MARCH 2012 PBAC MEETING OUTCOMES - "Subsequent" decisions not to recommend

DRUG AND FORM	TGA INDICATION	CURRENT PBS LISTING	LISTING REQUESTED BY SPONSOR	PBAC OUTCOME AND COMMENTS
Agomelatine, tablet, 25mg, Valdoxan® Servier Laboratories (Australia) Pty Ltd Major submission	Treatment of major depression in adults including prevention of relapse.	Not currently PBS listed.		The PBAC rejected the submission on the basis that superior clinical effectiveness and safety over serotonin selective reuptake inhibitors (SSRIs) had not been demonstrated. The PBAC further considered that non-inferior efficacy and superior safety to venlafaxine had not been demonstrated.
			Listing Requested: Restricted Benefit Major depressive disorders.	
			Comparator: Venlafaxine	Not accepted. The PBAC considered that the SSRIs are the more appropriate main comparators for agomelatine as agomelatine will be used in the first line treatment of depression.
			Clinical claim: Agomelatine is non-inferior in terms of comparative antidepressant efficacy, superior in terms of improving sleep and superior in terms of comparative safety compared to venlafaxine. Agomelatine is also superior in terms of comparative efficacy and superior in terms of comparative tolerability compared to SSRIs.	The PBAC reaffirmed that substantiation of a claim of non-inferiority to venlafaxine firstly requires demonstration of superiority over the SSRIs. However, the PBAC considered that the evidence provided in the submission was not sufficient to support the claim that agomelatine is superior in terms of comparative efficacy and safety to the SSRIs. Therefore, the PBAC considered that non-inferior efficacy and superior safety to venlafaxine had not been demonstrated.
			Economic claim: Cost minimisation versus venlafaxine.	As the cost minimisation analysis was based on the acceptance of non-inferior efficacy and safety of agomelatine to venlafaxine, the PBAC considered that the cost minimisation analysis was not supported by the clinical evidence presented in the re-submission.
			Sponsor's comments:	The sponsor disagrees with the decision and refers you to *www.servier.com.au* for further information.

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DRUG AND FORM	TGA INDICATION	CURRENT PBS LISTING	LISTING REQUESTED BY SPONSOR	PBAC OUTCOME AND COMMENTS
Ipilimumab, concentrate solution for I.V infusion, 50 mg in 10 mL, 200 mg in 40 mL, Yervoy® Bristol-Myers Squibb Australia Pty Ltd Major submission	As monotherapy, for the treatment of patients with unresectable or metastatic melanoma who have failed or are intolerant to prior therapy.	Not currently PBS listed.		The PBAC rejected the submission because of uncertain extent of clinical benefit, uncertain clinical place in therapy and high and uncertain cost effectiveness.
			Listing Requested: Section 100 (Highly Specialised Drugs Program) Private Hospital Authority Required Public Hospital Authority Required (STREAMLINED) Treatment of patients with unresectable stage III or stage IV malignant melanoma who have not responded to or were intolerant to prior systemic therapy for metastatic disease under certain circumstances.	
			Comparator: Dacarbazine and fotemustine	Accepted (as previously).
			Clinical claim: Ipilimumab 3 mg/kg is superior in efficacy to best supportive care (dacarbazine/fotemustine), and has a different safety profile.	The PBAC has previously considered that ipilimumab is inferior to best supportive care in terms of immune related adverse effects.
			Economic claim: Cost-effectiveness	The PBAC considered ipilimumab's cost-effectiveness to be high and uncertain, with uncertainty arising from the time horizon and the choice of utility weights used in the economic model.
			Sponsor's comments:	Bristol Myers Squibb is disappointed with the PBAC decision, but is committed to working with the PBAC to ensure that Yervoy is made available on the PBS for eligible Australian patients with unresectable metastatic melanoma

DRUG AND FORM	TGA INDICATION	CURRENT PBS LISTING	LISTING REQUESTED BY SPONSOR	PBAC OUTCOME AND COMMENTS
Naproxen with esomeprazole, tablet 500 mg -20 mg (as magnesium trihydrate), Vimovo® AstraZeneca Pty Ltd Major submission	Patients with an increased risk of gastrointestinal ulceration, who require NSAID therapy for symptomatic management of rheumatoid arthritis, ankylosing spondylitis and osteoarthritis with an inflammatory component and in whom lower doses of naproxen or other NSAIDs have proven insufficient. If a total daily dose of 1 gram naproxen is not required, Vimovo should not be used.	Not currently PBS listed.		The PBAC rejected the submission on the basis of an inappropriate comparator, uncertainty regarding the validity of the surrogate outcome for the purposes of demonstrating non-inferiority of more patient-relevant outcomes, and resultant uncertainty in the proposed cost-minimisation analysis.
			Listing Requested: <u>Restricted Benefit</u> Symptomatic treatment of osteoarthritis, rheumatoid arthritis or ankylosing spondylitis in a patient who requires a non-steroidal anti-inflammatory drug and is at high risk of developing gastrointestinal complications.	
			Comparator: Celecoxib	The PBAC considered that a mixed comparator of both meloxicam and celecoxib would be more appropriate than celecoxib alone.
			Clinical claim: Naproxen/esomperazole fixed dose combination (FDC) is non-inferior to celecoxib in terms of comparative effectiveness on all primary (pain and function) measures and non-inferior in a number of gastrointestinal safety and tolerability measures. Naproxen/esomeprazole FDC is superior to naproxen for the incidence of endoscopically detected ulcers.	The PBAC has previously accepted that naproxen/esomperazole FDC is non-inferior to celecoxib and naproxen in terms of comparative effectiveness on all primary (pain and function) measures. The PBAC did not consider that the evidence supported the claim that naproxen/esomeprazole FDC was superior to naproxen and non-inferior to celecoxib with respect to gastrointestinal toxicity using the surrogate outcome of endoscopically-detected ulcers.

