee was not aware of any evidence that correcting vision would reduce falls in comparison to other programmes which are proven to be effective in falls prevention.

The Committee considered that, as photodynamic therapy with verteporfin was a highly specialised procedure, it would be appropriate to seek an opinion from the Ophthalmology Sub-committee of PTAC on the appropriateness of funding it through the community section of the Pharmaceutical Schedule. Subsequently, if the sub-committee considers that it might be appropriate for verteporfin to be funded through the community section of the Pharmaceutical Schedule, then the application should be referred to them for further consideration.

Naltrexone hydrochloride (ReVia)

The Committee considered the naltrexone (ReVia) application together with responses submitted to PHARMAC as part of the December 2003-January 2004 consultation on the proposal to subsidise it for the treatment of alcohol dependence.

Members considered that General Practitioners (GPs) who specialise in alcohol and drug (A&D) treatments, but who work only part time for A&D services, should be allowed to make applications for a Special Authority and prescribe naltrexone. The Committee considered that such clinicians should be allowed to prescribe naltrexone while working for the A&D services but not when working in their normal GP practices, as the stated aim was to prescribe within an integrated multidisciplinary team. On the basis of the available evidence and given fiscal constraints the Committee recommended a three-month initial approval with an extension for another three months. Members considered that the proposed re-application criteria were reasonable. They considered that there was no good clinical trial evidence to show that patients who stayed on naltrexone for longer than six months (e.g. twelve months) benefited from such a treatment. They noted that there was some anecdotal evidence of benefit in some patients in Australia who stayed on naltrexone for twelve months or longer. The Committee considered, however, that at this stage it would not be appropriate to fund treatment for longer than six months in a year.

The Committee recommended the following Special Authority criteria for naltrexone:

- a) Subsidised for patients currently enrolled in a recognised comprehensive treatment programme for alcohol dependence in a service accredited against the New Zealand Alcohol and Other Drug Sector Standard or the National Mental Health Sector Standard.
- b) Applications and prescriptions to be made/written by clinicians working in an Alcohol and Drug Service. Note to be made on the Special Authority form indicating that the doctor works in an Alcohol & Drug Service and including the address of the service.
- c) Approvals and re-approvals are valid for three months. Approvals are granted for a maximum of six months treatment in a year (which can be either consecutive or intermittent) for any one patient per year.

The re-application criteria are: (1) compliance with the medication but patient is still unstable and requires further treatment; (2) compliance with the medication and patient achieved significant improvement but requires

further treatment; or (3) compliance with the medication and patient is well controlled but requires maintenance therapy. All re-application criteria are prescriber determined.

Products to be considered for delisting from the Pharmaceutical Schedule

The Committee noted that the Tender Medical Evaluation Subcommittee of PTAC had recommended the following products be considered for delisting from section B of the Pharmaceutical Schedule:

- Calcium 10% injections (chloride and gluconate salts)
- Tolnaftate solution 1% and cream 1%
- Salbutamol infusion 1 mg per ml, 5 ml infusion
- Propamidine isethionate eye drops 0.1%
- Dibromopropamidine isethionate eye ointment 0.15%
- Progesterone injection 50 mg per ml, 2 ml

Members also noted that PHARMAC intends to consult more widely before making the final decision to de-list any of the above products.

Calcium injection

The Committee noted calcium chloride 10% injection is mainly used in hospital as a third line agent in cardiac arrest. Members considered calcium chloride might be used in the community for the treatment of hypocalcaemic tetany. However they noted it is an irritant to veins and can cause arrhythmias, hypotension, and syncope. The Committee considered calcium gluconate was a safer treatment option for hypocalcaemia. The Committee considered calcium chloride 10% injection could be delisted from Section B of the Pharmaceutical Schedule but considered that calcium gluconate 10% injection should be retained on the Pharmaceutical Schedule.

