

JULY 2015 PBAC OUTCOMES – 1ST TIME DECISIONS NOT TO RECOMMEND

DRUG NAME, FORM(S), STRENGTH(S), SPONSOR, TYPE OF SUBMISSION	DRUG TYPE AND USE	LISTING REQUESTED BY SPONSOR / PURPOSE OF SUBMISSION	PBAC OUTCOME
<p>CARGLUMIC ACID</p> <p>200 mg dispersible tablet, 5 200 mg dispersible tablet, 60</p> <p>CARBAGLU®</p> <p>Emerge Health</p> <p>New listing</p> <p>(Major Submission)</p>	Hyperammonaemia	<p>Authority Required listing for the treatment of hyperammonaemia due to organic acidaemias including isovaleric acidaemia, methylmalonic acidaemia and propionic acidaemia.</p>	<p>The PBAC rejected the request to list carginic acid on the PBS for the treatment of hyperammonaemia on the basis that it considered that the PBS was not the appropriate mechanism for dispensing carginic acid. The Australian Society for Inborn Errors of Metabolism advised that carginic acid has only been used in the setting of hospital admission, and considered that the provision of carginic acid to neonates and older children would constitute routine care provided by hospitals in the context of acute decompensation episodes. In this regard, the PBAC considered that there was no unmet clinical need to be addressed through listing carginic acid on the PBS.</p>
		<p align="center">Sponsor Comment:</p>	<p>The sponsor had no comment.</p>
<p>ELIGLUSTAT</p> <p>eliglustat tartrate 100 mg hard capsule (equivalent to 84 mg eliglustat), 56</p> <p>CERDELGA®</p> <p>Sanofi-aventis (Genzyme)</p> <p>New listing</p> <p>(Major Submission)</p>	Gaucher Disease	<p>Section 100 (Highly Specialised Drugs Program) Authority Required listing for the treatment of Gaucher Disease Type 1.</p>	<p>The PBAC rejected the request to list eliglustat on the PBS for the treatment of Gaucher Disease type 1 on the basis that the results of the direct randomised trial (ENCORE) suggested inferiority, and that clinically important inferiority could not be excluded with confidence.</p>
		<p align="center">Sponsor Comment:</p>	<p>Genzyme firmly believes that Cerdelga provides significant clinical benefits through proven efficacy and safety for patients with Gaucher disease. This is the result of the largest Gaucher program ever developed with approvals in the United States, Europe and Japan. Genzyme is committed to bringing Cerdelga to patients around the world, where it is already the third most prescribed Gaucher treatment, and will explore ways to work with the Department of Health to make this important TGA-approved therapy available to Australian patients.</p>

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<p>FENTANYL CITRATE (BUCCAL)</p> <p>100 microgram tablet: buccal, 4 and 28 200 microgram tablet: buccal, 4 and 28 400 microgram tablet: buccal, 4 and 28 600 microgram tablet: buccal, 4 and 28 800 microgram tablet: buccal, 4 and 28</p> <p>FENTORA®</p> <p>Teva Pharma Australia Pty Ltd</p> <p>New listing</p> <p>(Major Submission)</p>	<p>Breakthrough pain</p>	<p>Authority Required (Palliative Care Schedule) listing for the treatment of breakthrough cancer pain.</p> <p align="center">Sponsor Comment:</p>	<p>The PBAC did not recommend the listing of fentanyl citrate buccal tablets for the treatment of breakthrough pain in patients undergoing palliative care for cancer. The PBAC considered that the submission had not adequately addressed other immediate-release opioids as an appropriate comparator. Further, the PBAC did not consider that the submission's utilisation estimates were reliable, and was concerned that no strategy was proposed by the sponsor to mitigate this risk.</p> <p>The Sponsor will work with the PBAC to resolve the outstanding matters and looks forward to bringing this treatment option to Australian patients.</p>
<p>IBRUTINIB</p> <p>140 mg capsules, 90</p> <p>IMBRUVICA®</p> <p>Janssen Cilag Pty Ltd</p> <p>New listing</p> <p>(Major Submission)</p>	<p>Chronic lymphocytic leukaemia (CLL) and small lymphocytic lymphoma (SLL)</p>	<p>Authority Required (STREAMLINED) listing for the treatment of relapsed or refractory CLL and relapsed or refractory SLL.</p>	<p>The PBAC did not recommend the listing of ibrutinib for the treatment of relapsed or refractory CLL and SLL. In making its recommendation, the PBAC considered that the patient population and clinical place of ibrutinib were not adequately defined, the size of the comparative clinical benefit could not be quantified and the cost effectiveness and financial implications were underestimated and unacceptably high.</p> <p>The submission requested PBS listing for ibrutinib therapy for patients with relapsed or refractory CLL or SLL and who were considered unsuitable for treatment or retreatment with a purine analogue.</p> <p>In regards to the submission, the PBAC:</p> <ul style="list-style-type: none"> noted that the TGA-approved indication for ibrutinib did not restrict use

