February 2007: 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.

Record of PTAC meeting held 16 & 17 November 2006

PTAC reviewed the record of the PTAC meeting held on 16 & 17 November 2006 and made the following minor amendments:

Etanercept (Enbrel) in Chronic Plaque Psoriasis – paragraph 12.4: replace "increased dosage and longer duration" with "increased dosage or longer duration".

Etanercept (Enbrel) in Chronic Plaque Psoriasis – paragraph 12.12: replace "chronic plaque sufferers" with "chronic plaque psoriasis sufferers".

Fulvestrant (Faslodex) – paragraph 13.7: replace "The incidence of thromboembolic events was 3.7%, higher for fulvestrant than for anastrazole." with "The incidence of thromboembolic events in patients treated with fulvestrant was 3.7%, which was higher than for patients treated with anastrazole".

Pegylated liposomal doxorubicin hydrochloride (Caelyx) – paragraph 18.5: replace "with a median survival was prolonged of 62.7 weeks" with "with a median survival of 62.7 weeks".

Adalimumab (Humira) for psoriatic arthritis – paragraph 20.1: delete last sentence in paragraph "The Committee considered that the evidence in support of the therapeutic claims was of moderate strength and good quality".

Trastuzumab (Herceptin) for HER2 positive early breast cancer

The Committee considered further information in relation to the application from Roche for the use of trastuzumab in HER2 positive early breast cancer. The Committee noted that this had been considered previously by PTAC at its February, May, August and November 2006 meetings. These minutes should be read in conjunction with the previous minutes found at http://www.pharmac.govt.nz/pdf/ptacmins.pdf.

The Committee reviewed the following material

- 6 January 2007 Lancet publication of the two-year median follow-up of the one-year treatment arm of the HERA trial (Smith et al) and the accompanying editorial (Hind et al);
- Power point presentation 'Phase III Trial Comparing AC-T with AC-TH and with TCH in the Adjuvant Treatment of HER2 positive Early Breast Cancer Patients: Second Interim Efficacy Analysis' BCIRG006 Trial; Slamon et al, presented at the San Antonio Breast Cancer Symposium (SABCS) 14-17 December 2006;
- Poster presentation 'Adjuvant Trastuzumab: Long-Term Results of E2198' Sledge et al, SABCS December 2006;

- 'Trastuzumab in Early Stage Breast Cancer' Huybrechts M, Hulstaert F, Neyt M, Vrijens F, Ramaekers D. Health Technology Assessment (HTA). Brussels: Belgian Health Care Knowledge Centre (KCE); 2006. KCE reports 34C (D/2006/10.273/25)

- New Zealand, Australian and USA trastuzumab Datasheets

The Committee noted that at its November 2006 meeting it considered that more clinical research was needed and that a study comparing 12 months trastuzumab with 9 weeks trastuzumab should be performed. The Committee further noted it recommended that, subject to an acceptable cost/QALY, including the cost of docetaxel, 9 weeks treatment with trastuzumab should be funded and gave this recommendation a high priority.

The Lancet article and editorial – 2-year median follow-up HERA data

The Committee noted that the two-year median follow-up data published in the Lancet in January 2007 confirmed the results presented at the American Society of Clinical Oncology (ASCO) 2006 conference that were considered by the Committee at its August 2006 meeting.

The Committee noted that data for patients treated with two years trastuzumab in the HERA trial is still to be reported.

The Committee noted that the hazard ratio (HR) for the two-year median follow-up was 0.64 (95% confidence interval 0.54-0.76), compared with the one-year median follow-up HR of 0.54 that had been considered by the Committee and used in PHARMAC's cost-utility analysis of trastuzumab. The Committee considered that these two-year follow-up data indicated a possible waning of treatment effect compared with the previous one-year follow-up data, and noted that the graphs in the Lancet paper indicated a possible convergence in disease-free survival between the sequential trastuzumab and standard treatment arms after the first six months' follow-up.

The Committee noted that 55 patients would need to be treated to prevent one death after two years' median follow-up ('number needed to treat' (NNT)), and that one of every 51 patients would suffer an adverse cardiac event over the same time period ('number needed to harm' (NNH)). The Committee noted that this NNH would reduce to one in 20 patients having any form of cardiac toxicity including non-symptomatic reductions in left ventricular ejection fractions (LVEF).

The Committee noted that the study design of HERA allowed switching of patients from the observation arm to trastuzumab treatment after publication of the one-year follow-up data. It was noted that 861 out of 1698 patients in the original observation treatment group had switched to trastuzumab. The Committee reiterated that due to this non-randomised switching the control group had been 'lost'; therefore, interpretation of future long-term efficacy and safety data for trastuzumab in this study would be significantly compromised.

BCIRG006 trial results

The committee reviewed 36-month median follow-up data from the Breast Cancer International Research Group (BCIRG) 006 study (as yet unpublished) as an interim analysis supplied in the form of MS PowerPoint slides of a presentation at SABCS in December 2006. The Committee noted that it had reviewed an interim analysis of 23-months median follow-up data during its May 2006 Meeting. The Committee noted that there were three treatment arms: the first containing chemotherapy only, with four cycles of doxorubicin and cyclophosphamide followed

by four cycles of docetaxel (AC-T); the second containing the same chemotherapy regimen plus one year of trastuzumab commenced concurrently with docetaxel (AC-TH); and the third comprising six cycles of docetaxel and carboplatin with one year of trastuzumab commenced concurrently with the chemotherapy (TCH).

The Committee noted that there was a significant improvement in both disease-free and overall survival in the trastuzumab treated patients in this study. The Committee considered that there appeared to be no clinical difference between the AC-TH (containing the anthracycline doxorubicin) treated patients compared with TCH (containing no anthracycline) treated patients, although the slide presentation did not present the results of a formal statistical comparison between the two arms. Members noted, however, that cardiac toxicity was lower in the TCH treatment group; therefore, it questioned the clinical benefit of anthracycline use in this study.

E2198 trial results

The Committee reviewed the 5-year follow-up results of study E2198 presented as a poster at SABCS in December 2006. This study compared short-duration trastuzumab (10 weeks) given concurrently with paclitaxel prior to anthracycline treatment, with the same treatment plus an additional 52 weeks trastuzumab after completion of anthracycline treatment.

