NOVEMBER 2010 PBAC MEETING 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 PBS listed. Alglucosidase is funded under the Life Saving Drugs Program for the treatment of infantile onset Pompe disease.		The PBAC rejected the re-submission to list alglucosidase on the PBS as a Section 100 Highly Specialised Drug for the treatment of patients with late onset Pompe disease on the basis of high and uncertain cost effectiveness. The PBAC did not recommend inclusion of alglucosidase in the Life Saving Drugs Program (LSDP) for the treatment of late onset Pompe disease as the drug fails to satisfy criterion four of the LSDP Guidelines in that no evidence satisfactory to the PBAC has been submitted to demonstrate that alglucosidase increases life expectancy in patients with late onset Pompe disease even though the drug may improve the quality of life of those patients taking the drug.
			Listing requested: Section 100 (Highly Specialised Drug Program) <u>Private hospital authority required</u> Patients with a confirmed clinical diagnosis of Pompe disease who have had their diagnosis confirmed by a documented deficiency of alfa-glucosidase enzyme activity in either skin fibroblasts, muscle tissue,	

			lymphocytes, mixed leukocytes or dried blood spots (<40% of normal levels) or through identification of a mutation in the GAA gene and who meet certain criteria.	
			Comparator: Standard (palliative) therapy including intensive respiratory support, cardiac care, dietary therapy and rehabilitative services.	Accepted (as previously)
			Clinical claim: The submission described alglucosidase as superior in terms of comparative effectiveness (as measured by forced vital capacity (FVC) and the six minute walk test (6MWT)) and inferior in terms of comparative safety over placebo (standard management).	The PBAC had previously accepted that alglucosidase therapy was associated with an improvement in the 6MWT and a stabilization of upright FVC compared to placebo. However, the PBAC considered that the link between improving or reducing the rate of decline of respiratory function and the increase in life expectancy is highly uncertain.
			Economic claim: Cost-effectiveness	Not accepted. The incremental cost-effectiveness ratio remained unacceptably high and uncertain.
			Sponsor's comments:	Genzyme Australasia remains committed to working with the PBAC and the LSDP to ensure that people with late-onset Pompe disease have funded access to alglucosidase alfa.

DRUG AND FORM	TGA INDICATION	CURRENT PBS LISTING	LISTING REQUESTED BY SPONSOR	PBAC OUTCOME AND COMMENTS
Quetiapine fumarate, tablet, 25 mg, 100 mg, 200 mg, 300 mg (as fumarate), Seroquel®, and tablets (modified release), 50 mg, 200 mg, 300 mg and 400 mg (as fumarate), Seroquel XR® AstraZeneca Pty Ltd Major submission	Treatment of acute mania associated with bipolar I disorder in combination with lithium or sodium valproate; Maintenance treatment of bipolar 1 disorder, as monotherapy or in combination with lithium or sodium valproate, for the prevention of relapse/recurrence of manic, depressive or mixed episodes; Treatment of acute mania associated with bipolar I disorder as monotherapy; and Treatment of depressive episodes associated with bipolar disorder. Treatment of schizophrenia, prevention of relapse	<u>Authority Required</u> (Streamlined) Schizophrenia; Monotherapy, for up to 6 months, of an episode of acute mania associated with bipolar I disorder; Maintenance treatment of bipolar I disorder, in combination with lithium or sodium valproate		The PBAC rejected listing on the basis that quetiapine as add-on therapy to lithium or valproate had not demonstrated non-inferiority to the comparator and as such was not acceptable for consideration in a cost minimisation analysis.
			Listing requested: <u>Authority Required (Streamlined)</u> Adjunctive therapy to mood stabilisers for up to 6 months, of an episode of acute mania associated with bipolar I disorder. Alternatively, if the PBAC was to recommend both quetiapine submissions to the November 2010 PBAC meeting, the sponsor proposed the following: <u>Authority Required (Streamlined)</u> Treatment of bipolar disorder	
			Comparator: Risperidone	Accepted.
			Clinical claim: The submission described quetiapine as non-inferior to risperidone in terms of comparative effectiveness and	Not accepted. In an indirect comparison between risperidone and quetiapine, the PBAC considered there to be important differences in

	and maintenance of clinical improvement during continuation therapy. Treatment of recurrent major depressive disorder in patients who are intolerant of, or have an inadequate response to alternative therapies. Treatment of generalised anxiety disorder.		equivalent in terms of comparative safety.	the trial populations, thereby questioning the validity of the results.
			Economic claim: Cost-minimisation.	Not accepted. The PBAC considered that non-inferiority of quetiapine to risperidone had not been demonstrated.
			Sponsor's comments:	The sponsor had no comment.

