MARCH 2013 PBAC MEETING OUTCOMES - "1st time" decisions not to recommend

DRUG AND FORM	DRUG USE AND TYPE	LISTING REQUESTED BY SPONSOR	PBAC RECOMMENDATION
ADALIMUMAB, injection, 40 mg in 0.8 mL pre-filled syringe, 40 mg in 0.8 mL pre-filled pen, Humira® AbbVie Pty Ltd Major submission	Chronic plaque psoriasis	Extend the current Authority required listing to include treatment of an adult patient with moderate to severe chronic plaque psoriasis who meets certain criteria.	The PBAC rejected the submission on the basis of uncertain cost-effectiveness.
		Sponsor's comments:	AbbVie is disappointed with the PBAC decision and will be considering its position regarding any future course of action.
CALCIPOTRIOL + BETAMETHASONE DIPROPIONATE, calcipotriol 0.005% (50 microgram/g) + betamethasone (as dipropionate) 0.05% (500 microgram/g) gel, 60 g, Daivobet® Leo Pharma Pty Ltd Minor submission	Psoriasis	To request a Restricted benefit listing for a larger size (60 g) for treatment of chronic stable plaque type psoriasis vulgaris in a patient who is not adequately controlled with either calcipotriol or potent topical corticosteroid monotherapy.	The PBAC rejected the submission on the basis of inadequate evidence of comparative effectiveness, safety and cost. The PBAC noted that the submission did not provide sufficient evidence to support claims that a 60 g gel pack was clinically justifiable.
		Sponsor's comments:	LEO Pharma acknowledges the PBAC recommendation and is committed to working with the Committee to address the stated issues.
CALCIPOTRIOL + BETAMETHASONE DIPROPIONATE calcipotriol 0.005% (50 microgram/g) + betamethasone (as dipropionate) 0.05% (500 microgram/g) gel, 30 g, Daivobet® Leo Pharma Pty Ltd Minor submission	Psoriasis	Extend the current Restricted benefit listing to include treatment of chronic stable plaque type psoriasis vulgaris in a patient who is not adequately controlled with either calcipotriol or potent topical corticosteroid monotherapy.(Current listing is for scalp only, extended listing will include body.)	The PBAC rejected the request on the basis of inadequate evidence of comparative effectiveness and safety between calcipotriol betamethasone gel and calcipotriol + betamethasone ointment, and cost.

		Sponsor's comments:	LEO Pharma acknowledges the PBAC recommendation and is committed to working with the Committee to address the stated issues.
CLOZAPINE, tablet, 25 mg & 100 mg, Clozaril® Novartis Pharmaceuticals Australia Pty Ltd Minor submission	Schizophrenia	Requests to change the existing Section 100 Highly Specialised Drugs Program Authority Required (+/- STREAMLINED) listing for treatment of schizophrenia in patients who are non-responsive to or intolerant of other neuroleptic agents to a Section 85 Authority Required listing.	The PBAC recommended retaining the existing Section100 HSD program listing for clozapine. The PBAC noted that there are a number of barriers to access of clozapine with the current prescribing and dispensing arrangements. The PBAC considered the benefits sought in the submission in terms of improved patient access could be achieved through amendments to the current Section 100 governance arrangements.
		Sponsor's comments:	The sponsor has no comments.
COBICISTAT, tablet (film coated), 150mg, Brand name to be confirmed, Gilead Sciences Major submission	Human immunodeficiency virus (HIV) infection	Section 100 Highly Specialised Drugs Program Private Hospital Authority Required and Public Hospital Authority required (STREAMLINED) for treatment of an HIV-infected patient as a pharmacokinetic enhancer of atazanavir.	The PBAC rejected the submission on the basis of unclear clinical need for cobicistat as a single-ingredient product, and inadequate evidence to support a claim of non-inferior comparative effectiveness and safety.
		Sponsor's comments:	The sponsor will engage with the PBAC once the TGA indication is finalised in order to move forward towards a PBS listing.
ECULIZUMAB, concentrated solution for I.V. infusion, 300 mg in 30 mL, Soliris® Alexion Pharmaceuticals Australasia Pty Ltd Major submission	Atypical Haemolytic Uraemic Syndrome (aHUS)	Section 100 Highly Specialised Drugs Program listing or inclusion on the Life Saving Drugs Program (LSDP) for treatment of atypical Haemolytic Uraemic Syndrome (aHUS).	The PBAC rejected eculizumab for PBS listing under Section 100 due to uncertainty regarding clinical effectiveness and unacceptable cost-effectiveness in treating newly diagnosed and long-term atypical Haemolytic Uraemic Syndrome (aHUS), and in patients with renal transplant to avoid renal and extra-renal thrombotic micro-

