

NOVEMBER 2015 PBAC OUTCOMES - DEFERRALS

DRUG NAME, FORM(S), STRENGTH(S), SPONSOR, TYPE OF SUBMISSION	DRUG TYPE AND USE	LISTING REQUESTED BY SPONSOR / PURPOSE OF SUBMISSION	PBAC OUTCOME
<p>AMINO ACID FORMULA with VITAMINS, MINERALS and LONG CHAIN POLYUNSATURATED FATTY ACIDS without PHENYLALANINE oral liquid, 20 x 500 mL</p> <p>PKU Baby</p> <p>Orpharma Pty Ltd</p> <p>New listing</p> <p>(Minor Submission)</p>	<p>Medicinal food</p>	<p>To request a Restricted Benefit listing for phenylketonuria.</p> <p>Sponsor comment:</p>	<p>The PBAC noted that the Nutritional Products Working Party (NPWP) deferred its consideration of the submission until further information could be provided by the Sponsor. The PBAC therefore deferred its recommendation until further advice could be provided by the NPWP on this submission in view of the additional information received from the sponsor.</p> <p>Orpharma will continue to work with the PBAC to achieve listing of PKU Baby.</p>
<p>AMINO ACID FORMULA with VITAMINS and MINERALS without PHENYLALANINE oral liquid: powder for, 30 x 20 g sachets</p> <p>PKU Go</p> <p>Orpharma Pty Ltd</p> <p>New listing</p> <p>(Minor Submission)</p>	<p>Medicinal food</p>	<p>To request a Restricted Benefit listing for phenylketonuria.</p> <p>Sponsor comment:</p>	<p>The PBAC noted that the Nutritional Products Working Party (NPWP) deferred its consideration of the submission until further information could be provided. The PBAC therefore deferred its recommendation until further advice could be provided by the NPWP on this submission in view of the additional information received from the sponsor.</p> <p>Orpharma will continue to work with the PBAC to achieve listing of PKU Go.</p>
<p>IBRUTINIB 140 mg capsules, 90</p> <p>Imbruvica</p> <p>Janssen Cilag Pty Ltd</p>	<p>Chronic lymphocytic leukaemia and small lymphocytic lymphoma</p>	<p>Re-submission to request Authority Required (STREAMLINED) listing for the treatment of relapsed or refractory chronic lymphocytic leukaemia and relapsed or</p>	<p>The PBAC deferred making a recommendation to list ibrutinib as an Authority Required (TELEPHONE) listing for the second-line treatment of chronic lymphocytic leukaemia (CLL) and small lymphocytic lymphoma (SLL).</p> <p>The PBAC noted that the requested restriction for second-line use in</p>

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<p>New listing (Minor Submission)</p>		<p>refractory small lymphocytic lymphoma.</p>	<p>patients unsuitable for treatment with fludarabine was narrower than the registered indications for ibrutinib. The PBAC considered that there was a potential for use in patients able to be treated with fludarabine and in the other registered indications including as first-line treatment for patients with 17p deletion and for patients with mantle cell lymphoma.</p> <p>The PBAC acknowledged that ibrutinib is an effective treatment for CLL and SLL based on the results of the RESONATE trial. However, the PBAC considered that the comparative clinical effectiveness of ibrutinib was overestimated in this trial as the comparator, ofatumumab monotherapy, is less effective than treatments used in clinical practice within Australia.</p> <p>The resubmission presented a revised economic evaluation with survival adjusted for patients crossing over from the comparator arm to ibrutinib in the RESONATE trial. The PBAC did not accept the revised survival results adjusted using the rank preserving structural failure time (RPSFT) methodology. The PBAC considered that the use of the RPSFT method was not valid for this resubmission because a key assumption of a common treatment effect was not met. As ofatumumab is an active treatment, there were difficulties interpreting the results in this resubmission because the RPSFT method relies on estimating effects during “on treatment” and “off treatment” time periods. That is, as treatment with ofatumumab results in a survival gain, those patients crossing over from ofatumumab treatment to ibrutinib will have a different survival outcome compared to those patients who are randomised to ibrutinib.</p> <p>The PBAC did not consider that ibrutinib was cost-effective at the price proposed in the resubmission. The PBAC recommended that the economic evaluation should be revised to obtain an ICER in the range of \$45,000 to \$75,000 per QALY with the modelling based on the survival results from the intention-to-treat (ITT) population in the RESONATE trial and a ten-year time horizon. The PBAC also considered that the approach in the resubmission to adjust the incremental effectiveness to account for the differences in the efficacy of the comparator arm in the trial compared to treatments used in Australian practice was appropriate.</p>