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Quetiapine, tablets, 25 mg, 100 mg, 200 mg and 300 mg (as fumarate), Seroquel®, and tablets (modified release), 50 mg, 200 mg, 300 mg and 400 mg (as fumarate), Seroquel XR® AstraZeneca Australia Pty Ltd Major submission	Treatment of acute mania associated with bipolar I disorder in combination with lithium or sodium valproate; Maintenance treatment of bipolar 1 disorder, as monotherapy or in combination with lithium or sodium valproate, for the prevention of relapse/recurrence of manic, depressive or mixed episodes; Treatment of acute mania associated with bipolar I disorder as monotherapy; and Treatment of depressive episodes associated with bipolar disorder. Treatment of schizophrenia,	<u>Authority Required</u> (Streamlined) Schizophrenia; Monotherapy, for up to 6 months, of an episode of acute mania associated with bipolar I disorder; Maintenance treatment of bipolar I disorder, in combination with lithium or sodium valproate		The PBAC rejected the submission on the basis that the main comparator was inappropriate and insufficient data were available to the PBAC to form a view about a comparison of quetiapine with lithium or paroxetine.
			Listing requested: <u>Authority Required (Streamlined)</u> Depressive episodes associated with bipolar disorder. Alternatively, if the PBAC was to recommend both quetiapine submissions to the November 2010 PBAC meeting, the sponsor proposed the following: <u>Authority Required (Streamlined)</u> Treatment of bipolar disorder	The PBAC did not consider the submission's proposal to list quetiapine with the simplified restriction "Treatment of bipolar disorder" to be appropriate as the evidence presented was limited to bipolar I disorder.
			Comparator: Olanzapine	Not accepted. Olanzapine is neither TGA registered nor PBS listed for the acute treatment of depressive episodes in bipolar disorder. The PBAC considered lithium in combination with an antidepressant as the most commonly prescribed treatment at present.

	prevention of relapse and maintenance of clinical improvement during continuation therapy. Treatment of recurrent major depressive disorder in patients who are intolerant of, or have an inadequate response to alternative therapies. Treatment of generalised anxiety disorder.		Clinical claim: Quetiapine is non-inferior to olanzapine. Quetiapine is more effective than placebo for treating bipolar depression in patients with both bipolar I and bipolar II.	Accepted. The PBAC had previously accepted non-inferiority with olanzapine, although clinical equivalence has only been demonstrated in bipolar I patients.
			Economic claim: Cost-utility	Not accepted. The PBAC considered the main comparator to be inappropriate.
			Sponsor's comments:	The sponsor had no comment.

DRUG AND FORM	TGA INDICATION	CURRENT PBS LISTING	LISTING REQUESTED BY SPONSOR	PBAC OUTCOME AND COMMENTS
Everolimus, tablets, 5 mg and 10 mg, Afinitor®, Novartis Pharmaceuticals Australia Pty Ltd Minor submission	Treatment of patients with advanced renal cell carcinoma after failure of treatment with sorafenib or sunitinib.	Not currently listed.		The PBAC rejected the submission on the basis of a high and uncertain cost-effectiveness ratio.
			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.	
			Comparator: Placebo	Accepted (as previously)
			Clinical claim: Everolimus has superior efficacy and inferior safety in metastatic renal cell carcinoma compared with placebo.	Partially accepted (as previously).
			Economic claim: Cost-effectiveness	Not accepted. The PBAC considered the magnitude of the clinical benefit in relation to survival is uncertain and that with plausible survival modelling, the ICER remains unacceptably high.
			Sponsor's comments:	Novartis is disappointed by this recommendation. Novartis remains committed to working with the PBAC to make everolimus available to

				patients with renal cell carcinoma, who have progressive disease.