Tolnaftate

The Committee noted that tolnaftate solution 1% and cream 1% are topical antifungal preparations with activity against superficial dermatophyte infections, and pityriasis versicolor. Members considered it was a narrow spectrum agent, with little clinical effectiveness against common fungal pathogens and noted it was sold over the counter at pharmacies. They considered that tolnaftate could be removed from the Pharmaceutical Schedule.

Salbutamol infusion

The Committee noted that injectable salbutamol was indicated for use in severe asthma, and use for tocolysis in premature labour. The Committee considered that the use of salbutamol in labour had been largely superseded by nifedipine, which is considered to have less toxicity, and similar efficacy. However, members considered that it was important for rural general practitioners to have access to salbutamol injection. They considered that the infusion could be removed from the Pharmaceutical Schedule.

Propamidine isethionate and dibromopropamidine isethionate

The Committee noted that propamidine is an anti-infective used in conjunctivitis, foreign body prophylaxis, acanthamoeba keratitis, and ophthalmia neonatorum. Members considered that there are alternative preparations listed on the Pharmaceutical Schedule with greater potency and clinical acceptance. The Committee considered there was no clear niche for these products, and considered they could be delisted.

Progesterone injection

The Committee noted that progesterone injection 50 mg per ml, 2 ml was used for the treatment of dysfunctional uterine bleeding, and has been used in assisted reproductive techniques. Members noted that the usage in the community was very low, and that pharmacies would often have to discard injections because of the low usage. The Tender Medical Evaluation Sub-committee considered that usage would be restricted mainly to fertility clinics, which have their own source of funding. The Committee considered that progesterone injection could be delisted from the Pharmaceutical Schedule. Members suggested, however, that fertility clinics be consulted to ensure that funding was available and/or sufficient.

Access to Multiple Sclerosis treatments

The Committee considered a letter and petition from an Otago Interest Group together with references provided by the Group and by PHARMAC staff. Members noted that the Otago Interest Group requested widening of access to the disease modifying agents in the treatment of multiple sclerosis. They also noted that PTAC had last considered access to multiple sclerosis treatments (specifically interferon alpha and beta) in May 2002 when it considered a recommendation from the Multiple Sclerosis Treatment and Assessment Committee (MSTAC) for access to be widened. MSTAC had recommended changing the entry criteria so that those with 3 or more relapses per year can have a lower baseline EDSS of 2 (compared with the current lower baseline EDSS of 3).

At the May 2002 meeting the Committee noted in summary that it had not seen a clear case for widening access to beta-interferon in MSTAC's initial report. It also did not consider that the trials proved that early treatment would have a positive impact on disease progression. PTAC noted that, under a fixed total pharmaceutical budget, funding of early treatment would come at the expense of other patients with more advanced disease who may have a lesser capacity to benefit.

The Committee noted at this meeting that no new positive evidence (compared with that presented in May 2002) had been provided with the Otago Interest Group submission. Members noted that the only additional information was a report (and cost-utility analysis) from the UK National Institute for Clinical Excellence (NICE) which states that, on the balance of clinical efficacy and cost effectiveness, NICE did not support funding either beta interferon or glatiramer.

The Committee noted that there are theoretical reasons supporting early treatment but that the theory has not been supported by the evidence that members have seen to date. They noted that there is no direct evidence that early intervention has long-term benefits. In addition, it noted that the cost of treatment was significant and suggested the Otago Interest Group approach the suppliers of beta-interferon regarding the price.

The Committee concluded that, given the insufficient evidence to date, it did not support widening access to disease modifying agents in the treatment of multiple sclerosis.

Access to adult growth hormone replacement therapy

The Committee considered a proposal from a working party of the NZ Society of Endocrinology for the funding of growth hormone for severely growth hormone deficient adults. The Committee, however, did not support the proposal in the present form. In making their recommendation members noted that intuitively treatment seemed like a sensible option for people with significant symptoms attributed to growth hormone deficiency. However, members noted that the evidence for improvement in quality of life was mostly based on observational studies and improvements were noted only in a few dimensions. There was no conclusive evidence on mortality benefits. The cost per QALY gained based on the cost utility analysis was very variable based on the models used but likely to be high. According to the University of Sheffield School of Health and Related Research, using the best-case scenario, estimated cost per QALY was £45,000. The incremental cost effectiveness ratio was £25,000 to £45,000. Members

also noted that there is a Cochrane review looking at improvement in quality of life and mortality benefits in adults with growth hormone deficiency, which may further clarify the value of this treatment.

