

**November 2011 PBAC MEETING OUTCOMES - "Subsequent" decisions not to recommend**

DRUG AND FORM	TGA INDICATION	CURRENT PBS LISTING	LISTING REQUESTED BY SPONSOR	PBAC OUTCOME AND COMMENTS
<p>BUDESONIDE with EFORMOTEROL FUMARATE DIHYDRATE, oral pressurised inhalation, 200 micrograms-6 micrograms per dose, Symbicort Rapihaler 200/6®</p> <p>AstraZeneca Pty Ltd</p> <p>Major submission</p>	<p>Symptomatic treatment of moderate to severe COPD (FEV<sub>1</sub> ≤ 50% predicted normal) in adults with frequent symptoms despite long-acting bronchodilator use, and/or a history of recurrent exacerbation.</p> <p>Symbicort is not indicated for the initiation of bronchodilator therapy in COPD.</p>	<p>Not currently PBS listed.</p>		<p>The PBAC rejected the resubmission on the basis of inadequate information regarding comparative costs, with remaining concerns that the quality use of medicine strategies proposed by the sponsor were unlikely to adequately counter the significant risk of leakage into off-label and unsubsidised asthma indications.</p>
			<p>Listing requested: <u>Restricted Benefit</u> Symptomatic treatment of chronic obstructive pulmonary disease (COPD), where the FEV<sub>1</sub> is less than 50 % predicted normal and there is a history of repeated exacerbations with significant symptoms despite regular beta-2 agonist bronchodilator therapy.</p> <p><u>NOTE:</u> Budesonide with eformoterol fumarate dihydrate is not indicated for the initiation of bronchodilator therapy in COPD.</p>	<p>The PBAC noted that the resubmission requested listing for the COPD indication only.</p> <p>The PBAC acknowledged the sponsor's proposed undertakings to prevent leakage into the non-registered Symbicort maintenance and reliever therapy (SMART) indication.</p>
			<p>Comparator: Symbicort 400/12 Turbuhaler device</p>	
			<p>Clinical claim: Nil</p>	<p>The PBAC accepted that Symbicort Turbuhaler and Symbicort Rapihaler were therapeutically equivalent.</p>

DRUG AND FORM	TGA INDICATION	CURRENT PBS LISTING	LISTING REQUESTED BY SPONSOR	PBAC OUTCOME AND COMMENTS
			Economic claim: Nil	The PBAC considered there was inadequate information provided regarding comparative costs. No economic analysis or costings were provided for the Rapihaler listing alone.
			Sponsor's comments:	AstraZeneca will continue to work towards PBS listing for Symbicort Rapihaler
CABAZITAXEL, solution concentrate for I.V. infusion, 60 mg in 1.5 mL, Jevtana®  Sanofi-Aventis Australia Pty Ltd  Minor submission	The proposed TGA indication is: Cabazitaxel in combination with prednisone or prednisolone is indicated for the treatment of patients with hormone-refractory metastatic prostate cancer previously treated with a docetaxel-containing regimen.	Not currently PBS listed		The PBAC rejected the resubmission on the basis of a high and uncertain cost-effectiveness ratio.
			Listing requested: <u>Authority Required</u> Treatment of hormone refractory metastatic carcinoma of the prostate in a patient previously treated with a docetaxel-containing regimen.	
			Comparator: Mitozantrone	Accepted (as previously).
			Clinical claim: Cabazitaxel is superior in terms of comparative effectiveness and inferior in terms of comparative safety over mitozantrone.	Accepted (as previously).

DRUG AND FORM	TGA INDICATION	CURRENT PBS LISTING	LISTING REQUESTED BY SPONSOR	PBAC OUTCOME AND COMMENTS
			Economic claim: Cost effectiveness	The PBAC considered the estimated base case ICER was still unacceptably high and there was remaining uncertainty about use beyond progression and also uncertainty regarding the clinical place of cabazitaxel in the treatment of hormone refractory metastatic carcinoma of the prostate.
			Sponsor's comments:	Sanofi is disappointed by the decision but is committed to continuing to work with the PBAC to ensure that Jevtana is made available on the PBS for Australian men who have prostate cancer
EVEROLIMUS, tablets, 5 mg and 10 mg, Afinitor®  Novartis Pharmaceuticals Australia Pty Ltd  Major submission	Treatment of patients with advanced renal cell carcinoma after failure of treatment with sorafenib or sunitinib.	The 5 mg and 10 mg tablets are not currently listed.	Listing requested: <u>Authority Required</u> Initial and continuing treatment, as the sole PBS-subsidised therapy, of Stage IV clear cell variant renal cell carcinoma in a patient with a WHO status of 2 or less, has progressive disease on sunitinib or following cessation of treatment with sunitinib due to toxicity, and who meets certain criteria.	The PBAC rejected the resubmission on the basis of a high and uncertain cost-effectiveness ratio.

