MARCH 2005 PBAC OUTCOMES - "Subsequent" Decisions not to Recommend

DRUG AND FORM	TGA INDICATION	CURRENT PBS LISTING	LISTING REQUESTED BY SPONSOR	PBAC OUTCOME AND COMMENTS
ALEFACEPT injection, 15 mg (IM) and 7.5 mg (IV), Amevive® Biogen Idec Australia Pty Ltd Major submission	Treatment of adult patients with moderate to severe chronic plaque psoriasis who are candidates for phototherapy or systemic therapy. Safety and efficacy beyond two courses have not been demonstrated.	Not PBS listed		Although the PBAC accepted both that there was a demonstrated clinical need for the drug and it was demonstrated to be effective, the Committee rejected the submission because of uncertain but unfavourable cost-effectiveness.
			Authority required listing for the initial treatment by a dermatologist of adults 18 years and over who have been diagnosed with severe chronic plaque psoriasis as defined by those who have failed to achieve an adequate response to two or more of the following treatments: ≥ 6 weeks of phototherapy, methotrexate at a dose of ≥ 10 mg/week for a minimum of ≥ 6 weeks or cyclosporin at a dose of 5 mg/kg/day for a minimum of 6 weeks, with the following criteria: CD4+ lymphocyte counts above the lower limit of normal within 2 weeks prior to dosing; and baseline PASI score of ≥ at any time since diagnosis or patients with psoriasis on the face, hands	The PBAC considered that, although progress has been made on defining the severity of disease, there are a number of outstanding issues to be resolved, such as ensuring that alefacept is used as last-line therapy, the timing of measurement of the PASI response and the time period before a treatment failure may be re-treated.

			and/or feet where at least 1 of the 3 subscales (erythema, scale or thickness) is severe and skin area affected is ≥30% of the face, hands and/or feet . Continuing PBS-subsidised treatment by a dermatologist of adults 18 years and over with severe chronic plaque psoriasis and who, at the time of application, have demonstrated a reduction of ≥ 50% of baseline PASI score at any time up to 24 weeks following commencement of initial treatment. For patients without a baseline PASI score, continuing PBS-subsidised treatment of those who have demonstrated a reduction in PASI score to ≤ 10 at any time up to 24 weeks following commencement of initial of treatment. Re-treatment may be initiated as needed, provided that CD4+ T-cell count is above the lower limit of normal and a minimum of 12 weeks has passed between courses of treatment.	
			Comparator: Placebo for a continuation of standard therapies	Accepted
			Clinical claim: Alefacept has significant advantages in	Partially accepted. However, the PBAC noted that differences in the

			effectiveness over the main comparator but is associated with more toxicity.	utility scores of reported studies have a substantial impact on the resulting cost-utility analysis. Although many patients may experience a high utility gain, the PBAC agreed that the claimed net effect for response to be implausible.
			Economic claim: Cost-effectiveness	Rejected. The PBAC concluded that the most favourable base case estimate of the model was based on assumptions which were biased in favour of alefacept.
			Sponsor's comments:	

ALENDRONATE tablet, 70 mg, Fosamax®; RISEDRONATE tablet, 5 mg and 35 mg, Actonel® and RALOXIFENE tablet, 60 mg, Evista® Merck Sharp & Dohme Pty Ltd Aventis Pharma Pty Ltd Eli Lilly Australia Pty	Alendronate 70 mg is indicated for treatment of osteoporosis, including glucocorticoid-induced osteoporosis Osteoporosis must be confirmed by: * the finding of low bone mass of at least 2 standard deviations below the gender specific mean for young	Alendronate and risedronate are PBS listed with authority required restrictions for Established osteoporosis[1] in patients with fracture due to minimal trauma. The fracture must have been demonstrated radiologically and the year of plain x-ray, or CT-scan or MRI scan must be included in the authority		PBAC rejected the application because of the uncertain extent of long-term clinical benefit and resulting uncertain cost-effectiveness.
			Initial treatment for patients at high risk of fracture. A high risk of fracture is diagnosed by: Patients[1] aged 60 years or older who have a bone mineral density (BMD) T-score -2.5 or less. The initial authority application must	PBAC was concerned that the requested restriction did not propose combinations of age and BMD thresholds which would constitute equivalent absolute risk of fracture to the average for patients with one or more prior