			angiopathy (TMA) and graft loss. The PBAC rejected eculizumab for inclusion on the LSDP because it failed to meet LSDP criteria 1, 2, 3, 4, 5 and 7 due to a number of uncertainties for the PBAC. The PBAC acknowledged the difficulties associated with obtaining clinical data for the use of eculizumab in the treatment of patients with aHUS disease given the rarity of the condition. The PBAC agreed that aHUS is rare and clinically definable, but did not agree at this time that eculizumab is a proven therapeutic modality for this condition based on this submission (criterion 1). The PBAC was not confident the disease would be identifiable with reasonable diagnostic precision using the proposed treatment algorithm and associated testing procedures (criterion 2). The PBAC did not agree the submission provided sufficient acceptable evidence that the disease causes a significant reduction in age-specific life expectancy (criterion 3) or that a patient's lifespan will be substantially extended as a direct consequence of the use of the drug (criterion 4). The PBAC noted that although the drug failed to meet PBS cost effectiveness criteria, the clinical effectiveness of the drug in treating newly diagnosed and long-term aHUS, and in patients with renal transplant to avoid renal and extra-renal TMA and graft loss remained unproven (criterion 5). The PBAC also stated that there are other non-drug therapeutic modalities which are recognised by medical authorities as suitable and cost effective treatments for this condition (criterion 7).

			The PBAC noted that any future proposals would need to be in the form of a major submission. The submission would need to include more robust data to support the clinical claim that eculizumab is safer and more effective than supportive care in treating newly diagnosed and long-term aHUS, and in patients with renal transplant to avoid renal and extra-renal TMA and graft loss. Refinements would need to be made to the proposed treatment algorithm and the evidence provided to support the reliability of associated testing procedures to improve the diagnostic precision with which the disease would be identified. Consideration should also be given to the submission of an application for PBS listing under Section 100. The PBAC noted that the submission meets the criteria for an independent review of the decision not to recommend listing on the PBS. The PBAC also acknowledged and noted the consumer comments on this item.
		Sponsor's comments:	The sponsor strongly disagrees with recommendations and rationale from PBAC that eculizumab for aHUS does not meet LSDP Funding Eligibility Criteria. Eculizumab has been approved by the TGA for this indication. The sponsor believes these PBAC recommendations are in conflict with the body of worldwide clinical evidence for eculizumab as a treatment in aHUS. The sponsor intends to work with the PBAC

			and resubmit to answer the committee's areas of uncertainty in their review and recommendations as soon as possible.
ELVITEGRAVIR, tablet, 85 mg and 150 mg, Brand name to be confirmed Gilead Sciences Major submission	Human immunodeficiency virus (HIV) infection	Section 100 Highly Specialised Drugs Program Private Hospital Authority Required and Public Hospital Authority Required (STREAMLINED) listing for continuing treatment of HIV infection, in combination with a boosted protease inhibitor and other antiretroviral agents, where the patient has previously received PBS-subsidised therapy for HIV infection.	The PBAC rejected the submission of the basis that, in the absence of the final TGA indication it was not possible to identify the clinical place of elvitegravir outside the context of a fixed dose combination. The PBAC therefore considered that it was not possible to formulate an appropriate PBS restriction, or to construct the appropriate price for elvitegravir.
		Sponsor's comments:	The sponsor will engage with the PBAC once the TGA indication is finalised in order to move forward towards a PBS listing.
ERIBULIN MESILATE, solution for injection, 1 mg in 2 mL, Halaven® Eisai Australia Pty Limited Major submission	Breast cancer	Section 100 Efficient Funding of Chemotherapy listing for the treatment of a patient with locally advanced or metastatic breast cancer who has progressed after at least two chemotherapeutic regimens for advanced disease.	The PBAC rejected the submission on the basis of unacceptably high and uncertain cost-effectiveness and because of a lack of clarity regarding the clinical place of the product.
		Sponsor's comments:	Whilst Eisai is disappointed with the decision of the PBAC Eisai is committed to working with the PBAC to address the issues and questions that have been raised, to ensure Halaven is listed on the PBS for eligible patients.
EVEROLIMUS, tablet, 5 mg and 10 mg, Afinitor® Novartis Pharmaceuticals Australia Pty Ltd	Breast cancer	Authority Required listing for treatment, in combination with an aromatase inhibitor, of post-menopausal women with hormone-receptor positive, HER2 negative advanced breast cancer after	The PBAC rejected the submission on the basis of uncertain clinical benefit and high and uncertain cost effectiveness.

