JULY 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
Cilostazol, tablets 50 mg and 100 mg, Pletal® PharmaLink Pty Ltd Major submission	Symptomatic improvement of intermittent claudication as indicated by increased maximal and pain-free walking distances, in patients who do not have rest pain and who do not have evidence of peripheral tissue necrosis.	Not currently listed		The PBAC rejected the submission on the basis of uncertain clinical benefit and a high and uncertain cost-effectiveness ratio.
			Listing requested: <u>Authority Required</u> For the symptomatic improvement of intermittent claudication as indicated by increased maximal and pain-free walking distances, in patients who do not have rest pain and who do not have evidence of peripheral tissue necrosis. Patients who do not experience a clinical benefit after 12 weeks of treatment must stop therapy.	The PBAC considered that a stopping rule at 12 weeks was inappropriate, given that the submission and Pre-Sub-Committee Response acknowledged that "the maximal effect of cilostazol is not reached until 24 weeks (or beyond)".
			Comparator: Placebo	Accepted (as previously).
			Clinical Claim: Cilostazol is statistically significantly superior to placebo for all primary and secondary endpoints but is associated with greater toxicity.	Accepted (as previously). However, the PBAC considered that as cilostazol is intended to be an add-on therapy to standard medical management (including lipid lowering agents in many patients), the incremental benefit of cilostazol treatment that would be realised in the intended PBS population is uncertain. The PBAC also noted that cilostazol has increased toxicity when combined with anti-platelet therapy and with other drugs which inhibit CYP3A4 and CYP2C19.

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DRUG AND FORM	TGA INDICATION	CURRENT PBS LISTING	LISTING REQUESTED BY SPONSOR	PBAC OUTCOME AND COMMENTS
			Economic Claim: Cost-effectiveness	Not accepted. The incremental cost-effectiveness ratio remained high and uncertain. The PBAC considered that methodological and dataset issues precluded derivation of a meaningful quality adjusted life year (QALY) and that the attempted cost per QALY is not reliable or informative.
			Sponsor Comments:	The sponsor had no comment.
Esomeprazole magnesium trihydrate, tablet, (enteric coated), equivalent to 40 mg esomeprazole, Nexium®, AstraZeneca Pty Ltd Minor submission	Gastroesophageal reflux disease (GORD). Patients requiring nonsteroidal anti-inflammatory drug therapy. Prevention of rebleeding of gastric or duodenal ulcers following treatment with Nexium IV solution by intravenous infusion. Pathological hypersecretory conditions including Zollinger-Ellison syndrome and idiopathic hypersecretion. In combination with appropriate antibiotics.	<u>Restricted Benefit</u> Healing of gastro-oesophageal reflux disease. NOTE: No applications for increased maximum quantities and/or repeats will be authorised.		The PBAC rejected the submission's request to remove the words 'and/or repeats' from the NOTE for esomeprazole 40 mg tablets as the total cost implication to the PBS is highly uncertain and likely to be high and utilisation is uncertain.
			Listing requested: <u>Restricted Benefit</u> Healing of gastro-oesophageal reflux disease. NOTE: No applications for increased maximum quantities ~~and/or repeats~~ will be authorised.	
			Comparator: Lansoprazole, omeprazole, pantoprazole, rabeprazole	Accepted
			Clinical Claim: Not applicable	

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DRUG AND FORM	TGA INDICATION	CURRENT PBS LISTING	LISTING REQUESTED BY SPONSOR	PBAC OUTCOME AND COMMENTS
			Economic Claim: The submission estimated costs to the PBS and presented a comparison of the Dispensed Price for Maximum Quantity equivalent doses of esomeprazole, omeprazole, pantoprazole, rabeprazole and lansoprazole.	The PBAC agreed that a more comprehensive economic evaluation of the impact on the PBS in the short, medium and long term would allow a more considered judgement of the cost implications.
			Sponsor Comments:	The sponsor has no comment.
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.	Not currently listed for this indication.		The PBAC rejected the submission on the basis of uncertain clinical benefit and a high and uncertain cost-effectiveness ratio.
			Listing requested: <u>Authority Required</u> Initial and continuing treatment of Stage IV clear cell variant renal cell carcinoma in a patient with a WHO status of 2 or less who meets certain criteria.	
			Comparator: Placebo	Accepted (as previously)

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DRUG AND FORM	TGA INDICATION	CURRENT PBS LISTING	LISTING REQUESTED BY SPONSOR	PBAC OUTCOME AND COMMENTS
			Clinical Claim: Everolimus has superior efficacy and inferior safety in metastatic renal cell carcinoma compared with placebo.	Partially accepted. The PBAC considered there was uncertainty about a conclusion of superior efficacy in metastatic renal cell carcinoma with everolimus compared with placebo based on the benefit in terms of progression-free survival, when no benefit in terms of overall survival or quality of life was observed in RECORD-1. Based on the supporting data the claim for inferior safety was considered reasonable.
			Economic Claim: Cost-effectiveness	Not accepted. The PBAC noted that the economic model was very sensitive to changes in the assumed overall survival benefit of everolimus and the estimated ICERs were therefore highly uncertain.
			Sponsor Comments:	The sponsor had no comment.
Imatinib, tablets, 100 mg and 400 mg, (as mesylate), Glivec® Novartis Pharmaceuticals	Anti-cancer drug	Not currently listed for adjuvant treatment of gastrointestinal stromal tumour (GIST).		The PBAC rejected the submission on the basis of uncertain clinical benefit and an unacceptably high and uncertain cost-effectiveness ratio.