One member agreed with the concept in principle but felt that further evidence (including copies of publications) in support of the proposal was required.

The Committee recommended that funding not be made available for adults who are severely deficient in Growth Hormone.

Growth hormone therapy for short children born small for gestational age

The Committee considered an application from the parents of a child seeking this treatment. Members noted that the basis for the request was a consensus development statement, which had been sponsored by Pharmacia, a supplier of growth hormone (GH).

The Committee noted that most studies used a height SDS of -2.0 as an entry criterion, however, in practice median height SDS scores at entry ranged from -2.8 to -3.5 SDS. Members noted that children born small for gestational age with height below -3.0 SDS could be considered for GH therapy under existing access criteria. Members also noted that there are insufficient and conflicting data contained within the studies presented to clarify whether there is any greater benefit in GH therapy according to height at entry.

The Committee noted that the predicted final height gain was between 4 and 6cm for short children who were born small for gestational age. This gain was less than that observed following treatment of other conditions, for which growth hormone is funded.

The Committee recommended that the current criteria for access to growth hormone not be adjusted at this time.

Enzyme replacement therapy for Fabry's disease

The Committee was asked by the Exceptional Circumstances panel to review the role of enzyme replacement therapy in Fabry's disease.

Members noted that there are two enzyme treatments available and, despite a five-fold difference in the dosing schedule used in trials, there was no apparent difference between either enzyme treatment. They noted that the evidence to date is either lacking or preliminary and inconclusive regarding the effects of treatment on pain, renal and cardiac function and cerebrovascular disease. They also noted the lack of evidence for long-term benefits.

The Committee considered that it would be premature to recommend that enzyme replacement therapies be subsidised for Fabry's disease.

Atorvastatin (Lipitor)

Revised Special Authority criteria for atorvastatin

The Committee noted the information provided by PHARMAC staff on atorvastatin.

Members considered that, in comparison to moderate dose statin therapy, high dose statin therapy results in a small change to a surrogate marker (cholesterol levels) of health outcomes while causing a significant increase in the risk of adverse events.

They considered that severe intolerance to statins was rare and was mostly a class effect, so that if a patient was intolerant to simvastatin it is likely he/she would be intolerant to all statins. They also considered that a small group of patients may have an idiosyncratic reaction to simvastatin that did not recur on another statin, and that an alternative statin should be available for these patients. Members considered that notes should be included on the revised Special Authority for atorvastatin explaining class effects for statins, and that if these types of intolerance occurred on simvastatin they were also likely to occur on another statin. They also considered that information on the frequency of intolerance to statins should be included in the notes.

The Committee considered that the number of Special Authority approvals for atorvastatin under the criterion of intolerance could be monitored such that if the number of patients gaining approval was significantly higher than would be expected based on clinical evidence, then availability under this criterion could be tightened. Based on clinical data the Committee did not expect to see an incidence of genuine intolerance greater than 5.0%, which, if a class effect, would be expected to occur with all statins.

The Committee considered that the lipid tests done during treatment with 80 mg simvastatin, and while trialling atorvastatin, should be carried out while the patient is in a fasted state. Members considered that, with the requirement for at least a 3 month trial of simvastatin 80 mg, the tests during treatment with it, did not need to be “at least one month apart”, and recommended that this be changed in the criteria to “at least one week apart”.

The Committee discussed the most appropriate treatment target for restricting access to atorvastatin. Members considered there should be one target only. There were differing views as to whether the target should be total or LDL cholesterol. The Committee recommended that wider consultation should occur on this issue.