Major submission		failure of treatment with letrozole or anastrozole.	
		Sponsor's comments:	Novartis will continue to work with the PBAC to make everolimus available to women with hormone-receptor positive HER2 negative advanced breast cancer.
FENTANYL, single dose spray 6-pack, 50 micrograms, 100 micrograms and 200 micrograms; 10-dose spray bottle, 50 micrograms, 100 micrograms and 200 micrograms; 20-dose spray bottle, 50 micrograms, 100 micrograms and 200 micrograms, Instanyl® Takeda Pharmaceuticals Australia Pty Ltd Major submission	Pain	Palliative Care Schedule listing for treatment of breakthrough pain in a patient with cancer who is receiving opioids for their persistent pain and where further escalation in the dose of morphine for breakthrough pain results in intolerable adverse effects.	The PBAC rejected the submission because of the poor quality of the clinical data presented in support of the claim of superiority of nasal fentanyl over oral transmucosal fentanyl and uncertainty regarding the effectiveness of nasal fentanyl compared with oral transmucosal fentanyl.
		Sponsor's comments:	The sponsor has no comments.
INFLIXIMAB, powder for IV infusion, 100mg, Remicade® Janssen Pty Ltd Major submission	Ulcerative colitis	Extend the current Section 100 Highly Specialised Drugs Program Public and Private Hospital Authority Required listings to include treatment of acute severe ulcerative colitis not responding to IV corticosteroids in a patient aged 6 years or greater and who meets certain criteria.	The PBAC rejected the submission on the basis that the comparator should have also included cyclosporine, the evidence base for infliximab's efficacy was limited to a small number of trials in the acute ulcerative setting and uncertainty in the economic modelling that potentially results in high and unacceptable cost effectiveness ratio.
		Sponsor's comments:	Janssen is disappointed with the PBAC outcome and are working with the PBAC to understand the issues raised.
INSULIN DEGLUDEC, injection, 100 units per mL and 200 units per mL, 3 mL, Tresiba FlexTouch®; injection, 100 units per mL, 3 mL, Tresiba Penfill® Novo Nordisk Pharmaceuticals Pty Ltd	Diabetes	Unrestricted listing (for use in the treatment of patients with type 1 or 2 diabetes).	The PBAC rejected the application to list insulin degludec on the basis that the claim of superior safety over insulin glargine was not adequately justified, and cost-effectiveness was therefore not supported.

Major submission		Sponsor's comments:	Novo Nordisk is disappointed with the PBAC's recommendation but will continue to work constructively with the PBAC to ensure that insulin degludec is made available for patients and physicians dealing with the burden of diabetes as soon as possible.
LENALIDOMIDE, capsule, 5 mg and 10 mg, Revlimid® Celgene Pty Ltd Minor submission	Multiple myeloma	Amend the current Section 100 Highly Specialised Drugs Program Public and Private Hospital Authority Required listings to remove the requirement for prior treatment with thalidomide in multiple myeloma patients with progressive disease.	The PBAC rejected the submission on the basis of insufficient clinical evidence to support the claim of superior effectiveness in comparison to thalidomide.
		Sponsor's comments:	Celgene will work with the Department of Health and the PBAC to provide the clinical evidence required.
MOMETASONE FUROATE 0.1% (1 mg/g) hydrogel, 15 g, Zatamil® Ego Pharmaceuticals Pty Ltd Minor submission	Skin lesions	Restricted benefit listing for a 15 g hydrogel formulation for treatment of corticosteroid-responsive dermatoses.	The PBAC rejected the requested listing on the basis of inadequate evidence provided on comparative effectiveness and safety for the new hydrogel formulation of mometasone furoate compared with the currently PBS-listed cream, lotion and ointment formulations of mometasone furoate.
		Sponsor's comments:	We are working with the PBAC to resolve the issues.
MOMETASONE FUROATE 0.1% (1 mg/g) hydrogel, 45 g, and ointment 45 g, Zatamil® Ego Pharmaceuticals Pty Ltd Minor submission	Skin lesions	Restricted benefit listing for 45 g hydrogel and ointment formulations for treatment of corticosteroid-responsive dermatoses.	The PBAC rejected the requested listing of a larger size of hydrogel formulation of mometasone on the basis of inadequate evidence provided on comparative effectiveness and safety for the new hydrogel formulation of mometasone furoate compared with the currently PBS-listed cream, lotion and ointment formulations of mometasone furoate. The PBAC also rejected the requested listing