The Committee noted similar clinical outcomes in the short-duration concurrent regimen compared with the extended (52 weeks) trastuzumab treatment. The Committee considered that although the study was not designed to test efficacy, and was not powered to determine equivalence, the results supported the efficacy of short-duration concurrent trastuzumab therapy when administered before anthracycline containing chemotherapy, as demonstrated in the FinHer study, and supported the rationale for the SOLD study which would compare long versus short durations of concurrent trastuzumab regimen.

New Zealand Datasheet, Australian Product Information and USA Prescribing Information

The Committee noted that a key issue around its recommendation for funding 9 weeks treatment with trastuzumab (concurrent with chemotherapy) is that this treatment regimen is not currently covered by the Medsafe-approved Datasheet in New Zealand which specifies that trastuzumab is to be administered following completion of adjuvant chemotherapy (i.e. sequential treatment).

The Committee noted that the USA Prescribing Information recommends that trastuzumab is administered for 12 months starting concurrently with paclitaxel and that the Australian Product Information allows for 12 months sequential, 12 months concurrent or 9 weeks concurrent treatment regimens to be used.

The Committee specifically noted that the Australian Product Information states that 'The optimal dosage regimen and treatment duration have not been defined. A favourable risk/benefit ratio has been demonstrated with the following regimens:

- Three weekly regimen (HERA trial): Treatment with HERCEPTIN was commenced following surgery and completion of neoadjuvant or at least 4 cycles of adjuvant chemotherapy.

- Weekly regimen (B31/N9831 trials): Treatment with HERCEPTIN was commenced following surgery and completion of 4 cycles (12 weeks) of doxorubicin and

cyclophosphamide (AC) chemotherapy, then together with paclitaxel for 12 weeks, then as a single agent for a further 40 weeks.

- Weekly regimen (FinHer trial): Treatment with HERCEPTIN was commenced following surgery and was given concurrently with docetaxel or vinorelbine for a total of 9 weeks.'

The Committee considered that the Australian Product Information was consistent with its view that there was still uncertainty about the best way of administering trastuzumab.

The Committee noted that trastuzumab currently has provisional consent in New Zealand and, therefore, there may be an opportunity for Medsafe to align the New Zealand datasheet with that in Australia. The Committee resolved to write to Medsafe to request that it initiate a review of the datasheet, given the Committee's concerns that the datasheet specified sequential 12 months trastuzumab treatment, which the Committee considered may be inappropriate (given that the two-year median follow-up data from HERA, alongside the results of Arm B of study N9831, raised significant doubts about the magnitude of efficacy of sequential 12 months trastuzumab, and that concurrent regimens may be, at least as, if not more efficacious than sequential).

Cost-Utility Analysis

The Committee received a verbal update from PHARMAC staff regarding the trastuzumab cost-utility analysis (CUA), which had been updated to indicate the cost-effectiveness of the nine-week concurrent treatment regimen (as per FinHer). The Committee noted that the updated analysis included the cost of docetaxel (Taxotere), and made the conservative assumption that the cardiotoxicity risks and costs would be the same as seen in the HERA trial (because FinHer may have been underpowered to detect these risks).

The Committee noted that the base-case results of the revised CUA were less than $20,000/QALY under conservative scenarios for effectiveness. The Committee considered that the inputs for the revised CUA were sound and noted that the cost-effectiveness of nine-week concurrent treatment with trastuzumab was comparable to other pharmaceuticals funded by PHARMAC.

The Committee noted the Belgian Health Technology Assessment report and considered that the conclusions outlined in the report were reasonable and consistent with the Committee's views.

General Discussion

The Committee reiterated its view that there was still uncertainty about the best way of administering trastuzumab in terms of optimal treatment duration, dose and schedule (sequential to, or concurrent with, chemotherapy), minimising cardiovascular toxicity, and long-term clinical outcomes.

Specifically, the Committee considered that data from Arm B of study N9831 raised significant doubts about the efficacy of sequential 12 months trastuzumab. The Committee noted that it had requested in May 2006 that full data from the N9831 trial be provided by the supplier, but thus far this had not been provided. The Committee considered that there was now likely to be

longer-term follow-up of outcomes (disease free survival and mortality) in this study, and that all the updated data from all three arms of the trial should be made available to the Committee.

The Committee reiterated its recommendation from its November 2006 meeting that 9 weeks treatment with trastuzumab (concurrent with chemotherapy and before anthracycline) should be funded and gave this recommendation a high priority.

The Committee considered that more clinical research was needed to determine if long duration concurrent treatment (52 weeks) is any better than short duration concurrent treatment (9 weeks) and reiterated that a comparative study should be performed. The Committee noted CaTSoP's advice from it's October 2006 meeting that the proposed SOLD study was well designed and would answer some of the questions relating to the optimal dose, duration and scheduling of trastuzumab in early HER2 positive breast cancer.

Rituximab (MabThera)

The Committee considered an application from Roche to widen the Special Authority criteria for rituximab (MabThera) in the Pharmaceutical Schedule to include use in combination with chemotherapy for patients with low-grade, symptomatic (stage III/IV), follicular non-Hodgkin's lymphoma (NHL).

The Committee noted that rituximab is currently funded for the treatment of patients with relapsed low-grade NHL, patients with large B-cell NHL concurrently with CHOP (cyclophosphamide, vincristine, doxorubicin and prednisone) or alternative anthracycline-containing chemotherapy and patients with B-cell post transplant lymphoproliferative disorder.

The Committee noted that follicular lymphoma is the most common form of indolent lymphoma, accounting for about 70% of low-grade (indolent) lymphomas and approximately 20% of all cases of NHL. The Committee further noted that low-grade (indolent) NHLs often grow very slowly, with median survival without treatment of between eight to ten years. In asymptomatic patients, treatment may be postponed for a long time, a so-called 'watch and wait' approach. In symptomatic patients, treatment may include radiotherapy with or without chemotherapy.

The Committee noted that in September 2006 NICE issued guidance recommending rituximab in combination with CVP (cyclophosphamide, vincristine and prednisone) as an option for the treatment of symptomatic stage III and IV follicular lymphoma in previously untreated patients.

The Committee considered evidence from three phase III studies, and one phase II study.

The Committee considered that the strongest evidence was provided from a phase III, open label, study (M39021) comparing CVP with R-CVP (CVP plus rituximab, Marcus et al Blood 2005). This study enrolled patients with stage III or IV disease and good performance status (0 to 2 Eastern Clinical Oncology Group (ECOG) criteria).