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			<p>to patients unsuitable for re-treatment with a purine analogue and also recommended use in first-line patients with CLL with 17p deletion and mantle cell lymphoma. Usage of ibrutinib beyond restriction was a possibility.</p> <ul style="list-style-type: none"> considered that ibrutinib is an effective treatment, but the increased effect over the treatment that would be replaced in Australia was difficult to quantify but may be smaller than proposed in the submission. <p>considered that submission could not establish the cost effectiveness of the treatment at the sponsor's requested price.</p>
		Sponsor Comment:	<p>Although disappointed that the PBAC were unable to recommend ibrutinib in the requested setting, Janssen are committed to working with the Department and PBAC in order to ensure timely access to ibrutinib. Janssen believe there is an unmet clinical need for an effective and well tolerated treatment for relapsed or refractory CLL and SLL patients who are unsuitable for treatment or retreatment with a purine analogue.</p>
<p>MANNITOL</p> <p>powder for inhalation, 40 mg capsules, 280</p> <p>BRONCHITOL®</p> <p>Pharmaxis Ltd</p> <p>Change to listing</p> <p>(Minor Submission)</p>	Cystic fibrosis	Amendment of the PBS restriction to consolidate the wording and to enable use in combination with dornase alfa.	<p>The PBAC did not recommend amending the current listing of dry powder inhaler (DPI) mannitol to permit the combination use of DPI mannitol with dornase alfa on the basis of unproven cost-effectiveness. However, the PBAC did recommend some amendments to simplify the listing of DPI mannitol.</p>
		Sponsor Comment:	<p>Pharmaxis is disappointed that the PBAC could not recommend a change to amend the Bronchitol listing to bring it in line with best clinical practice. Pharmaxis welcomes the PBAC's recommendation of simplification of the current wording and will continue to look at ways to amend the current listing to enable Bronchitol to be used in addition to best supportive care for appropriate patients.</p>
<p>NITISINONE</p> <p>2 mg capsule, 60</p> <p>5 mg capsule, 60</p> <p>10 mg capsule, 60</p> <p>ORFADIN®</p>	Tyrosinaemia	Re-submission for section 100 (Highly Specialised Drugs Program) Authority Required listing for the treatment of hereditary tyrosinaemia type 1 (HT-1).	<p>The PBAC rejected the request to list nitisinone on the PBS for the treatment of HT-1 on the basis of an uncertain and unacceptably highestimate of cost effectiveness.</p> <p>The PBAC noted the clinical need for nitisinone for the treatment of HT-1 and that patients are currently being treated with the drug through hospitals.</p>

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<p>A. Menarini Australia Pty Ltd</p> <p>New listing</p> <p>(Minor Submission)</p>		<p align="center">Sponsor Comment:</p>	<p>The PBAC considered that treatment with nitisinone plus diet therapy is superior in terms of comparative effectiveness and inferior in terms of comparative safety compared with diet alone.</p> <p>The PBAC noted that adverse events that may be associated with treatment with nitisinone for HT-1 include eye disorders, haematological events and developmental and cognitive disorders. The relationship of these events to nitisinone treatment is unknown. The PBAC considered that neuropsychological assessments of patients being treated with nitisinone over time were important and should be implemented in a systematic fashion.</p> <p>The PBAC considered that the cost per quality adjusted life year gained was uncertain and unacceptably high due to the high cost of the drug, weight based dosing and the impact of newborn screening practices on the estimates of comparative effectiveness.</p> <p>A.Menarini Australia Pty Ltd is committed to partnering with the department to find a solution to allow nitisinone to be reimbursed for patients with tyrosinaemia type 1.</p>
<p>NIVOLUMAB</p> <p>nivolumab concentrate solution for infusion, 10 mg/mL, 1 x 4 mL vial, concentrate solution for infusion, 10 mg/mL, 1 x 10 mL vial, concentrate solution for infusion</p> <p>OPDIVO®</p> <p>Bristol Myers Squibb</p>	<p>Melanoma</p>	<p>Section 100 (Efficient Funding of Chemotherapy – Public and Private Hospital) Authority Required listing for the treatment of unresectable Stage III or Stage IV malignant melanoma.</p>	<p>The PBAC decided not to recommend nivolumab for the treatment of unresectable or metastatic (Stage III or IV) melanoma. In reaching this conclusion, the PBAC did not accept that ipilimumab, as presented in the submission, was the appropriate comparator. The PBAC considered that pembrolizumab was the appropriate comparator for the treatment of unresectable or metastatic (Stage III or IV) melanoma.</p> <p>The PBAC also considered that, for the main comparison of nivolumab and ipilimumab, the extent of superior comparative effectiveness and safety had not been adequately established by the submission and, due to several issues with the economic model, the resulting ICER was highly uncertain. For the preliminary comparison of nivolumab and pembrolizumab, the limited information provided did not support a recommendation to list nivolumab as an alternative to pembrolizumab.</p>