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		Sponsor comment:	Janssen is pleased to note that the PBAC agree that ibrutinib is a safe and effective treatment for CLL and SLL. However, Janssen is disappointed by the PBAC's decision to defer its decision and is working with the PBAC on how best to account for cross-over in the trial to help make ibrutinib available on the PBS as soon as possible. The substantial proportion of ofatumumab randomised patients who crossed-over to receive ibrutinib contribute to a biased estimate (underestimate) of the comparative efficacy of ibrutinib. Consequently, not addressing this issue biases against the cost-effectiveness analysis of ibrutinib.
IDELALISIB 100 mg tablet, 60 150 mg tablet, 60 Zydelig Gilead Sciences Pty Ltd New listing (Major Submission)	Follicular lymphoma	Re-submission to request Authority Required (STREAMLINED) listing for the treatment of relapsed/refractory follicular lymphoma that has progressed despite prior treatment with rituximab and an alkylating agent	The PBAC deferred its decision for the Authority Required listing of idelalisib for the treatment of follicular lymphoma because idelalisib was not considered to be cost-effective at the price proposed. Given that no further data is likely to become available to inform this consideration, the PBAC deferred the submission to enable the Department to negotiate a reduced price. The PBAC wished to see the results of its request for a price reduction to an otherwise accepted sensitivity analysis of the economic evaluation.
		Sponsor comment:	Gilead looks forward to working with the Department to make idelalisib available to patients for the treatment of follicular lymphoma
IDELALISIB 100 mg tablet, 60 150 mg tablet, 60 Zydelig Gilead Sciences Pty Ltd New listing (Major Submission)	Chronic lymphocytic leukaemia	Re-submission to request Authority Required (STREAMLINED) listing for the treatment chronic lymphocytic leukaemia in patients with progressive disease despite previous treatment.	The PBAC deferred its decision for the Authority Required listing of idelalisib in combination with rituximab for the second-line treatment of relapsed chronic lymphocytic leukaemia (CLL) and small lymphocytic leukaemia (SLL) in patients who are unfit for chemotherapy as idelalisib was not considered to be cost-effective at the price proposed. The PBAC therefore considered that the submission should be deferred to enable the Department to negotiate a reduced price, adopting a pragmatic approach that would reduce the ICER to a more appropriate range.
		Sponsor comment:	Gilead looks forward to working with the Department to make idelalisib available to patients for the treatment of chronic lymphocytic leukemia