The Committee noted a high drop out rate in this study with only 68% of patients treated with CVP and 85% of patients treated with R-CVP receiving all eight scheduled cycles, likely due to withdrawal from treatment due to inadequate therapeutic response.

The Committee noted that in this study patients treated with R-CVP had an increased time to treatment failure (TTF: 27 months vs. 7 months), time to treatment progression (TTP: 32 months vs. 15 months), duration of response (35 months vs 14 months) and response rate (RR: 81% vs 57%), compared with chemotherapy alone. The Committee noted that overall survival, at median follow-up of 30 months, was 89% in patients treated with R-CVP versus 85% in patients treated with CVP (not statistically significant).

The Committee noted that the number of patients with at least one adverse event was comparable between the treatment groups, CVP (95%) and R-CVP (97%); however, more patients in the R-CVP group than in the CVP group experienced an adverse event within 24 hours of an infusion (71% vs 51%). The incidence of grade 3 or 4 neutropenia was higher in the R-CVP treatment group (24%) compared with CVP (14%); however, there was no difference in overall infection rate. The Committee considered that there would be costs associated with treatment of rituximab-related neutropenia.

The Committee noted that the supplier provided a cost-effectiveness analysis based on data from the M39021 study. [ ] However, the Committee noted that no quality-of-life data were provided, making the assessment of quality-adjusted life year (QALY) gains difficult. The Committee also noted that it was unclear whether patients who received R-CVP as first-line treatment and then relapsed would be offered a second treatment course of rituximab.

The Committee **recommended** that rituximab be listed on the Pharmaceutical Schedule for use in combination with chemotherapy for patients with low-grade, symptomatic (stage III/IV), follicular non-Hodgkin's lymphoma (NHL). The Committee gave this recommendation a low to medium priority.

The Committee recommended that the application be referred to the Cancer Treatments Subcommittee (CaTSoP) for advice regarding appropriate combination chemotherapy regimens and whether or not relapsed patients should be able to access a second course of rituximab.

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, and, (vi) The budgetary impact (in terms of the pharmaceutical budget and the Government's overall health budget) of any changes to the Pharmaceutical Schedule*

Escitalopram oxalate (Lexapro)

Treatment of severe depression

The Committee considered an application from Lundbeck for the listing of escitalopram on the Pharmaceutical Schedule for severe depression. The Committee noted that the supplier had applied for escitalopram funding three times previously: for depression under the then-current endorsement criteria for selective serotonin reuptake inhibitors (SSRIs) other than fluoxetine (reviewed by the Mental Health Subcommittee in February 2003), for treatment-resistant depression (considered by PTAC in May 2004) and for severe depression (considered by PTAC in February 2005). Members noted that neither the Mental Health Subcommittee, nor PTAC,

had made a positive recommendation to list escitalopram and the application was formally declined by PHARMAC's Chief Executive under Delegated Authority in April 2005.

Members noted that PTAC and the Mental Health Subcommittee had previously considered that there were no major safety concerns with escitalopram and that it was well tolerated.

The Committee noted that the current application included a meta-analysis (conducted by the supplier) of several clinical studies in which escitalopram was compared with SSRIs (paroxetine, citalopram, fluoxetine and sertraline) and venlafaxine. Most trials contained subsets of patients with severe depression. Members noted that most individual studies did not show clear superiority of escitalopram over SSRIs, although there were two trials where superiority was shown (one versus paroxetine and one versus citalopram; both trials were considered to be of good quality).

The Committee noted that results of the meta-analysis suggested that escitalopram was associated with a higher response rate and a higher remission rate versus a combined group including SSRI and venlafaxine treated patients with severe depression. Compared with SSRIs only and citalopram alone, escitalopram appeared to be associated with greater efficacy and higher response rates, whereas there were no significant differences in efficacy observed between venlafaxine alone and escitalopram.

Members noted that the safety analysis in the meta-analysis considered all patient groups enrolled in the studies, not just patients with severe depression. Results did not reveal any significant safety concerns associated with the use of escitalopram, and suggested that escitalopram may be better tolerated than the comparators. The Committee considered that the tolerability benefits of escitalopram would likely be more apparent at higher doses, compared with equipotent doses of other SSRIs.

The Committee noted that details of the meta-analysis were not provided by the supplier and the analysis was likely to be influenced greatly by the two trials of escitalopram (one versus paroxetine and one versus citalopram) that demonstrated superior efficacy of escitalopram.

Members noted that the December 2004 NICE clinical guidance document entitled "Depression: Management of Depression in Primary and Secondary Care" concluded that there is insufficient evidence or limited evidence of superiority of escitalopram over other treatments in treating depression. However, members noted that severe depression was not considered separately in this review. Members considered that severe depression responds differently to treatment compared with milder forms of depression, in that there is less of a placebo response and more obvious medication responses.

The Committee expressed reservations about the cost-effectiveness analysis provided by the supplier, in particular with respect to the price of paroxetine which was based on the current full subsidy rather than the impending reduced subsidy for generic paroxetine.

The Committee considered that although statistically significant efficacy and tolerability differences were seen in the meta-analysis conducted by the supplier, this would not translate into a great enough benefit in clinical practice to justify the high cost of escitalopram, particularly given the availability of low-cost alternatives.

The Committee **recommended** that the application to list escitalopram on the Pharmaceutical Schedule for severe depression be declined.

The Decision Criterion relevant to this recommendation is: (iii) *The availability and suitability of existing medicines, therapeutic medical devices and related products and related things*.

Treatment of obsessive compulsive disorder (OCD)

The Committee considered an application from Lundbeck for the listing of escitalopram on the Pharmaceutical Schedule for the treatment of OCD. The Committee noted that the supplier had provided details of two unpublished clinical studies in support of its application: one versus paroxetine and one versus placebo. The Committee considered that paroxetine was an appropriate comparator for escitalopram in OCD, but noted that citalopram and fluoxetine are also used for the treatment of OCD (although only fluoxetine is registered for this indication in New Zealand). The Committee noted that clomipramine was also indicated for treatment of OCD, but considered that clomipramine was no longer commonly used for this indication.

The Committee noted that one clinical study showed a trend towards superiority of escitalopram 20 mg over paroxetine 40 mg for OCD in terms of reduced risk of relapse and better tolerability, but that these differences were not statistically significant and the studies were unpublished.