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New Listing (Major Submission)		Sponsor Comment:	The sponsor continues to work with the PBAC to ensure nivolumab is available to Australian patients via the PBS in the earliest possible timeframe.
<p>SITAGLIPTIN SITAGLIPTIN and METFORMIN SITAGLIPTIN and METFORMIN XR</p> <p>sitagliptin 100 mg tablet, 28 sitagliptin 50 mg tablet, 28 sitagliptin 25 mg tablet, 28</p> <p>sitagliptin 50 mg + metformin hydrochloride 1000 mg tablet, 56 sitagliptin 50 mg + metformin hydrochloride 850 mg tablet, 56 sitagliptin 50 mg + metformin hydrochloride 500 mg tablet, 56</p> <p>sitagliptin 100 mg + metformin hydrochloride 1000 mg tablet: modified release, 28 sitagliptin 50 mg + metformin hydrochloride 1000 mg tablet: modified release, 56</p> <p>JANUVIA®</p>	Type 2 diabetes mellitus (in combination with insulin)	<p>Authority Required (STREAMLINED) listing for use in combination with insulin in patients with type 2 diabetes mellitus (T2DM).</p> <p>Sponsor Comment:</p>	<p>The PBAC rejected the request to list sitagliptin, sitagliptin+metformin and sitagliptin+metformin XR in combination with insulin for T2DM on the PBS. In making its recommendation, the PBAC considered that the clinical need and place of therapy were not well defined and the clinical effectiveness (in terms of reduction in mean daily insulin dose) was uncertain. In particular, the PBAC noted that the addition of sitagliptin to insulin regimens (±metformin) resulted in an increased mean daily insulin dose.</p> <p>MSD respectfully believes that the PBAC has misinterpreted the trial results in reaching this recommendation. Sitagliptin reduces relative insulin use in patients treated to target with insulin, and delivers better glycaemic outcomes, less hypoglycaemia and less weight gain compared to up-titrating insulin alone. MSD will clarify this in a minor submission to the PBAC.</p>

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<p>JANUMET® JANUMET XR®</p> <p>Merck Sharp & Dohme (Australia) Pty Limited</p> <p>Change to listing (Major Submission)</p>			
<p>TIOTROPIUM BROMIDE</p> <p>tiotropium 2.5 microgram inhalation: solution for, 60 actuations</p> <p>SPIRIVA® RESPIMAT®</p> <p>Boehringer Ingelheim Pty Limited</p> <p>Change to recommended listing (Major Submission)</p>	<p>Asthma</p>	<p>Restricted Benefit listing for the treatment of severe asthma.</p>	<p>The PBAC did not recommend the listing of tiotropium bromide as add-on therapy for the treatment of severe uncontrolled asthma. In making its recommendation, the PBAC considered that the economic model was not reliable and the true cost-effectiveness of tiotropium bromide in this setting was probably high and highly uncertain.</p> <p>The PBAC noted the comments from The Lung Foundation and The Centre of Research Excellence in Severe Asthma and agreed that there is a need for additional treatments for severe uncontrolled asthma.</p> <p>The PBAC was concerned that tiotropium bromide could be used beyond the restriction to treat people with less severe asthma than what was supported by the clinical evidence and in which cost-effectiveness was not tested.</p> <p>On the basis the combined analysis of the head to head trials, the comparison of tiotropium bromide and placebo resulted in:</p> <ul style="list-style-type: none"> • Approximately a 100 mL reduction in trough FEV1 over a median duration of follow-up of exposure of 24 weeks. • Approximately 56 days difference in time until at least 25% of patients experienced a severe exacerbation with a 48 week follow up. • Approximately 134 days difference in time without an exacerbation (any severity) for 50% of the patients with a 48 week follow-up. <p>On the basis of direct comparison evidence presented by the submission, for every 100 patients treated with tiotropium bromide in comparison to</p>

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			placebo with a 48 week follow-up: <ul style="list-style-type: none"> • Approximately 13 fewer patients would have had an exacerbation (any severity) • Approximately 8 fewer patients would have had a respiratory, thoracic or mediastinal disorder.