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<p>LENALIDOMIDE 5 mg capsule 10 mg capsule 15 mg capsule 25 mg capsule</p> <p>Revlimid</p> <p>Celgene Pty Ltd</p> <p>Change to listing (Major Submission)</p>	<p>Multiple myeloma</p>	<p>To request extension to Section 100 HSD Authority Required listing of lenalidomide to include use in the treatment of patients with symptomatic multiple myeloma who are ineligible for stem cell transplant.</p> <p>Sponsor comment:</p>	<p>The PBAC acknowledged there is a high clinical need for oral therapies in the treatment of multiple myeloma (MM). However, the PBAC deferred making a recommendation for the submission seeking to list lenalidomide in combination with dexamethasone (Rd) as first line therapy for patients who are newly diagnosed with multiple myeloma (NDMM) due to the appropriate comparators, the inclusion of many favourable assumptions to Rd in the presented model and a highly uncertain and high ICER for the requested treatment setting.</p> <p>Celgene will work with the Department to address concerns raised in the evaluation.</p>
<p>LENVATINIB</p> <p>4 mg capsule, 30 10 mg capsule, 30</p> <p>Lenvima®</p> <p>Eisai Australia</p> <p>New listing (Major submission)</p>	<p>Stage III or IV differentiated thyroid cancer</p>	<p>The submission requested Section 85 Authority Required listing for lenvatinib for treatment of radioactive iodine refractory differentiated thyroid cancer stage III or IV.</p>	<p>The PBAC deferred the submission for lenvatinib for the treatment of radioactive iodine refractory differentiated thyroid carcinoma (RAI-R DTC) pending further discussion with the sponsor regarding the eligible patient population, price, and finalisation of the TGA registration process. The PBAC considered that lenvatinib was not cost-effective at the price presented in the submission.</p> <p>On the basis of the direct randomised trial, the comparison of lenvatinib and placebo resulted in:</p> <ul style="list-style-type: none"> • an approximate difference in median progression-free survival of 14.7 months • no statistically significant difference in overall survival for the ITT population. This result may have been affected by the early termination and crossover observed in the trial. <p>On the basis of an indirect comparison using placebo as the common reference, the comparison of lenvatinib and sorafenib resulted in:</p> <ul style="list-style-type: none"> • an approximate difference in median progression-free survival of 11.8 months (based on median PFS with lenvatinib and HR for indirect comparison) • no statistically significant difference in overall survival. <p>On the basis of direct randomised evidence versus placebo, for every 100</p>

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			<p>patients treated:</p> <ul style="list-style-type: none"> • approximately 27 additional patients on lenvatinib are likely to experience serious adverse events; whereas approximately 11 additional patients on sorafenib are likely to experience serious adverse events • approximately 39 additional patients on lenvatinib are likely to experience hypertension of at least Grade 3 severity; whereas approximately 7 additional patients on sorafenib are likely to experience hypertension of at least Grade 3 severity • approximately 3 additional patients on lenvatinib are likely to experience a hand-foot skin reaction of at least Grade 3 severity; whereas approximately 20 additional patients on sorafenib are likely to experience a hand-foot skin reaction of at least Grade 3 severity.
		Sponsor comment:	Eisai is continuing to work with the PBAC to make lenvatinib available for Australian patients with advanced thyroid cancer
<p>NINTEDANIB 100 mg capsule, 60 150 mg capsule, 60</p> <p>Ofev</p> <p>Boehringer Ingelheim Pty Ltd</p> <p>New listing</p> <p>(Major Submission)</p>	Idiopathic pulmonary fibrosis	Re-submission to request an Authority Required listing for the treatment of idiopathic pulmonary fibrosis.	<p>The PBAC deferred the decision to recommend nintedanib for PBS listing for IPF subject to a lower revised ICER, incorporating a continuation rule and a price reduction.</p> <p>The PBAC recognised the high clinical need for an effective treatment for IPF and the significant debilitating effects of the disease on quality of life, as noted in the consumer comments received for this item.</p> <p>The PBAC noted the resubmission presented the same three head-to-head randomised trials comparing nintedanib to placebo as in the March 2015 submission: Trial 30 (n=432), Trial 32 (n=515) and Trial 34 (n=551). On the basis of a meta-analysis of this direct evidence versus placebo, nintedanib was associated with:</p> <ul style="list-style-type: none"> • Approximately a 118.89 mL/year reduction in the annual rate of decline in FVC. • Approximately a 3.31% reduction in absolute decline in forced vital capacity percent predicted (FVC%Pred) from baseline to week 52. • Approximately a 65% reduction in the risk of independently adjudicated acute IPF exacerbations over 52 weeks, but no significant difference in