The Committee noted that the supplier analysis had used the current full subsidy for paroxetine rather than the impending reduced subsidy for generic paroxetine, and had assumed an efficacy benefit of escitalopram over paroxetine that it did not accept as valid. The Committee considered that escitalopram was likely to be significantly less cost-effective than had been estimated by the supplier.

The Committee considered that at this time there was insufficient evidence to support claims of a benefit of escitalopram over other currently funded treatments for OCD, and **recommended** that the application to list escitalopram on the Pharmaceutical Schedule for obsessive compulsive disorder be declined.

The Decision Criterion relevant to this recommendation is: (iii) *The availability and suitability of existing medicines, therapeutic medical devices and related products and related things*.

Ziprasidone (Zeldox)

The Committee noted that it had first considered an application from Pfizer to list ziprasidone on the Pharmaceutical Schedule in November 2001 and that the application had subsequently been reviewed twice by the Mental Health Subcommittee of PTAC (in April 2002 and October 2006). It was noted that PTAC had requested a review of the history of the application following the October 2006 meeting of the Mental Health Subcommittee.

The Committee noted that one of the key benefits of ziprasidone, as previously identified by PTAC and the Mental Health Subcommittee, is its reduced propensity to cause weight gain relative to other atypical antipsychotic agents, particularly olanzapine.

Members noted that the two unpublished supporting studies provided in the initial application had now been published. In addition, several new studies had subsequently been published that supported the previous conclusions drawn by PTAC and the Mental Health Subcommittee.

The Committee considered that, in terms of efficacy, ziprasidone was comparable to risperidone, quetiapine and haloperidol, but may be slightly less effective than olanzapine. However, it was noted that higher doses of ziprasidone might be needed to achieve an antipsychotic effect than had been used in some clinical trials. Members considered that, like other antipsychotic agents, ziprasidone would be used in combination with antidepressants, mood stabilisers and/or benzodiazepines, as appropriate.

Members considered that the need to take ziprasidone twice a day could negatively affect compliance.

Members noted that in clinical trials ziprasidone was generally well tolerated (with tolerability comparable to olanzapine) and was not associated with significant weight gain or worsening of lipid profile at one year compared with placebo. Members noted that switching from olanzapine or risperidone to ziprasidone was associated with weight loss in clinical trials.

The Committee considered that patients who had experienced significant weight gain on other atypical antipsychotic agents would benefit most from ziprasidone. It was noted that Maori and Pacific Island patients could be at even greater risk of weight gain from atypical antipsychotic agents.

The Committee considered that if restrictions were placed on the use of ziprasidone it would be primarily for financial reasons. The Committee proposed the following Special Authority criteria:

> **Special Authority for Subsidy - Form xxxx**
> Initial application only from a psychiatrist. Approvals valid for 2 years for applications meeting the following criteria:
> Both:
> 1 Patients suffering from schizophrenia and related psychoses; and
> 2 Either:
> 2.1 Significant weight gain while taking olanzapine which has not been resolved by switching to quetiapine or risperidone; or
> 2.2 Significant weight gain while taking quetiapine or risperidone.
> Renewal only from a psychiatrist. Approvals valid for 2 years where the treatment remains appropriate and the patient is benefiting from treatment.
> Note
> Initial prescriptions to be written by psychiatrists or psychiatric registrars and subsequent prescriptions can be written by General Practitioners.

The Committee considered that the use of ziprasidone in patients who had gained weight on other atypical antipsychotic agents could reduce medical costs associated with weight gain, although members noted there was limited evidence that this would be the case.

Members considered that if ziprasidone was listed in the Pharmaceutical Schedule subject to the proposed Special Authority criteria, it would result in a reduction in the use of olanzapine and, to a lesser extent, risperidone and quetiapine.

The Committee **recommended** that ziprasidone be listed on the Pharmaceutical Schedule under the above restrictions, with a high priority.

The Decision Criteria relevant to this recommendation are: (i) *The health needs of all eligible people within New Zealand*; (ii) *The particular health needs of Maori and Pacific peoples*; (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*; 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.*

Modafinil (Modavigil)

The Committee considered an application from CSL Biotherapies to list modafinil on the Pharmaceutical Schedule for the treatment of narcolepsy. The Committee noted that modafinil is approved for the treatment of excessive sleepiness associated with chronic pathological conditions, including narcolepsy, obstructive sleep apnoea/hypopnoea syndrome and moderate to severe chronic shift work sleep disorder. The Committee noted that Medsafe approval of modafinil for use in narcolepsy was subject to treatment being initiated by specialists in the area of narcolepsy. The Committee noted that there were several off-label uses for modafinil, including the treatment of attention deficit hyperactivity disorder (ADHD). Members noted that there was significant potential for abuse/diversion of modafinil, e.g., for students and athletes.

The Committee considered two key 9-week, randomised, double-blind placebo-controlled studies provided in support of the application: Study 301 published in 1998 (n = 283) and Study 302 published in 2000 (n = 271) investigating the efficacy of modafinil for reduction of excessive daytime sleepiness associated with narcolepsy. Both studies included a 9-week randomised treatment phase, followed by a 2-week discontinuation phase and then a 40-week open-label extension phase. During the initial 9-week randomised phase patients received modafinil 200 mg, modafinil 400 mg or placebo. The modafinil groups combined were statistically significantly superior to placebo on all subjective and objective efficacy measures (including Epworth Sleepiness Scale, Multiple Sleep Latency Test, Maintenance of Wakefulness Test, Clinical Global Impression of Change), and no significant differences were seen between modafinil groups. Data from the studies provided by the supplier but not included in the publications showed only small reductions in the number of unwanted sleep episodes/day and the number of episodes of desire to sleep/day in the modafinil groups, as recorded in patients' sleep logs,.

The Committee noted that combined results of the 40-week open-label extension phases of the two studies (during which ~75% of patients received modafinil 400 mg/day) suggested that the effectiveness of modafinil was maintained during long-term treatment, and that there was no evidence of tolerance developing.

Members noted the data demonstrating improvements in quality-of-life measures and patients' perceptions of general health during modafinil treatment.

Side-effects of modafinil in the trials included headache, nausea, nervousness, back pain, rhinitis and diarrhoea, but there were fewer accidental injuries in the modafinil groups.

Overall, the Committee considered that the clinical studies provided in support of the application were of good strength and quality.