The Committee noted the LDL cholesterol targets specified by the New Zealand Guideline Group (NZGG) of 2.0 mmol/l for patients with venous CABG, and 2.5 mmol/l for other patients, qualified by a statement that treatment targets should be adjusted individually according to the patient’s level of cardiovascular risk. Members also noted that the LDL cholesterol targets were listed under the NZGG’s highest grade of recommendation (A).

The Committee considered that the LDL cholesterol target of 2.5 mmol/l was low relative to the European guideline target for most patients of 3.0 mmol/l, and suggested that the use the European targets could be more appropriate for some patient groups.

The Committee considered that the four-week initial approval period for atorvastatin should be extended to eight weeks to provide additional time for dose titration.

The Committee considered that applications for a Special Authority for atorvastatin should be by relevant specialists and by general practitioners.

The Committee considered that it was not necessary to specify “or the maximum tolerated dose” after simvastatin 80 mg in the proposed Special Authority criteria, because patients who could not tolerate 80 mg simvastatin were covered by the criterion of severe documented intolerance.

Taking into account the recommendations above, the Committee recommended the following Special Authority criteria for atorvastatin, following reference pricing, be changed as follows (changes from the Sub-committee’s recommendations marked in bold and strikethrough):

Special Authority - Retail Pharmacy:

- a) Initial approval for patients with a calculated absolute risk of cardiovascular disease of $\geq 15\%$ over 5 years who:

- have severe documented intolerance to simvastatin; or
- have been compliant with a dose of simvastatin 80 mg ~~(or the maximum tolerated dose)~~ per day for at least 2 months; and
- do not reach target total and LDL cholesterol levels defined as follows:

| | | |
|---------------------------|--|--|
| Patients with venous CABG | Total cholesterol < 3.5 mmol/L | LDL cholesterol < 2.0 mmol/L |
| Other patients | < 5.0 4.0 mmol/L | < 2.5 3.0 mmol/L |

- ~~have total and LDL cholesterol levels that are not still improving. To confirm that cholesterol levels are not still improving, two lipid tests must be carried out during treatment with simvastatin 80 mg (or the maximum tolerated dose). The tests must:~~
 - **be carried out while the patient is in a fasted state (with the exception of patients with IDDM);**
 - be carried out at least one ~~month~~ **week** apart; and
 - have results for total and LDL cholesterol that have reduced by <10% in the second test.
- b) Initial approvals are valid for ~~four~~ **eight** weeks.
- c) Reapprovals:
- Patients are required to have their lipid levels tested during the ~~four~~ **eight** week initial approval period for atorvastatin. For a reapproval to be granted the test must ~~show that:~~
 - **be carried out while the patient is in a fasted state (with the exception of patients with IDDM);**
 - **show that** total or LDL cholesterol levels have reduced by >10% in comparison to the patient's last test prior to atorvastatin treatment; or
 - for patients with venous CABG, **show that** target total or LDL cholesterol levels have been reached.
- d) Reapprovals are valid indefinitely.
- e) Applications can be made by a relevant specialist **or a general practitioner.**
- f) Prescriptions can be written by a relevant specialist or a general practitioner.

Note:

The following indications of intolerance to simvastatin, are known as class effects for all statins, and hence are likely to mean that the patient may also be intolerant of atorvastatin:

- Constipation, flatulence (may occur in $\geq 1\%$ of patients)
- Asthenia, abdominal pain, headache (may occur in $\geq 1\%$ of patients)
- Myopathy, rhabdomyolysis (may occur in <1% of patients)
- Elevated serum transaminases levels (may occur in <1% of patients)

Statins have been shown to be generally well tolerated in clinical studies, with the rate of discontinuation due to adverse reactions being less than 5%, and similar to the discontinuation rate for patients taking a placebo.