JULY 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
Australia Pty Ltd Major submission			Listing requested: Authority Required listing for the adjuvant treatment of an adult patient at high risk of recurrence following complete resection of primary gastrointestinal stromal tumour (GIST) which has been histologically confirmed by the detection of CD117 on immunohistochemical staining, at a dose not exceeding 400 mg/day for a period of 12 months.	The PBAC noted that although the restriction limits to 12 months based on the duration of treatment in Trial Z9001, the appropriate treatment length of treatment is still unknown.
			Comparator:	Accepted (as previously).
			Clinical Claim: Superior in terms of comparative efficacy over placebo.	Partially accepted. The PBAC noted that clinical trial demonstrated significantly increased recurrence-free survival with imatinib compared with placebo. However, the PBAC considered that recurrence-free survival may not be a valid surrogate for overall survival in GIST patients, and that until definitive data become available in 2015, considerable uncertainty will remain around the estimate of the comparative treatment effect for overall survival.
			Economic Claim: Cost-effectiveness	Not accepted. The incremental cost-effectiveness ratio remained unacceptably high and uncertain.
			Sponsor Comments:	The sponsor had no comment.

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DRUG AND FORM	TGA INDICATION	CURRENT PBS LISTING	LISTING REQUESTED BY SPONSOR	PBAC OUTCOME AND COMMENTS
Risedronate sodium, tablets, 5 mg and 30 mg, Actonel ®, 35 mg, Actonel Once-a Week®, 150 mg, Once-a-Month ®; Risedronate sodium and calcium carbonate, pack containing 4 tablets risedronate sodium 35 mg and 24 tablets calcium carbonate 1.25 g (equivalent to 500 mg calcium), Actonel Combi®; Risedronate sodium and calcium carbonate with colecalciferol, pack containing 4 tablets risedronate sodium 35 mg and 24 sachets containing granules of calcium carbonate 2.5 g (equivalent to 1 g calcium) with colecalciferol 22 micrograms, Actonel Combi D® Sanofi-Aventis Australia Pty Ltd Major submission	Treatment of osteoporosis; Treatment of glucocorticoid-induced osteoporosis; Preservation of bone mineral density in patients on long term corticosteroid therapy.	No change to the listing requested.		The PBAC reaffirmed its previous advice to the Minister that alendronate and its combinations and risedronate and its combinations should be treated as interchangeable on an individual patient basis in the treatment of osteoporosis, and reaffirmed its previous advice that alendronate, risedronate and tiludronate should be treated as interchangeable on an individual patient basis in the treatment of Paget disease of bone.
			Request the PBAC to re-consider its advice to the Minister that risedronate sodium and its combination formulations are interchangeable with alendronate and its combination formulations on an individual patient basis in the treatment of osteoporosis and in the treatment of Paget disease. An additional minor submission asserted that alendronate was associated with an increased risk of serious atrial fibrillations compared with risedronate.	
			Comparator: Alendronate	Accepted

			Clinical Claim: Due to the very significant scientific and clinical differences which have effects on efficacy (bone turnover markers, fracture, onset of fracture efficacy and speed of reversal effect) and safety (GI tolerability and ONJ) as well as strengths available and PBS listings, alendronate and risedronate cannot be considered to be interchangeable at the individual patient level.	Not accepted. The PBAC considered that the patient relevant outcomes are fractures and there are no supporting data that the differences either in bone turnover markers or BMD results in differences in fracture rate or risk. The PBAC considered there was no evidence for an advantage of risedronate over alendronate in the speed of onset of fracture reduction rate. The PBAC noted that there were no statistically significant differences between risedronate and alendronate in GI events in most of the studies presented including the FACTS head-to-head trials. The PBAC considered that there is no acceptable data which supports a lower risk of ONJ with risedronate. The PBAC considered that the meta-analysis presented did not provide evidence of a difference between alendronate and risedronate with respect to the incidence of atrial fibrillations. The PBAC also noted that the sponsor provided no new data in regard to Paget disease of bone.

			Economic Claim: Cost-effectiveness	Not accepted. The PBAC considered that in view of the overwhelming body of evidence which failed to show a clinical advantage in fracture reduction or tolerability of risedronate over alendronate there was no basis on which to support a cost effectiveness analysis and the original cost minimisation approach accepted by the PBAC was appropriate.
			Sponsor Comments:	Sanofi-aventis maintains that there are significant chemical, pharmacological and clinical differences between alendronate and risedronate which are taken into consideration by physicians when deciding which treatment is most suitable for an individual patient. We contend that these drugs are therefore not interchangeable on an individual patient basis.