The Committee considered that modafinil 200-400 mg could have similar effects to methylphenidate 20–30 mg and dexamphetamine 10–20 mg, with potential for fewer adverse

effects and lower risk of tolerance, but noted that this would require confirmation in comparative studies.

The Committee considered that if modafinil was listed in the Pharmaceutical Schedule for narcolepsy it would replace dexamphetamine and methylphenidate, although members noted there could be a risk of modafinil being used in combination with these agents. The Committee considered that modafinil would be used in combination with agents used for the treatment of cataplexy (eg, tricyclic antidepressants and SSRIs).

The Committee did not consider that there were problems with access to current treatments, and noted that the restrictions on the use of dexamphetamine and methylphenidate were appropriate.

The Committee considered that modafinil would most benefit patients with narcolepsy with excessive daytime sleepiness, particularly those who cannot tolerate or who have contraindications to currently funded treatments. The Committee considered that modafinil could benefit patients where there was a significant risk of abuse or diversion with dexamphetamine or methylphenidate; however, members noted there could be a significant risk of diversion with modafinil itself if it was listed in the Pharmaceutical Schedule.

The Committee did not consider that there was a significant unmet health need in the population of patients with excessive daytime sleepiness associated with narcolepsy, although members noted that there could be a small minority of patients whose needs were not being met.

The Committee considered that if modafinil was listed in the Pharmaceutical Schedule it should be restricted to patients with diagnosed excessive daytime sleepiness associated with narcolepsy who could not tolerate methylphenidate and dexamphetamine or in whom methylphenidate and dexamphetamine were contraindicated. Members noted that the restrictions would be on the basis of cost and a lack of evidence that modafinil is as, or more, effective than methylphenidate and dexamphetamine. Proposed criteria for a diagnosis of excessive daytime sleepiness associated with narcolepsy were as follows:

> All of:
> 1. Excessive daytime sleepiness occurring almost daily for three months or more; and
> 2. Hypersomnia not better explained by another disorder; and
> 3. Either:
> 3.1 Definite history of cataplexy and a Multiple Sleep Latency Test (MSLT) with a mean sleep latency less than or equal to 8 minutes; or
> 3.2 A MSLT with a mean sleep latency of less than or equal to 8 minutes and 2 or more sleep onset rapid eye movement (REM) periods; and
> 4. The MSLT must be preceded by nocturnal polysomnography and sleep prior to the MSLT must be at least 6 hours.

The Committee **recommended** that modafinil be listed on the Pharmaceutical Schedule (because of the small unmet health need) subject to the above criteria, with a low priority.

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*.

Dipyridamole 200 mg modified release (Persantin), dipyridamole 200 mg modified release with 25 mg acetylsalicylic acid (Asasantin) and the dipyridamole Special Authority criteria

The Committee considered an application from Boehringer Ingelheim for the listing of a 200 mg long-acting dipyridamole capsule (Persantin), and a combination 200 mg long-acting dipyridamole with 25 mg aspirin capsule (Asasantin). The application also included a widening of access to dipyridamole to allow Persantin and Asasantin to be used as a first-line treatment for the prevention of ischaemic stroke and transient ischaemic attacks (TIA). In addition the Committee considered a letter and some articles from Harry McNaughton (Honorary Medical Director, Stroke Foundation of New Zealand) suggesting that dipyridamole plus aspirin, rather than aspirin alone, should be considered as first-line treatment for the secondary prevention of a stroke.

Members noted that the Committee had previously considered Persantin, Asasantin and widening access to dipyridamole as proposed.

The Committee considered the results of the ESPRIT (2006) trial which sought to resolve uncertainty as to whether combined aspirin and dipyridamole was more effective than aspirin alone for the secondary prevention of vascular events after stroke. The Committee noted that during the trial (mean follow-up 3.5 years), 13% (173) of the patients treated with a combination of aspirin and dipyridamole experienced at least one primary outcome event (death, non-fatal stroke, non-fatal myocardial infarction, or major bleeding complication) compared to 16% (216) of the aspirin alone patients. This equated to a hazard ratio of 0.80, a 20% reduction in relative risk, an absolute risk reduction of 1% per year, and a number needed to treat of 104 to prevent 1 primary outcome event per year. The Committee also noted that there was a 34.2% (470) drop out rate with dual therapy, mainly due to headaches, compared to 13.3% (184) when treated with aspirin alone. In addition, the Committee noted that there were no quality- of-life data to support the use of combined therapy for stroke patients, that most first outcome events, including secondary prevention of ischaemic stroke, did not reach significance, and that there was no significant effect on mortality.

The Committee also noted the results of other literature including ESPS 1, ESPS 2, a meta-analysis by Leonardi-Bee et al (2005), the Anti Thrombotic Collaboration trial (2002), and a Cochrane review (De Schryver et al, 2003).

The Committee noted that the proposed listing criteria includes patients who suffer ischaemic events within the last two years; however, the ESPRIT and ESPS 2 trials only included patients within six months and three months of an ischaemic event respectively.

The Committee considered that the actual number of Persantin and Asasantin patients would be higher than the number estimated in the application.

The Committee considered that the evidence supporting combined therapy (aspirin and dipyridamole) was weak and that the side-effects and the price of combined therapy were significant when compared to aspirin therapy alone. As a result the Committee **recommended** that the application to list Persantin and Asasantin be declined.

The Committee noted that clopidogrel is available for aspirin intolerant patients and considered that clopidogrel would be preferred over dipyridamole for these patients, as data suggests that dipyridamole monotherapy has limited efficacy for secondary prevention of TIAs and strokes.

The Committee also noted that the current Special Authority restricted the prescribing of dipyridamole to vascular surgeons, cardiologists, neurologists, neurosurgeons or general physicians. The Committee noted that it had previously recommended that general practitioners and ophthalmologists should be able to prescribe dipyridamole and recommended that access be widened accordingly.

The Committee noted that the wording of the current Special Authority criteria required a patient to have multiple transient ischaemic episodes despite aspirin therapy, or when aspirin intolerant, before they are eligible for dipyridamole. The Committee considered that for clarity, this should be amended to a single transient ischaemic episode or ischaemic stroke despite aspirin therapy or when aspirin intolerant.

The Committee noted that removing the current Special Authority would reduce prescriber administration and considered that this should be performed subject to budgetary constraints.

