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

DRUG AND FORM	TGA INDICATION	CURRENT PBS LISTING	LISTING REQUESTED BY SPONSOR	PBAC OUTCOME AND COMMENTS
EFALIZUMAB 125 mg injection, Raptiva® Serono 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 12 months have not been established.	Not PBS listed		The PBAC rejected the submission because of unacceptable cost-effectiveness.
			Section 100 (Highly Specialised Drug) listing for: <u>Initial treatment</u>: Initial treatment for up to 16 weeks as mono-systemic therapy (i.e. not in conjunction with acitretin, methotrexate or cyclosporin) by a dermatologist for adults 18 years and over for severe chronic plaque psoriasis where lesions have been present for at least 6 months from the time of initial diagnosis; AND who have signed a patient agreement form indicating that they understand and acknowledge that PBS-subsidised treatment will cease if the predetermined response criteria do not support continuation of PBS-subsidised treatment; AND who have failed to achieve an adequate response to two out of three therapies comprising phototherapy (UVB or PUVA) for	Although not a reason for rejection, there were some outstanding issues with the requested restriction in its intended aim in terms of rigorously identifying both eligible patients and then adequate responders. Most dermatologists work in private practice and thus listing under section 100 would be likely to disadvantage a large number of patients.

			3 treatments per week for at least 6 weeks, methotrexate at a dose of 10 – 15 mg weekly for at least 6 weeks and cyclosporin at a dose of 2 – 5 mg/kg/day for at least 6 weeks. Continuing PBS-subsidised treatment by a dermatologist for adults 18 years and over with severe chronic plaque psoriasis who, at the time of the application, demonstrate an adequate response to treatment with EFALIZUMAB as manifested by a PASI score which is reduced by 50% or more after at least 12 weeks of treatment compared with the pre-treatment value.	
			Comparator: Placebo	Accepted
			Clinical claim: Efalizumab has significant advantages in effectiveness over the main comparator but is associated with more toxicity.	Accepted. PBAC agreed that efalizumab is an effective drug in terms of a PASI 50 improvement.
			Economic claim: Cost-effectiveness	Partially accepted. Despite the concerns about the derivation of the utility values, PBAC considered that the incremental cost per extra QALY gained was reasonably robust, but also considered that the base case cost-effectiveness ratio

				was high.
			Sponsor's comments:	Serono wishes to continue to work with the PBAC to achieve a positive recommendation for funding of Raptiva for eligible patients.
INSULIN GLARGINE, 100 IU per mL, Lantus® Sanofi Aventis Group Major submission	Treatment of type I and type II diabetes mellitus in adults who require insulin for the control of hyperglycaemia. Treatment of type 1 diabetes mellitus in children aged 6-15 years.	Not PBS listed		Although PBAC continues to agree that there are patients who will potentially benefit from the advantage in hypoglycaemic rates with insulin glargine over insulin NPH, the submission was rejected on the grounds of uncertain overall benefit in the insulin-dependent diabetic population as a whole and of an uncertain and unacceptably high cost-effectiveness ratio.
			Unrestricted listing	Accepted
			Comparator: Neutral protamine hagedorn (NPH) insulin	Accepted.
			Clinical claim: Insulin glargine is no worse than NPH in terms of effectiveness as measured by reduction in HbA1C, but is less toxic in terms of hypoglycaemic events	Accepted. PBAC noted that the analysis presented showed reductions in hypoglycaemic events per patient for insulin glargine compared with insulin NPH. However, the absolute sizes of the reductions in the different types of hypoglycaemic events with insulin glargine were small and glargine

				does not totally remove the risk of hypoglycaemic events.
			Economic claim: Cost-effectiveness	Rejected. The absolute differences in hypoglycaemic event rates used in the modelled economic evaluation were higher than those observed in the clinical trials and were not accepted. The utility values used in the economic model were considered poorly justified.
			Sponsor's comments:	The sponsor disagrees with the decision and will be considering its position regarding any future course of action.
TERIPARATIDE (rbe), injection, 3 mL prefilled pen, 250 micrograms per mL Forteo® Eli Lilly Australia Pty Limited Major submission	Treatment of osteoporosis in postmenopausal women and the treatment of primary osteoporosis in men when other agents are considered unsuitable and when there is a high risk of fractures.	Not PBS listed		The PBAC acknowledged there is a clinical need for an effective treatment in this patient group, but rejected the submission because of the inappropriate comparator and the resulting uncertain clinical benefit and uncertain cost effectiveness of teriparatide.
			Initial treatment for severe established osteoporosis in men and postmenopausal women with evidence of one severe painful osteoporotic vertebral fracture. Evidence of the fracture/deformity must be demonstrated	Although not a reason for rejection, the PBAC agreed that any restriction would need to be in accordance with the TGA-approved indication, but noted that the sponsor had no objections to any change in its requested restriction

			radiologically and the year of plain x-ray or CT-scan or MRI scan must be included in the authority application. A severe vertebral fracture is defined as 40% reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body, or, greater than 40% reduction in any of these heights compared to the vertebral body above or below the affected vertebral body. Continuing treatment where the patient has previously been issued with an authority prescription for this drug. Teriparatide is available with a lifetime maximum of 18 months teriparatide therapy (18 pens), a maximum of 18 pens will be reimbursed through the PBS. Teriparatide must be initiated only by a specialist/consulting physician treating osteoporosis	to reflect this.
			Comparator: Placebo	Rejected. Despite apparent “failure” of an anti-resorptive in this situation, the evidence available does not support an argument that these agents are ineffective in treating this patient sub-group and

				that treatment would continue to be offered given the greater clinical need. Thus, an anti-resorptive, specifically alendronate as the most frequently prescribed drug in the group, was considered to be the appropriate comparator.
			Clinical claim: Teriparatide is superior to placebo but is more toxic.	Given the conclusion that placebo is not the appropriate comparator, the comparative clinical data and the economic model did not give an informative basis for the PBAC to consider the listing of teriparatide in this patient group.
			Economic claim: Cost-effectiveness	Rejected. In addition to the use of an inappropriate comparator, PBAC also considered that there was uncertainty due to many of the clinical assumptions and many of the data inputs into the model, particularly the derivation of the utility estimates.
			Sponsor's comments:	The sponsor disagrees with aspects of the PBAC decision and is considering seeking an Independent Review. The sponsor refers to its website for further information: www.lilly.com.au