DRUG AND FORM	TGA INDICATION	CURRENT PBS LISTING	LISTING REQUESTED BY SPONSOR	PBAC OUTCOME AND COMMENTS
			Comparator: Best supportive care.	Accepted (as previously).
			Clinical claim: Everolimus has superior efficacy and inferior safety in metastatic renal cell carcinoma compared with placebo.	The claim for inferior safety was accepted. However, the PBAC considered that there was still uncertainty about a conclusion of superior efficacy and whether there is a survival gain associated with everolimus and if so, the magnitude of the gain.
			Economic claim: Cost effectiveness	The PBAC considered the estimated base case ICER was unacceptably high.
			Sponsor's comments:	The sponsor has no comment.
LIRAGLUTIDE (rys), injection solution, pre-filled pen, 6 mg per mL, 3 mL, 2 and 3, Victoza®	An adjunct to diet and exercise for treatment of adults with type 2 diabetes mellitus to	Not currently PBS listed		The PBAC rejected the resubmission on the basis of uncertain cost effectiveness.

DRUG AND FORM	TGA INDICATION	CURRENT PBS LISTING	LISTING REQUESTED BY SPONSOR	PBAC OUTCOME AND COMMENTS
<p>Novo Nordisk Pharmaceuticals Pty Ltd</p> <p>Major submission</p>	<p>achieve glycaemic control: - in dual combination, added to metformin or a sulphonylurea, in patients with insufficient glycaemic control despite the use of maximally tolerated or clinically adequate doses of metformin or sulphonylurea monotherapy; or - in triple combination, added to metformin and a sulphonylurea in patients with insufficient glycaemic control despite dual therapy.</p>		<p>Listing requested: Re-submission for an Authority required listing for treatment of type 2 diabetes: 1) as triple combination therapy with metformin and a sulphonylurea; 2) as dual combination therapy with metformin or a sulphonylurea in patients for whom a combination of metformin and a sulphonylurea is contraindicated or not tolerated.</p>	
			<p>Comparator: Exenatide</p>	<p>Accepted (as previously).</p>
			<p>Clinical claim: Liraglutide (1.8 mg daily) is superior in terms of comparative effectiveness and equivalent in terms of comparative safety to exenatide (10 µg twice daily).</p>	<p>The PBAC considered there is clinical uncertainty about the relationship between intensive glycaemic control and diabetes related complications, including the use of HbA1c as a surrogate for cardiovascular outcomes as noted in recent publications.</p>
			<p>Economic claim: Cost effectiveness</p>	<p>The PBAC considered the cost effectiveness remained uncertain. The PBAC did not accept the disutilities nor the inclusion of a reduction in major hypoglycaemic events incorporated into the model.</p>

DRUG AND FORM	TGA INDICATION	CURRENT PBS LISTING	LISTING REQUESTED BY SPONSOR	PBAC OUTCOME AND COMMENTS
			Sponsor's comments:	Novo Nordisk does not agree with the PBAC determination regarding the clinical uncertainty about the relationship between glycaemic control and diabetes related complications and is extremely disappointed that this has resulted in a further delay in the listing of Victoza on the PBS. However, we are committed to working with the all stakeholders to find a way forward in order to make Victoza available for people with type 2 diabetes in Australia.
MANNITOL, capsule containing powder for oral inhalation, 40 mg (for use in inhaler device), Bronchitol®	Treatment of cystic fibrosis (CF) in both paediatric and adult populations six years and above as either an add-on therapy to	Not currently PBS listed		The PBAC rejected the resubmission because of uncertainty about the comparator and on the basis of uncertain clinical effectiveness and uncertain cost effectiveness.

DRUG AND FORM	TGA INDICATION	CURRENT PBS LISTING	LISTING REQUESTED BY SPONSOR	PBAC OUTCOME AND COMMENTS
Pharmaxis Ltd  Major submission	dornase alfa or in patients intolerant to, or inadequately responsive to dornase alfa.		Listing requested: <u>Authority Required</u> Treatment of cystic fibrosis (CF) in paediatric (six years and above) and adult patients as a monotherapy alternative to dornase alfa in a patient who has previously failed PBS-subsidised initiation criteria for dornase alfa; OR in a patient who has discontinued dornase alfa despite a previous successful trial and is considering recommencing therapy; OR in a patient currently on dornase alfa or where a change of therapy might improve outcome based on clinical global assessment.	The PBAC noted that there was potential for use of mannitol outside the requested monotherapy PBS listing.
			Comparator: Dornase alfa	The PBAC considered that hypertonic saline or usual care (placebo) are also appropriate comparators. The PBAC considered that there could be some substitution of dornase alfa by mannitol, and hence dornase alfa as part of a mixed comparison may be reasonable.
			Clinical claim: Dry powder inhaler mannitol monotherapy is non-inferior to dornase alfa in terms of comparative effectiveness (FEV <sub>1</sub> outcomes) and similar in terms of comparative safety.	The PBAC considered the clinical efficacy and safety versus dornase alfa remained uncertain.