Alendronate sodium cholecalciferol (Fosamax Plus)

The Committee considered an application from Merck Sharpe and Dohme to list Fosamax Plus (alendronate sodium 70 mg with cholecalciferol 2800 IU tablet) on the Pharmaceutical Schedule under the same Special Authority restrictions that currently apply to Fosamax (alendronate 70 mg tablet).

The Committee noted that Fosamax Plus is a once weekly treatment and is indicated for the treatment of osteoporosis in selected patients where vitamin D supplementation is recommended.

The Committee noted that Fosamax Plus would treat the same patient population currently being treated with Fosamax, as current treatment guidelines recommend calcium and vitamin D supplementation for all patients with osteoporosis.

The Committee noted that Fosamax Plus presented no additional clinical risk to patients compared to Fosamax.

The Committee noted that the listing of Fosamax Plus on the Pharmaceutical Schedule as proposed would be cost neutral.

The Committee noted that the dose of cholecalciferol in Fosamax Plus was 2800 IU. The Committee considered that, while this dosage is consistent with that recommended for healthy subjects, many studies show that a dose of 600-800 IU daily (4200 IU weekly) is required in patients with osteoporosis. This advice is contained in a recent Cochrane review of the use of vitamin D in osteoporosis as well as in the ANZBMS guideline referred to in the supplier's submission.

The Committee noted that in New Zealand, supplementation with cholecalciferol was only available as a monthly tablet of 1.25 mg (Cal-D Forte) or else given as a daily multivitamin supplement.

The Committee considered that despite the guidance, only a minority (perhaps one third) of patients with osteoporosis receive any form of vitamin D supplementation, and that compliance with co-prescribed cholecalciferol was difficult to maintain given the intermittent dosing currently used in New Zealand.

The Committee considered that although the dosage of cholecalciferol was too low for the proposed patient population, supplementation with 2800 IU cholecalciferol weekly would be preferable to no treatment. Prescribers would be able to monitor vitamin D levels and offer additional supplements if necessary

The Committee considered that there was no clinical reason not to list Fosamax Plus on the Pharmaceutical Schedule, but considered that it offered limited clinical gain.

The Committee considered that Fosamax Plus would have the same or similar therapeutic effect to the separate components, alendronate and cholecalciferol, and that reference pricing could therefore be considered.

The Committee **recommended** that Fosamax Plus be listed on the Pharmaceutical Schedule with a low priority.

The Decision Criterion relevant to this recommendation is: (i) *The health needs of all eligible people within New Zealand*.

Methylphenidate long-acting (once-daily) formulation (Ritalin LA)

The Committee considered an application from Novartis to list a long-acting (once-daily) formulation of methylphenidate (Ritalin LA) on the Pharmaceutical Schedule for the treatment of attention deficit hyperactivity disorder (ADHD). The Committee noted in the studies provided by the supplier that this formulation of methylphenidate has a bimodal pharmacokinetic profile (similar to that of two doses of the immediate release form given four hours apart), with an extended duration of action up to 12 hours. Members noted that the capsules can be opened and the contents sprinkled on food with no alteration of pharmacokinetics once consumed.

The Committee noted the results of a randomised, double-blind placebo-controlled trial conducted in 136 children aged 6–14 years with ADHD in which long-acting methylphenidate demonstrated significant improvements in Inattentive and Impulsive Behaviour subscale scores. In addition, results of two trials in which methylphenidate long-acting was compared with methylphenidate extended-release once-daily formulation (Concerta) indicated that methylphenidate long-acting (20 mg or 40 mg) provided similar or better efficacy to Concerta up to 4 and 8 hours, and similar efficacy to Concerta between 8 and 12 hours. Members noted that no new safety concerns for methylphenidate were identified from these studies. The Committee considered that the evidence provided in the application was of moderate strength and quality.

Members noted that the cost-effectiveness of methylphenidate preparations was sensitive to price. It was noted that methylphenidate long-acting was substantially less expensive than Concerta.

The Committee considered that methylphenidate long-acting provided similar efficacy to currently funded methylphenidate preparations (immediate- and sustained-release), and that the main differences lay in the number of pills and frequency of administration. It was considered that methylphenidate long-acting would be used instead of immediate- and sustained-release methylphenidate in eligible patients, but members noted that patients might still take a short-acting tablet at the same time as the long-acting tablet.

The Committee considered that the patients who would most benefit from methylphenidate long-acting would be those for whom compliance with existing formulations was a problem and those for whom there was a significant risk of diversion associated with taking tablets to school for a midday dose. Members considered that, within this patient group, Maori and Pacific peoples could have a greater unmet need than the population as a whole.

The Committee considered that if funded, methylphenidate long-acting should be restricted by Special Authority as follows:

1 Patient with ADHD; and
2 Either:
  2.1 Current methylphenidate medication has not been effective due to significant administration and/or compliance difficulties; or
  2.2 There is significant concern regarding the risk of diversion or abuse of short-acting methylphenidate.

Members noted that the Mental Health Subcommittee had indicated that up to 50% of patients taking currently funded methylphenidate preparations could be eligible for a once-daily preparation of methylphenidate under these criteria. Members noted that significant savings had been achieved by the recent tender awarded to generic methylphenidate sustained-release, and that funding methylphenidate long-acting would essentially undo these savings.

The Committee **recommended** that methylphenidate long-acting (once-daily) formulation (Ritalin LA) be listed on the Pharmaceutical Schedule with a medium priority. The Committee further **recommended** that PHARMAC staff conduct further literature searching to help with cost-effectiveness estimates.

The Decision Criteria relevant to this recommendation are: (i) *The health needs of all eligible people within New Zealand*; (ii) *the particular health needs of Maori and Pacific peoples*; (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; 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*.

Lopinavir / ritonavir (Kaletra)

The Committee reviewed an application from Abbott regarding the listing of a new tablet formulation of lopinavir/ritonavir (Kaletra) on the Pharmaceutical Schedule for the treatment of patients with HIV infection under the same Special Authority Criteria as the current soft-gel capsule formulation.

The Committee noted that the new tablet formulation, containing 200mg lopinavir with 50mg ritonavir, would replace the current soft-gel capsule formulation.

The Committee considered evidence, provided in the form of conference posters, from four bioavailability studies.

The Committee considered that data from these studies demonstrated that the new tablet formulation was bioequivalent to the current soft-gel capsule formulation.