Ltd Major submission	adults or by * the presence of osteoporotic fracture FOSAMAX is also indicated for the prevention of glucocorticoid-induced osteoporosis in those patients on long term corticosteroid therapy. Risedronate 35 mg is indicated for: Treatment of osteoporosis. Treatment of glucococorticoid-induced osteoporosis. Preservation of bone mineral density in patients on long term corticosteroid therapy. Raloxifene is indicated for the prevention and treatment of osteoporosis in post-menopausal women.	application. A vertebral fracture is defined as a 20% or greater reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body, or a 20% or greater reduction in any of these heights compared to the vertebral body above or below the affected vertebral body. Continuing treatment for established osteoporosis[1] in patients with fracture due to minimal trauma where the patient has previously been issued with an authority prescription for this drug. The raloxifene listing is limited to postmenopausal osteoporosis only.	state the date, site (femoral neck or lumbar spine) and score of the qualifying BMD measurement. The patient's date of birth must be included in the authority application. For all initial authority applications, the radiological and/or laboratory reports supporting eligibility must be available for audit by the HIC. Continuing treatment for established osteoporosis[1] in patients bone mineral density (BMD) T-score -2.5 or less where the patient has previously been issued with an authority prescription for this drug. [1] the raloxifene listing is limited to postmenopausal osteoporosis only.	minimal trauma fractures.
			Comparator: No therapy or 'watchful waiting' (patient monitoring and standard managements with calcium and vitamin D)	Accepted.
			Clinical claim: Alendronate, risedronate and raloxifene have significant clinical advantages over placebo and have similar or less toxicity	Partially accepted. PBAC noted the three therapies statistically significantly reduced the rate of morphometric vertebral fractures. There were however, differences between therapies regarding the efficacy on non-vertebral fractures.

			Economic claim: Cost-effectiveness	Rejected. PBAC considered the claimed treatment effects in the model were not supported by the extent and clinical importance of the treatment effect demonstrated in the randomised trials.
			Sponsor's comments: Merck Sharp & Dohme Pty Ltd	The sponsor will be considering its position regarding any future course of action, and refers you to its website for further information. Weblink: www.msd-australia.com.au
			Aventis Pharma Pty Ltd	The sponsor is considering its position regarding any future course of action.
			Eli Lilly Australia Pty Ltd	The sponsor will be considering its position regarding any future course of action, and refers you to its website for further information. Weblink: www.lilly.com.au

ATOMOXETINE capsule, 10 mg, 18 mg, 25 mg, 40 mg and 60 mg,	Treatment of Attention Deficit Hyperactivity Disorder (ADHD) as defined by DSM-IV	Not PBS listed		The PBAC rejected the submission because the conclusion from the trial evidence for atomoxetine is that it is non-inferior to the

Strattera® Eli Lilly Australia Pty Ltd Major submission	criteria in children 6 years of age and older, adolescents and adults.			stimulants in terms of clinical benefits overall and thus atomoxetine is of uncertain but unfavourable cost-effectiveness due to its increased costs.
			Authority required listing for initial treatment for attention deficit hyperactivity disorder in patients aged 6 years and older. Treatment should be initiated by a specialist medical practitioner treating ADHD. Continuing treatment for ADHD where the patient has previously been issued with an authority prescription for this drug.	Accepted
			Comparator: Stimulants – dexamphetamine and methylphenidate and Placebo, for no therapy.	Accepted.
			Clinical claim: Atomoxetine has similar effectiveness to stimulants but has less toxicity. Atomoxetine is significantly more effective than placebo and has similar toxicity.	Partially accepted. PBAC noted that although atomoxetine is superior to placebo there was a trend for atomoxetine being inferior to stimulants, although this is unlikely to be clinically important. PBAC considered the claim for a superior toxicity profile for atomoxetine was not adequately justified.