DRUG AND FORM	TGA INDICATION	CURRENT PBS LISTING	LISTING REQUESTED BY SPONSOR	PBAC OUTCOME AND COMMENTS
			Economic claim: Cost minimisation	The PBAC considered that the issues regarding the place in therapy of mannitol, the comparator and the clinical efficacy made the economic evaluation uncertain.
			Sponsor's comments:	Pharmaxis are committed to making Bronchitol available to the CF Community, and working with the PBAC in their efforts to reduce uncertainty.
MIGLUSTAT, capsule, 100 mg, Zavesca®  Actelion Pharmaceuticals Australia Pty Ltd  Major submission	Treatment of progressive neurological manifestations in adult and paediatric patients with Nieman Pick type C (NP-C) disease.	Not currently PBS listed  Listed on the Life Saving Drugs Program (LSDP) for treatment of type 1 Gaucher disease.		The PBAC rejected the resubmission on the basis that the clinical evidence presented failed to show that miglustat meets eligibility criterion 4 and 5 of the LSDP.
			Listing requested: To be considered for the LSDP, the drug must have been accepted by the PBAC as Inclusion on the Life Saving Drugs Program (LSDP) for the treatment of progressive neurological manifestations in adults and paediatric patients with NP-C disease.	<i>Comment: To be considered for the LSDP, the drug must have been accepted by the PBAC as clinically effective, but rejected for Pharmaceutical Benefits Scheme (PBS) listing because it failed to meet the required cost effectiveness criteria.</i>
			Comparator: Placebo	The PBAC considered, at the July 2010 meeting, that placebo plus standard medical management (standard care) was the appropriate comparator for miglustat in the treatment of NP-C disease.

DRUG AND FORM	TGA INDICATION	CURRENT PBS LISTING	LISTING REQUESTED BY SPONSOR	PBAC OUTCOME AND COMMENTS
			Clinical claim: Miglustat is superior to placebo in terms of effectiveness in patients with NP-C.	The PBAC did not accept the clinical claim based on the data presented in the submission that miglustat is superior to placebo in terms of effectiveness. The PBAC has previously accepted that miglustat is not as safe as placebo in terms of safety.
			Economic claim: Nil	The PBAC considered in July 2010 that miglustat is not cost effective.
			Sponsor's comments:	Actelion is disappointed with the PBAC's decision not to recommend the inclusion of Zavesca for NP-C on the Life Saving Drugs Program. Zavesca is the only TGA approved medication for the treatment of NP-C in Australia. Actelion is committed to working with the PBAC to explore ways of ensuring Zavesca is made more accessible to people with NP-C.
PLERIXAFOR, solution for injection, 20 mg in 1 mL, 1.2 mL, Mozobil®	Use in combination with G-CSF to mobilise haematopoietic stem cells (HSCs) to the	Not currently PBS listed		The PBAC rejected the resubmission on the basis of a high and uncertain cost-effectiveness ratio.

DRUG AND FORM	TGA INDICATION	CURRENT PBS LISTING	LISTING REQUESTED BY SPONSOR	PBAC OUTCOME AND COMMENTS
Genzyme Australasia Pty Ltd  Major submission	peripheral blood for collection and subsequent autologous transplantation in patients with lymphoma and multiple myeloma.		Listing requested: <u>Section 100 listing – Highly Specialised Drug program Public and Private Hospital Authority Required</u> 1. Patients with lymphoma who require autologous stem cell transplant (ASCT) and have failed previous stem cell collection attempts. 2. Patients with multiple myeloma who require ASCT and have failed previous stem cell collection attempts.	The PBAC noted that the intent of requested restriction is to include patients who have failed previous attempts at peripheral blood stem cell collection as well as those who are currently failing, i.e. “immediate rescue”, which was acknowledged by the sponsor in its Pre-PBAC Response. Therefore, the restriction would be required to accommodate the different populations.
			Comparator: G-CSF in combination with chemotherapy (ifosfamide +, carboplatin + etoposide for lymphoma; and cyclophosphamide for multiple myeloma) in patients with lymphoma and multiple myeloma who have failed previous stem cell collection attempts.	Accepted (as previously).
			Clinical claim: Plerixafor can be an effective means to achieve mobilisation in patients who have previously failed mobilisation attempts.	Accepted (as previously).

DRUG AND FORM	TGA INDICATION	CURRENT PBS LISTING	LISTING REQUESTED BY SPONSOR	PBAC OUTCOME AND COMMENTS
			<p>Economic claim: Cost effectiveness</p>	<p>The PBAC considered that there is major uncertainty arising from the low quality of clinical data about the incremental numbers of patients proceeding to transplant and from the attempt to translate these increments into LYG.</p> <p>Therefore, the PBAC considered that the estimated incremental cost per quality-adjusted life year (QALY) gained for lymphoma and for multiple myeloma are highly uncertain due to the considerable uncertainty associated with the economic model.</p>
			<p>Sponsor's comments:</p>	<p>Genzyme is disappointed by the decision but is committed to continuing to work with the PBAC to ensure that Mozobil is made available on the PBS for eligible patients with lymphoma and multiple myeloma</p>