The Committee noted the Cardiovascular Sub-Committee's recommendation that patients being treated with 80 mg atorvastatin and patients with genetic lipid disorders (Group NHF A2) be grand-parented to remain on atorvastatin without the need for a trial of simvastatin. Members considered that the criteria for grand-parenting should be tightened to only include those patients:

- being treated with 80 mg atorvastatin with documented evidence of an adequate trial of simvastatin, or with documented evidence that they had been titrated from a lower dose atorvastatin to a dose of 80 mg (copies of the documented evidence to provided along with the application); or
- with homozygous familial hypercholesterolemia being treated with 80 mg atorvastatin.

Rosuvastatin (Crestor)

The Committee reviewed the supplier's application and the information provided by PHARMAC staff on rosuvastatin.

It considered rosuvastatin to be more potent than other statins currently available. In particular it considered 10 mg rosuvastatin to be equivalent in reducing cholesterol levels to 80 mg simvastatin and 40 mg atorvastatin.

The Committee noted that the supplier's application for the registration of an 80 mg dose had been withdrawn. Members considered there to be safety issues with the use of rosuvastatin, particularly at higher doses (for example myopathy, rhabdomyolysis, proteinuria, nephritis, and haematuria). The Committee raised a particular concern about renal toxicity with the use of rosuvastatin, noting that proteinuria had not previously been considered a class effect for statins.

The Committee noted that rosuvastatin had recently been recommended for approval for use in Australia at a dose range from 5 mg to 20 mg per day, but only for use in patients with hypercholesterolemia.

The Committee considered that P-glycoprotein interactions of rosuvastatin with other pharmaceuticals have not been fully explored, notably with alterations in cyclosporin pharmacokinetics. Members considered that if rosuvastatin were to be listed on the Schedule it should be restricted under Special Authority for patients whose cholesterol is not adequately controlled on maximum dose atorvastatin.

The Committee considered that other agents for the treatment of raised cholesterol levels with good safety and clinical outcome data were available but there was not adequate long-term safety and clinical outcome data for rosuvastatin. The Committee therefore recommended declining rosuvastatin for listing on the Schedule at this time.

Carvedilol (Dilatrend): access criteria

The Committee noted the supplier's application and the information provided by PHARMAC staff on carvedilol.

The Committee considered that the dose of metoprolol used in the COMET study was below the dose used the MERIT-HF study, which may have accounted for the lower health benefits. Members also noted, however, that the price of metoprolol would increase on 1 July 2004.

The Committee considered that the additional survival benefits from the use of carvedilol in comparison to metoprolol in the COMET study should be investigated further, and recommended that PHARMAC staff conduct a cost-utility-analysis for members' consideration.

Hormone replacement therapy: cost utility analysis

The Committee noted that the PHARMAC Board had requested PHARMAC staff undertake a cost utility analysis (CUA) of hormone replacement therapy (HRT). The Committee noted that PHARMAC staff were seeking PTAC's opinion on the CUA and whether any restrictions should be placed on the use of HRT in the Pharmaceutical Schedule.

The Committee considered that the assumptions used in the rapid cost-utility analysis of HRT were reasonable, and members did not identify any important factors excluded from the rapid analysis that would have an impact on the results.

The Committee noted that the CUA presented by PHARMAC staff helped to clarify the evidence surrounding HRT use. Members noted that in younger perimenopausal women HRT was associated with a small risk of harm, but this was greater in older post-menopausal women (typically over 60 years of age). They also noted that time of menopause for women was variable.

The Committee noted in the CUA that, extrapolating from published analyses of excess risks associated with HRT use found in major RCTs and observational studies, for every 417 postmenopausal women aged 60-69 treated with HRT for one year, one will suffer a stroke or pulmonary embolus or develop breast cancer (number-needed-to-harm). However, members considered that HRT is necessary in a small group of perimenopausal women for treating severe vasomotor symptoms unresponsive to other treatment. They also noted that the use of HRT appeared to be continuing to decrease.

The Committee considered that HRT treatment to be highly effective in symptomatic perimenopausal patients, with likely gains in overall quality-adjusted life expectancy. Members considered that no restrictions should be placed on the use of HRT.