			of a larger size of ointment formulation of mometasone because the PBAC considered that listing the 45 g pack size may lead to the larger size being the standard prescribed quantity, resulting in many patients being prescribed a larger quantity than necessary; and this may result in higher usage by some patients with associated safety and quality use of medicines (QUM) issues.
		Sponsor's comments:	We are working with the PBAC to resolve the issues.
PROTEIN HYDROLYSATE FORMULA, powder, 900 g, Karicare Aptamil Gold+ Allerpro 1® Nutricia Australia Pty Ltd Minor submission	Medicinal food	Authority required listing for cows' milk protein enteropathy in infants up to12 months of age.	The PBAC rejected the request on the basis of inadequate evidence of an advantage over Karicare Aptamil Pepti-Junior to justify the requested price.
		Sponsor's comments:	The sponsor will consider a re-submission.
PROTEIN HYDROLYSATE FORMULA, powder, 900 g, Karicare Aptamil Gold+ Allerpro 2® Nutricia Australia Pty Ltd Minor submission	Medicinal food	Authority required listing for cows' milk protein enteropathy and intolerance to soy protein in infants 6 to 24 months of age.	The PBAC rejected the request on the basis of inadequate evidence of an advantage over Karicare Aptamil Pepti-Junior to justify the requested price.
		Sponsor's comments:	The sponsor will consider a re-submission.
RANIBIZUMAB, solution for intravitreal injection, 2.3 mg in 0.23 mL, Lucentis® Novartis Pharmaceuticals Australia Pty Ltd Major submission	Visual impairment	Extend the current Authority required listing to include treatment, by an ophthalmologist, of a patient with visual impairment due to diabetic macular oedema, as diagnosed by fluorescein angiography.	The PBAC rejected the submission on the basis of uncertainty about the cost effectiveness ratio, uncertainty about comparative long term safety, and lack of clarity in the extent of benefit measured as an average difference of 5 letters for the treated eye.
		Sponsor's comments:	Novartis will continue to work with the PBAC to make ranibizumab available on the PBS for patients with visual impairment due to diabetic macular oedema.

RISEDRONATE risedronate sodium 35 mg tablet, 4, Acris® RISEDRONATE (&) CALCIUM CARBONATE risedronate sodium 35 mg tablet [4 tablets] (&) calcium (as carbonate) 500 mg tablet [24 tablets], 28, Acris Combi® Alphapharm Pty Ltd Minor submission RISEDRONATE SODIUM, tablet, 35 mg, Risedro Once a Week® Aspen Pharma Pty Ltd Minor submission RISEDRONATE SODIUM, tablet, 35 mg (enteric coated), Actonel EC®; RISEDRONATE SODIUM and CALCIUM CARBONATE, pack containing 4 enteric coated tablets risedronate sodium 35 mg and 24 tablets calcium carbonate 1.25 g (equivalent to 500 mg calcium), Actonel EC Combi® Sanofi-Aventis Australia Pty Ltd Minor Submission	Osteoporosis	To allow PBAC to consider whether a brand equivalence indicator be applied between the immediate release tablet and the enteric coated formulations of risedronate 35 mg.	The PBAC recommended that presentations containing enteric coated risedronate 35 mg should <u>not</u> be marked as equivalent for the purposes of substitution by the pharmacist at the time of dispensing to presentations containing immediate release risedronate 35 mg as the difference in the dosing instructions for the two presentations could result in patient confusion when switching from one presentation to the other.
		Sponsor's comments:	*Alphapharm Pty Ltd* The sponsor is disappointed that, despite acknowledging therapeutic equivalence between the EC and IR formulations when taken according to directions, the committee did not recommend a brand equivalence indicator. *Aspen Pharma Pty Ltd* The sponsor has no comments. *Sanofi-Aventis Australia Pty Ltd* The sponsor has no comments.
TESTOSTERONE, topical solution for transdermal application, 30 mg in 1.5 mL, Axiron®	Testosterone replacement therapy	Seeks review of the March 2012 recommended relativity ratio between testosterone solution and testosterone	The PBAC rejected the submission's proposed change to the recommended relativity ratio of testosterone solution 70 mg

Eli Lilly Australia Pty Ltd Minor submission		gel.	and testosterone gel 50 mg, in the absence of new clinical data for dose equivalence.
		Sponsor's comments:	The sponsor has no comments.
TOBRAMYCIN, powder for inhalation, capsule 28 mg, Tobi® Podhaler® Novartis Pharmaceuticals Australia Pty Ltd Major submission	Cystic fibrosis	Authority required (STREAMLINED) listing for management of a proven Pseudomonas aeruginosa infection in a patient aged 6 years or older with cystic fibrosis.	The PBAC rejected the submission on the basis of uncertainty in the comparative benefit of tobramycin inhalation powder (TIP) over tobramycin solution for inhalation (TSI), and on the basis that TIP's comparative tolerability compared to TSI was potentially less favourable; resulting in the cost-utility approach to the economic analysis being considered inappropriate.
		Sponsor's comments:	Novartis will continue to work with the PBAC to make tobramycin inhalation powder available on the PBS for patients with cystic fibrosis.