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			<p>investigator-reported acute IPF exacerbations.</p> <ul style="list-style-type: none"> • No significant difference in disease specific quality of life. • Insufficient evidence to support a significant difference in OS. <p>On the basis of direct evidence presented by the submission, for every 100 patients treated with nintedanib in comparison to placebo:</p> <ul style="list-style-type: none"> • Approximately 43 additional patients would have diarrhoea over 52 week duration of follow-up. • Approximately 9 additional patients would have vomiting over 52 week duration of follow-up. • Approximately 4 fewer patients would have dyspnoea over 52 week duration of follow-up.
		Sponsor comment:	The sponsor had no comment.
<p>SORAFENIB 200 mg tablet, 60</p> <p>Nexavar</p> <p>Bayer Australia Ltd</p> <p>Change to listing</p> <p>(Major Submission)</p>	Differentiated thyroid cancer	Re-submission to request an Authority Required (STREAMLINED) listing for the treatment of locally advanced or metastatic, radioactive iodine refractory differentiated thyroid cancer (RAI-R DTC).	<p>The PBAC deferred its decision on sorafenib for the treatment of locally advanced or metastatic RAI-R DTC as the re-submission had not provided a reliable estimate of the cost-effectiveness of sorafenib in this setting, and wished to see the results of its preferred re-specifications for the base case of the economic model. The PBAC considered, as previously, that the clinical data did not adequately demonstrate a statistically significant gain in OS and therefore the life-years gained of 9.12 months estimated by the modelled economic evaluation was implausibly large.</p> <p>On the basis of direct randomised evidence presented by the submission, for patients treated with sorafenib in comparison to placebo plus best supportive care, there would be:</p> <ul style="list-style-type: none"> • an approximate difference in median progression-free survival of 5 months • an unknown possible difference in median overall survival. <p>For every 100 patients treated with sorafenib in comparison to placebo plus best supportive care:</p> <ul style="list-style-type: none"> • approximately 38 additional patients would experience at least one treatment-emergent adverse event of Grade 3 or greater severity over a period of 10 – 12 months of treatment with sorafenib (compared to 8 – 9 months of observation in the placebo plus best supportive care arm) • approximately 20 additional patients would experience a hand-foot skin

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			<p>reaction of at least Grade 3 severity over a period of 10 – 12 months of treatment with sorafenib (compared to 8 – 9 months of observation in the placebo plus best supportive care arm)</p> <ul style="list-style-type: none"> • approximately 7 additional patients would experience hypertension of at least Grade 3 severity over a period of 10 – 12 months of treatment with sorafenib (compared to 8 – 9 months of observation in the placebo plus best supportive care arm).
		Sponsor comment:	Bayer is disappointed regarding the deferral outcome, however will continue to work with the PBAC and the Department of Health to bring access to this innovative therapy for an area of high unmet clinical need.
<p>TRIGLYCERIDES MEDIUM CHAIN oral liquid, 12 x 500 mL pouches</p> <p>Peptamen Junior Liquid Peptamen Junior Advance</p> <p>Nestlé Health Science (Nestlé Australia Ltd)</p> <p>New listing</p> <p>(Minor Submission)</p>	Medicinal food	<p>To request a Restricted Benefit listing for dietary management of conditions requiring a source of medium chain triglycerides limited to fat malabsorption due to liver disease, short gut syndrome, cystic fibrosis and gastrointestinal disorders.</p>	<p>The PBAC noted that the Nutritional Products Working Party (NPWP) deferred its consideration of the submission until further information could be provided by the Sponsor. The PBAC therefore deferred its recommendation until further advice could be provided by the NPWP on this submission in view of the additional information received from the sponsor.</p>
		Sponsor comment:	<p>Nestle Health Science has provided the relevant information requested by the Nutritional Products Working Party (NPWP) and looks forward to the PBAC's consideration of the submission in March 2016.</p>