March 2009 PBAC OUTCOMES – "Subsequent" decisions not to recommend

DRUG AND FORM	TGA INDICATION	CURRENT PBS LISTING	LISTING REQUESTED BY SPONSOR	PBAC OUTCOME AND COMMENTS
ALGLUCOSIDASE alfa, powder for I.V. infusion, 50 mg, Myozyme® Genzyme Australasia Pty Ltd Major submission	Long-term treatment of patients with a confirmed diagnosis of Pompe disease (acid alfa-glucosidase deficiency).	Not currently listed		The PBAC rejected the application for listing alglucosidase on the PBS because of unacceptably high cost effectiveness. The PBAC also did not recommend inclusion of alglucosidase on the LSDP because it considered it did not meet criterion 2 of LSDP criteria as there remained uncertainty associated with the extent to which a patient's life would be extended as a direct consequence of treatment.
			Section 100 (Highly Specialised Drug) Private hospital authority required Late onset Pompe disease Or, to be considered for inclusion in the Life Saving Drugs Program (LSDP)	The PBAC considered there would be a need to establish treatment initiation and continuation guidelines.
			Comparator: Standard (palliative) therapy including intensive respiratory support, cardiac care, dietary therapy and rehabilitative services.	Accepted.
			Clinical Claim: Alglucosidase is associated with greater efficacy than placebo (supportive care) and would be expected to stop disease progression but is associated with greater toxicity.	Partially accepted. The PBAC accepted that alglucosidase therapy is associated with an improvement in the 6-minute walk test (6MWT) and lung function compared with placebo. However, the PBAC raised some concern about the uncertainty associated with assuming that these surrogate outcomes can be extrapolated to improvements in morbidity and mortality in patients diagnosed with the disease later in life.

			Economic Claim: Cost-effective.	Not accepted. The cost-effective analyses were unacceptably high, and uncertain due to the uncertain clinical benefit.
			Sponsor Comments:	The PBAC reaffirmed its previous recommendation for the Government to consider including alglucosidase on the Life Saving Drugs Program for use in infantile onset Pome disease. Genzyme Australasia will continue to work with the PBAC and the LSDP to ensure that all appropriate Pompe disease patients have funded access to Myozyme by addressing the concerns raised by the PBAC.

CETUXIMAB, solution for I.V. infusion, 100 mg in 20 mL, 100 mg in 50 mL and 500 mg in 100 mL, Erbitux® Merck Serono Australia Pty Ltd Minor submission	Treatment of patients with metastatic colorectal cancer that has been demonstrated to express epidermal growth factor receptor (EGFR) and whose disease has progressed or is refractory to irinotecan based therapy. Cetuximab can be used at the doses recommended either in combination with irinotecan or as a single agent; In combination with radiation therapy, for the treatment of patients with locally advanced squamous cell cancer of the head and neck.	<u>Authority Required</u> Initial treatment of stage III, IVa or IVb squamous cell cancer of the larynx, oropharynx or hypopharynx for the week prior to radiotherapy, where cisplatin is contraindicated according to the TGA-approved Product information; Initial treatment of stage III, IVa or IVb squamous cell cancer of the larynx, oropharynx or hypopharynx, in combination with radiotherapy, where cisplatin is not tolerated. <u>Authority Required</u> Continuing treatment of stage III, IVa or IVb squamous cell cancer of the larynx, oropharynx or hypopharynx, in combination with radiotherapy, where cisplatin is either contraindicated or not tolerated.		The PBAC rejected the application because of high and uncertain cost-effectiveness.
			<u>Authority required</u> PBS-subsidised treatment of patients with metastatic colorectal cancer with a WHO performance status of 2 or less, in combination with irinotecan, where: a) Patients have received and failed 5-fluorouracil or capecitabine, received and failed an irinotecan based therapy and received and failed or are unsuitable for an oxaliplatin based therapy. b) There is evidence that the patient has KRAS wild type in the tumour material. .	The PBAC had previously considered there was no evidence of benefit with further irinotecan treatment following disease progression.
			Comparator: Best supportive care	Accepted.

			Clinical Claim: Cetuximab plus best supportive care (BSC) is superior in terms of overall survival compared to BSC.	Not accepted. The PBAC considered the extent of survival benefit remains uncertain as it is based on post-hoc analyses and extrapolation.
			Economic Claim: Cost effective	Not accepted. The ICER remains both high and uncertain due to uncertain survival benefit and a number of assumptions in the modelled economic evaluation, in particular drug and adverse event costings.
			Sponsor Comment	Merck Serono Australia is disappointed with this recommendation and will continue to work with the PBAC to ensure access to this targeted therapy for patients with metastatic colorectal cancer.
ECULIZUMAB, solution concentrate for I.V. infusion, 300 mg in 30 mL, Soliris® Alexion Pharmaceuticals Australasia Pty Ltd Major submission	Treatment of patients with paroxysmal nocturnal haemoglobinuria (PNH) to reduce haemolysis.	Not currently listed		The PBAC rejected the application for listing eculizumab on the PBS on the basis of an unacceptably high and highly uncertain cost-effectiveness. The PBAC considered that eculizumab meets the criteria for inclusion on the LSDP but that specific requirements for initiation and continuation of treatment would need to be developed by independent experts to identify those patients with paroxysmal nocturnal haemoglobinuria (PNH) who would benefit most from treatment with eculizumab.
			Section 100 (Highly Specialised Drug) <u>Private hospital authority required</u> Treatment of patients with paroxysmal nocturnal haemoglobinuria to reduce haemolysis. Or Inclusion on the Life Saving Drugs Program (LSDP) for treatment of paroxysmal nocturnal haemoglobinuria to reduce haemolysis.	
			Comparator: Best supportive care	Accepted.