The Committee noted that the new formulation appeared to have some advantages over the soft-gel capsule formulation, in particular a reduced pill burden, 4 tablets per day compared with 6 soft-gel capsules, and no requirement for refrigeration. The Committee also noted that the new tablet formulation may be associated with lower incidence of adverse effects, especially diarrhoea, which was reduced from 50% to 17% across the studies.

The Committee noted that the supplier indicated that it would provide the tablets at the same price as the soft-gel capsules. The Committee considered that the new formulation represented an improvement over the current soft-gel capsule formulation with no additional cost to PHARMAC.

The Committee **recommended** that lopinavir/ritonavir (Kaletra) tablets be listed on the Pharmaceutical Schedule for the treatment of patients with HIV infection under the same Special Authority Criteria as the current soft-gel capsule formulation. The Committee considered this recommendation a medium priority.

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, and, (vi) The budgetary impact (in terms of the pharmaceutical budget and the Government's overall health budget) of any changes to the Pharmaceutical Schedule*

Topiramate (Topimax)

The Committee considered an application from Janssen-Cilag to widen access to topiramate for the prophylaxis of migraine. The Committee noted that the supplier had provided three large randomised controlled trials in support of the application, two comparing topiramate with placebo and one comparing topiramate with propanolol or placebo. In the latter study topiramate 200 mg/day appeared to provide equivalent efficacy to propranolol 160 mg/day. The Committee noted that a pooled analysis of the three randomised controlled trials indicated that prophylactic treatment with topiramate resulted in a significant 45% reduction in migraine days compared to placebo. However, topiramate was associated with an increase in adverse events (e.g., paraesthesias, difficulties with concentration, nausea, fatigue, insomnia and weight loss).

The Committee noted that topiramate appeared to reduce the frequency of migraine by approximately two migraines per month, and that topiramate at a dose of 100 mg/day provided a ≥50% reduction in monthly migraines in approximately 50% of patients.

The Committee noted findings from a Cochrane review of anticonvulsant drugs for migraine prophylaxis (last updated May 2004) which indicated that anticonvulsants as a class (gabapentin, sodium valproate, divalproex sodium, carbamazepine, clonazepam, lamotrigine and topiramate) decreased migraine frequency by approximately 1.4 attacks per month compared with placebo, with the strongest evidence supporting use of sodium valproate and divalproex sodium. The Committee noted that the Cochrane review found that the number needed to treat for a halving in the number of migraine attacks with topiramate was 3.5, whereas the number needed to harm for topiramate ranged from 2.3 to 32.9, depending on the adverse event.

The Committee considered that the evidence provided by the supplier was of good quality and moderate strength, although members expressed reservations about the ability of the randomised controlled trials to maintain double blinding during the titration phase. Members considered that topiramate provided efficacy similar to beta-blockers and other agents used for migraine prophylaxis (including propranolol, low-dose amitriptyline, pizotifen, verapamil and sodium valproate), but that it was associated with serious side-effects (including cognitive impairment and weight loss), especially when compared with propanolol.

Members considered that topiramate would most likely be used for prophylaxis of migraine following failure of other agents. Members noted there were currently no problems with access to funded alternatives.

The Committee considered that topiramate would most benefit patients who could not tolerate or were unresponsive to other funded alternatives, and that if funded for migraine prophylaxis it should be restricted to such patients. The Committee noted that it would be difficult to define treatment failure in this regard.

The Committee **recommended** that access to topiramate be widened for migraine prophylaxis for patients who had failed, or were unable to tolerate, funded alternatives, with a low priority. However, the Committee noted that expanding access to topiramate in this manner would pose a large financial risk for PHARMAC, as patients could potentially access topiramate very quickly after trying the alternatives. [

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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*.

Sunitinib (Sutent)

The Committee considered an application from Pfizer to list Sunitinib (Sutent) in the Pharmaceutical Schedule for the treatment of patients with gastrointestinal stromal tumour (GIST) that is refractory to imatinib due to treatment failure or intolerance.

The Committee noted that sunitinib is a small molecule multi-receptor kinase (RTK) inhibitor. Some RTKs are implicated in tumour growth, angiogenesis, and metastatic progression of cancer. Sunitinib has been identified as an inhibitor of platelet-derived growth factor receptors (PDGFRα and PDGFRβ), vascular endothelial growth factor receptors (VEGFR1, VEGFR2 and VEGFR3), stem cell factor receptor (KIT), Fms-like tyrosine kinase-3 (FLT3), colony stimulating factor receptor Type 1 (CSF-1R), and the glial cell-line derived neurotrophic factor receptor (RET).

Refractory gastrointestinal stromal tumour (GIST)

The Committee noted that Imatinib (Glivec) is currently listed in the Pharmaceutical Schedule for the treatement of unresectable and/or metastatic malignant gastrointestinal stromal tumour (GIST). The Committee noted that surgical resection remains the treatment of choice for GIST and offers the only chance of a cure, whilst the goals of drug therapy are to induce remission, reduce morbidity, and prevent complications.

The Committee noted that in New Zealand there is good data available on the number of patients diagnosed and treated with imatinib. In the year ending June 2006, 24 patients had started on imatinib for the treatment of GIST, of these 1/24 patients died and 9/24 had treatment withdrawn due to imatinib failure or intolerance.

The Committee considered evidence from a Phase III study (Demetri et al Lancet, 2006) in which 312 patients with imatinib refractory (intolerant or unresponsive) GIST were randomised (2:1) to sunitinib (n=207), 50 mg daily for four weeks followed by a two week break (then repeated), or placebo (n=105). The Committee noted that patients enrolled in this study had good performance status (ECOG 0 or 1) and adequate renal, cardiac, hepatic and haematological function.

The Committee noted that if disease progression occurred during the study, patients were unblinded and given the option to continue (or start) open-label sunitinib. At the time of data cut off 65% of patients on sunitinib and only 32% of patients on placebo continued to receive blinded treatment.

The Committee noted that the primary endpoint, time to tumour progression, was improved by 20.9 weeks (27.3 vs 6.4). A median survival calculation was not performed; however, at the time of cut-off 29 (14%) of sunitinib patients had died, compared with 27 (26%) of placebo patients.

The Committee noted that 83% of sunitinib-treated patients and 59% of placebo-treated patients reported at least one adverse event, with the most common sunitinib-related adverse events being fatigue, diarrhoea, skin discolouration, and nausea. Serious adverse events were reported more frequently in the sunitinib-treated patients (34% vs 22%).