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DRUG AND FORM	TGA INDICATION	CURRENT PBS LISTING	LISTING REQUESTED BY SPONSOR	PBAC OUTCOME AND COMMENTS
			Economic claim: Cost-minimisation	The PBAC considered there to be uncertainty in the proposed cost-minimisation analysis due to the uncertainty regarding the validity of the surrogate outcome (endoscopically-detected ulcers).
			Sponsor's comments:	AstraZeneca will continue to work with the PBAC to make Vimovo available on the PBS for people suffering from arthritis who are at increased gastrointestinal risk from NSAID therapy.

DRUG AND FORM	TGA INDICATION	CURRENT PBS LISTING	LISTING REQUESTED BY SPONSOR	PBAC OUTCOME AND COMMENTS
Tapentadol, tablet, 50 mg, 100 mg, 150 mg, 200 mg and 250 mg (as hydrochloride) (sustained release), Palexia SR® CSL Limited Major submission	The management of moderate to severe chronic pain un-responsive to non-narcotic analgesia. There is currently no clinical trial data available regarding the safety and efficacy of tapentadol SR in patients with pain due to malignancy.	Not currently PBS listed.		The PBAC rejected the submission because of uncertain clinical benefit, uncertain cost-effectiveness and hence uncertain basis for justifying the requested price.
			Listing Requested: <u>Restricted Benefit</u> Treatment of chronic severe disabling pain not responding to non-narcotic analgesics.	
			Comparator: Oxycodone controlled release (CR) as the main comparator and tramadol sustained release (SR) as the secondary comparator.	Accepted.
			Clinical claim: Tapentadol SR is equivalent in terms of comparative effectiveness and superior in terms of comparative safety (related to constipation and nausea/vomiting) to oxycodone CR. Tapentadol SR is non-inferior in terms of comparative effectiveness non-inferior in terms of comparative safety to tramadol SR.	The PBAC accepted (as previously) the clinical claim with respect to comparative effectiveness compared with oxycodone CR, however it did not accept the claim of superior safety due to uncertainty in the data provided regarding constipation severity. The claim of non-inferiority in terms of comparative effectiveness and safety compared with tramadol SR was accepted.
			Economic claim: Cost-effectiveness (compared to oxycodone CR). Cost-minimisation (compared to tramadol SR).	The PBAC considered tapendatol's cost-effectiveness compared to oxycodone CR to be uncertain. The PBAC also considered the cost-minimisation comparison with tramadol SR to be uncertain due to the way the equi-effective dose ratio was estimated.

DRUG AND FORM	TGA INDICATION	CURRENT PBS LISTING	LISTING REQUESTED BY SPONSOR	PBAC OUTCOME AND COMMENTS
			Sponsor's comments:	CSL disagrees with the PBAC's decision, but is committed to working with the PBAC to ensure tapentadol SR is available for patients with chronic severe disabling pain not responding to non-narcotic analgesics.

DRUG AND FORM	TGA INDICATION	CURRENT PBS LISTING	LISTING REQUESTED BY SPONSOR	PBAC OUTCOME AND COMMENTS
Velaglucerase alfa, powder for I.V. infusion, 400 units in 4 mL, Vpriv® Shire Australia Pty Limited Minor submission	Long-term enzyme replacement therapy for paediatric and adult patients with Type 1 Gaucher disease associated with at least one of the following clinical manifestations: anaemia, thrombocytopaenia, hepato-splenomegaly.	Not currently PBS listed.		The PBAC considered that velaglucerase alfa was clinically effective but failed to meet the required cost effectiveness criteria for listing on the Pharmaceutical Benefits Scheme (PBS). However, the PBAC considered that velaglucerase alfa meets all the criteria for inclusion on the Life Saving Drugs Program (LSDP), and recommended that it is suitable for the Government to consider for inclusion on the LSDP.
			Listing Requested: Life Saving Drugs Program (LSDP) Treatment of Type 1 Gaucher disease in a patient who meets certain criteria.	*Comment: To be considered for the LSDP, the drug must have been accepted by the PBAC as clinically effective, but rejected for PBS listing because it failed to meet the required cost effectiveness criteria.*
			Comparator: Imiglucerase.	Accepted (as previously).
			Clinical claim: Velaglucerase is non-inferior in terms of comparative effectiveness and equivalent in terms of comparative safety compared to imiglucerase.	Accepted (as previously).
			Economic claim: Cost-minimisation.	Accepted.
			Sponsor's comments:	Shire Australia welcomes the PBAC decision that Velaglucerase alfa has met all the criteria for inclusion on the Life Saving Drugs Program (LSDP). Shire looks forward to working with the LSDP to ensure that Velaglucerase alfa is made available to eligible Gaucher Disease patients in Australia as soon as possible.