			Clinical Claim: Eculizumab is therapeutically superior to best supportive care (BSC) with similar safety issues.	Not accepted. The PBAC considered that uncertainty remained in the comparative mortality benefit and in the comparative safety of eculizumab over BSC due to the lack of long term placebo controlled mortality studies or comparative safety studies to BSC."
			Economic Claim: Cost effective	Not accepted. In view of the uncertain long term clinical benefit, there was uncertainty about the cost-effectiveness analyses.
			Sponsor Comments:	The sponsor agrees that eculizumab is an appropriate drug to be listed under the Life Savings Drug Program."
ESSENTIAL AMINO ACID FORMULA without PHENYLALANINE, with CARBOHYDRATE, FAT, VITAMINS, MINERALS and TRACE ELEMENTS, sachets, 15.8 g, 40, Lanaflex®, Nutricia Australia Pty Ltd. Minor submission	Lanaflex does not require registration with the TGA. It is classified with the Australian and New Zealand Food Authority (ANZFA) as a "Food for Special Medical Purposes" and complies with this standard.	Not currently listed.		The application was rejected because of uncertain clinical benefit, uncertain extent of use and use of an inappropriate comparator.
			<u>Restricted benefit</u> Dietary management of adults with proven phenylketonuria who no longer adhere to a phenylalanine restricted diet.	
			Comparator: XP Maxamum® as the main comparator, and also offers comparisons to PKU Express Cooler® and Lophlex LQ®.	Not accepted. Other phenylalanine free formulae were considered more appropriate comparators.
			Clinical Claim: Lanaflex is a useful addition to the current dietary management options for individuals with PKU, over the age of 18 years, who are no longer following a phenylalanine restricted diet.	Not accepted. The PBAC considered there was uncertainty with respect to clinical benefit, and use in a patient group that no longer adhered to a phenylalanine restricted diet.

			Economic Claim: None provided	
			Sponsor Comments:	Nutricia accepts the position of the PBAC regarding listing of Lanaflex at this time. We would like to clarify with the PBAC the interpretation of information regarding the indication and usage of Lanaflex and will consider our position regarding any future course of action towards successful listing.
LEVODOPA with CARBIDOPA MONOHYDRATE, intestinal gel, 20 mg – 5 mg (base) per mL, 100 mL, Duodopa® Solvay Pharmaceuticals Major submission	Treatment of advanced idiopathic Parkinson's disease with severe motor fluctuations despite optimized oral treatment. A positive clinical response to Duodopa administered via a temporary nasoduodenal tube should be confirmed before a permanent percutaneous endoscopic gastronomy (PEG) tube is inserted.	Not currently listed.		The application was rejected because of uncertain clinical benefit and an unacceptably high and uncertain cost effectiveness ratio.

			Section 100 (Highly Specialised Drug) <u>Public and Private Hospital Authority Required</u> Initial Treatment, commenced in a hospital based Movement Disorder clinic specialising in the treatment of advanced Parkinson's Disease with Duodopa. Patients should have adequate cognitive function to manage administration with a portable continuous infusion pump. <u>Section 85 - Authority Required</u> Continuation of treatment with Duodopa intestinal gel commenced in a hospital based specialised Movement Disorder clinic.	Partially accepted. The gel was not considered to meet all the criteria for listing as a Highly Specialised Drug.
			Comparator Standard medical management including deep brain stimulation.	Accepted
			Clinical Claim: levodopa-carbidopa intestinal gel has advantages in effectiveness over standard medical management.	Not accepted. The PBAC considered there was uncertainty with the clinical importance of the trial results, and significant safety concerns associated with percutaneous endoscopic gastrostomy (PEG).
			Economic Claim: Cost utility	Not accepted. The PBAC noted a number of concerns with the modelled economic evaluation. In particular, the inclusion of patient carer utilities, and omission of safety and quality of life issues associated with PEG.
			Sponsor Comments:	The sponsor has no comment.

PARICALCITOL, injection, 2 micrograms in 1 mL and 5 micrograms in 1 mL; capsules, 1 microgram, 2 micrograms, Zemplar®, Abbott Australasia Pty Ltd Major submission	Treatment of the biochemical manifestations of secondary hyperparathyroidism associated with chronic kidney disease.	Not currently listed		The application was rejected because of uncertain clinical benefit and uncertain cost effectiveness.
			Section 100 (Highly Specialised Drugs) <u>Private Hospital Authority Required</u> Treatment by a nephrologist of patients with chronic kidney disease (Stage 5) receiving dialysis who have secondary hyperparathyroidism (iPTH value > 300 pg/mL or 31.8 pmol/L). <u>Section 85 Authority Required</u> (Oral formulation only) Treatment by a nephrologist of patients with chronic kidney disease (Stage 5) receiving dialysis who have secondary hyperparathyroidism (iPTH value > 300 pg/mL or 31.8 pmol/L)	The PBAC noted paricalcitol did not meet all the criteria for listing as a Highly Specialised Drug.
			Comparator: Calcitriol	Accepted.
			Clinical Claim: Paricalcitol is superior in terms of comparative effectiveness (in terms of survival and hospitalisations) and equivalent in terms of comparative safety over calcitriol.	Not accepted. The PBAC considered clinical superiority in terms of survival and hospitalisations was not established due to the use of non-randomised data.
			Economic Claim: Cost utility	Not accepted. In view of the uncertain clinical benefit there was uncertainty about the cost-utility analyses.
			Sponsor Comments:	The sponsor has no comment.

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