			Economic claim: Cost-effectiveness	Rejected. The PBAC noted a number of problems with the modelled economic evaluation, which favoured atomoxetine.
			Sponsor's comments:	The sponsor will be considering its position regarding any future course of action, and refers you to its website for further information. Weblink: www.lilly.com.au

EPOPROSTENOL vial, 500 microgram and 1.5 mg, Flolan® GlaxoSmithKline Australia Ltd Major submission	For long-term intravenous treatment of primary pulmonary hypertension (PPH) in New York Heart Association (NYHA) functional Class III and Class IV patients.	Not PBS listed		The PBAC rejected the submission because of uncertainty about the determination of equi-effective doses and uncertainty about the resulting cost-minimisation analysis.
			Initial treatment of certain patients who have been assessed by a physician from a designated hospital to have WHO Functional Class III primary pulmonary hypertension a mean right atrial pressure greater than 8mm Hg, as measured by RHC, unless a RHC is contraindicated on clinical grounds OR WHO functional class IV primary pulmonary hypertension.	The PBAC did not agree with the proposed restriction's continuation criteria for epoprostenol which is less stringent than that for bosentan or iloprost.

			Continuing PBS-subsidised treatment of patients with WHO Functional Class III or IV primary pulmonary hypertension who have received approval for initial subsidised treatment and have completed the initial treatment course and have been assessed by a physician from a designated hospital to have achieved a response to treatment.	
			Comparator: Bosentan	Accepted.
			Clinical claim: Epoprostenol sodium is at least no worse than bosentan in terms of effectiveness, but has greater toxicity.	Accepted. PBAC concluded that epoprostenol is therapeutically no worse than bosentan.
			Economic claim: Cost-minimisation	PBAC did not accept the submission's proposed equi-effective doses of epoprostenol 9.2ng/kg/min and bosentan 125mg twice daily. Other evidence presented showed a dose of 21ng/kg/min at the end of the first year of treatment. This suggests that the dose of epoprostenol will continue to increase beyond the 8- to 12-week time horizon of the key trials. PBAC considered an

				alternative proposal to address this concern to be clinically inappropriate.
			Sponsor's comments:	The sponsor disagrees with the decision and will clarify the decision with the PBAC.

PALIVIZUMAB vial, 50 mg and 100 mg, Synagis® Abbott Australasia Pty Ltd Major submission	For the prevention of serious lower respiratory tract disease caused by respiratory syncytial virus (RSV) in children at high risk of the disease. Safety and efficacy were established in children with bronchopulmonary dysplasia (BDP), infants with a history of prematurity (gestational age ≤ 35 weeks at birth) and children with haemodynamically significant congenital heart disease.	Not PBS listed		The PBAC rejected the submission because the extent of clinical benefit demonstrated for palivizumab was insufficient to justify the overall costs and cost off-sets associated with its use in the requested restriction and thus uncertain but unfavourable cost-effectiveness.
			Section 100 listing for children with haemodynamically significant congenital heart disease and who are ≤ 2 years of age, at the time of first inoculation. Children with a history of prematurity (gestational age ≤ 35 weeks at birth) who are less than 3 months of age at the time of first inoculation. Inoculations should commence	PBAC was not convinced that palivizumab qualified as a section 100 highly specialised drug.

			one month before the RSV season and continue for the duration of the season but can also start at any time during the season.	
			Comparator: Placebo	Accepted
			Clinical claim: Pavilizumab prophylaxis is more effective than placebo, with similar toxicity.	Partially accepted. PBAC noted that the Impact trial provides evidence of the drug's effectiveness in reducing hospital admissions due to RSV. However, the data from the Impact trial may be outdated and may be less valid, given improvements in neonatal management in the last seven years.
			Economic claim: Cost-effectiveness	Rejected. PBAC considered that the long-term consequences of palivizumab regarding asthma are uncertain and there was thus considerable uncertainty about the extent of the risk assumed in the modelled evaluation.
			Sponsor's comments:	