The Committee considered that although sunitinib did appear to have some effect in imatinib refractory GIST patients the selection of 'well' patients in this study and the ability of placebo patients to cross-over to sunitinib limited it's usefulness in determining the effect in a realistic clinical setting.

The Committee noted that although the supplier did not provide a cost-effectiveness, or cost-utility analysis, it did submit a cost-utility analysis to the Scottish Medicines Consortium (SMC) of sunitinib versus best supportive care (i.e. imatinib discontinued regardless of treatment

modality). The report from the SMC indicates that the suppliers model estimated the cost/QALY at around £65,000 (NZ$180,000) The Committee noted that the SMC did not recommend the use of sunitinib in the NHS in Scotland, its primary reason being that cost-effectiveness had not been demonstrated.

The Committee considered that given the high cost of sunitinib compared with imatinib (approximately twice the cost) and limited evidence for its long-term survival effectiveness in imatinib-refractory patients, the Committee **recommended** that the application be declined.

The Committee **recommended** that its minutes be referred to the Cancer Treatment Subcommittee of PTAC (CaTSoP) for noting.

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, and, (vi) The budgetary impact (in terms of the pharmaceutical budget and the Government's overall health budget) of any changes to the Pharmaceutical Schedule*

Everolimus (Certican)

The Committee reviewed a submission from Novartis in response to its August 2006 minute regarding the listing of everolimus (Certican) on the Pharmaceutical Schedule for the prophylaxis of organ rejection in patients following allogeneic renal or cardiac transplant.

The Committee considered that although the evidence provided suggests that everolimus reduces cardiac allograft vasculopathy (CAV), the long-term clinical benefits of this are unclear. The Committee considered that a correlation between reduced CAV and long-term graft or patient survival for patients treated with everolimus had not been demonstrated.

The Committee noted that it was aware of potential advantages and disadvantages relating to everolimus treatment in the studies provided; however, it considered that the supplier had not demonstrated the place in therapy for everolimus compared with other treatment options.

The Committee reiterated its **recommendation** that the application be declined, because the place in therapy for everolimus was not clear at this time.

The Committee **recommended** that its minutes and the application be referred to the Transplant and Immunosuppressant Subcommittee of PTAC for advice regarding appropriate endpoints and the place in therapy for everolimus compared with other treatment options.

Pemetrexed (Alimta)

The Committee reviewed a letter from Eli Lilly in response to its August 2006 minute regarding the listing of pemetrexed disodium (Alimta) on the Pharmaceutical Schedule for the treatment of

patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) after prior platinum-based chemotherapy (second-line).

The Committee noted that it had reviewed all studies provided by the supplier during its August 2006 meeting. The Committee noted that in the phase II study by Smit et al (Annal Oncol. 2003; 14: 455-460) vitamin supplementation was omitted which would have a negative effect on the incidence of neutropenic sepsis. The Committee clarified that it had been referring to the Smit et al trial only in its 17 August 2006 minute where it had stated that 'other trials' showed a higher incidence of neutropenic sepsis when compared with data from the open label phase III trial (JMEI, J Clin Oncol. 2004 May 1;22(9):1589-97) .

The Committee noted the supplier's comment that although the overall duration of hospital days was higher in patients treated with pemetrexed the incidence of hospitalisations due to drug-related events was higher in docetaxel-treated patients. The Committee disagreed with the supplier's position that for the purposes of economic analysis only hospitalisation for adverse events considered to be study drug related are appropriate. The Committee considered that increased hospital resource utilisation associated with pemetrexed use is important, regardless of reason. The Committee considered that the use of and duration of hospitalisation was an appropriate economic and clinical parameter for it to consider, and noted that there were longer hospital stays in the pemetrexed-treated patients compared with docetaxel (1772 vs. 1410 bed days).

The Committee **recommended** that its minute be provided to the Cancer Treatments Subcommittee of PTAC for comment.

The Committee reiterated its August 2006 **recommendation** that the application be declined on the basis that the evidence showed no additional efficacy benefit of pemetrexed compared with docetaxel which is currently funded for second-line treatment of NSCLC.

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, and, (iv) the clinical benefits and risks of pharmaceuticals.*

Imiquimod (Aldara)

The Committee noted the email correspondence between the Committee members since the November 2006 PTAC meeting regarding appropriate Special Authority criteria. The Committee also noted the April 2005 and December 2006 assessments of imiquimod cream (Aldara) for superficial basal cell carcinoma performed by the Scottish Medicines Consortium and RADAR (Rational Assessment of Drugs and Research) respectively.

The Committee considered that some form of confirmation of the lesion being a basal cell carcinoma was appropriate and that this could be in the form of a histological assessment or the opinion of a dermatologist, or other prescriber with an appropriate scope of practice.

The Committee considered that surgical excision was the preferred treatment as it had the highest cure rate and, therefore, should be used first-line whenever possible

When considering the place of imiquimod therapy in a patient's treatment, the Committee noted that fluorouracil sodium has a specialist restriction. The Committee considered that this restriction should be removed.

The Committee considered that it was likely that imiquimod would be used for lesions in the H zone of the face by practitioners even though imiquimod has not been evaluated for the treatment of superficial basal cell carcinoma (BCC) within 1 cm of the hairline, eyes, nose mouth or ears.

The Committee noted that imiquimod is not indicated for recurrent, invasive, infiltrating, or nodular BCC.

The Committee **recommended** that the following Special Authority criteria should be applied to imiquimod cream, as follows:

> **Imiquimod (Aldara) Special Authority**
>
> Tick boxes
>
> Primary treatment of confirmed superficial basal cell carcinoma where other standard treatments, including simple surgical excision, are contraindicated or inappropriate.
>
> Prescriber has a scope of practice that includes the management of superficial basal cell carcinoma
>
> Presciption is limited to a maximum of 12 sachets per treatment course
>
> Notes
>
> Surgical excision remains first-line treatment for superficial BCCs as it has a higher cure rate than imiquimod and allows histological assessment of tumour clearance.
>
> Aldara cream has not been evaluated for the treatment of superficial BCC within 1 cm of the hairline, eyes, nose, mouth or ears.
>
> Imiquimod is not indicated for recurrent, invasive, infiltrating, or nodular BCC.

The Committee **confirmed** its previous recommendation that imiquimod be listed on the Pharmaceutical Schedule with a medium priority for the treatment of superficial basal cell carcinoma.