Tiotropium (Spiriva)

The Committee noted that it had reviewed applications for tiotropium on two previous occasions, with the Committee seeking respiratory medicine input from [REDACTED] and the opinions of the Respiratory Sub-committee of PTAC at its last review. Members noted that the opinions of the Respiratory sub-specialists were largely positive for the listing of tiotropium on the Pharmaceutical Schedule, particularly regarding the reduction in hospital admission rates observed in the two 12 month efficacy trials. They also noted that admissions for chronic obstructive pulmonary disease (COPD) exacerbations accounted for a large proportion of the treatment costs incurred for COPD. Some members were sceptical about the likely impact of tiotropium on hospital admissions and cautioned that this product had potential for high expectations (and therefore expenditure) without delivering savings in other areas.

The Committee noted the Special Authority criteria for tiotropium recommended by the Respiratory Subcommittee of PTAC. Members noted that access to pulmonary rehabilitation is not uniform around New Zealand. They considered that the Special Authority criteria recommended by the Respiratory subcommittee to be appropriate. They recommended that the priority for listing should remain high, subject to confirmation of supposed benefit by way of a cost-utility analysis.

Members noted the following relevant decision criteria cited by the Respiratory Sub-committee:

- (i) the health needs of all eligible people within New Zealand:* the subcommittee noted that there was a large number of patients with COPD in New Zealand who might benefit from the treatment with tiotropium;
- (ii) the particular health needs of Maori and Pacific peoples:* the subcommittee considered that high burden of disease associated with COPD was especially among Maori and Pacific Islanders
- (iii) the availability and suitability of existing medicines, therapeutic medical devices and related products and related things:* the subcommittee considered that the case for this drug was substantially greater than that for the current widespread use of inhaled corticosteroids;
- (iv) the clinical benefits and risks of pharmaceuticals:* the subcommittee considered that

the magnitude of benefits associated with tiotropium use in COPD are clinically relevant; the subcommittee considered that tiotropium is associated with very low risk and the only significant adverse effect is that of a dry mouth; the subcommittee considered that tiotropium provides additional health benefits over and above other pharmaceuticals funded by PHARMAC, e.g. short-acting beta agonists and ipratropium; (vi) *the budgetary impact (in terms of the pharmaceutical budget and the Government's overall health budget) of any changes to the Pharmaceutical Schedule*: potentially significant budgetary impact; depending on the access criteria the budgetary impact could potentially be greater than forecasted by the supplier in its submission.

Montelukast sodium (Singulair)

The Committee reviewed the further evidence and proposal from Merck Sharp & Dohme (MSD) for the listing of montelukast sodium on the Pharmaceutical Schedule. Members noted that it had reviewed applications for montelukast on three previous occasions and had considered that montelukast did not have an established place in asthma therapy and that it was less effective than standard doses of beclomethasone dipropionate (BDP). [REDACTED]

The Committee noted the further evidence provided by the supplier included some original studies as well as new studies published since the original application.

The Committee considered that, despite the new studies presented, montelukast sodium has similar efficacy to standard dose inhaled corticosteroid therapy with at best a modest steroid-sparing effect at the higher steroid doses. The Committee noted that the one comparative study with inhaled LABAs showed similar efficacy. However, the Committee noted that the Dahlen study on aspirin intolerant patients appeared to show benefit in this group of patients, with a small group of patients exhibiting substantial benefit. The data provided for young children was of poor quality and demonstrated limited clinical benefit.

The Committee considered that montelukast sodium could be targeted to patients who are aspirin intolerant, and those patients who are apparently refractory to high dose-inhaled corticosteroid therapy. Members considered that, for these patients, a high priority should be given for listing on the Pharmaceutical Schedule. They considered that montelukast could also be considered for patients with exercise-induced asthma, but considered that this should be given a moderate priority for listing on the Pharmaceutical Schedule. The Committee did not support listing for other patient groups mentioned in this application.