

NOVEMBER 2017 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 |
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| <p>AMINO ACID FORMULA WITH VITAMINS, MINERALS AND LONG CHAIN POLYUNSATURATED FATTY ACIDS, WITHOUT PHENYLALANINE</p> <p>Oral powder 400 g (PKU Start)</p> <p>PKU Start®</p> <p>Vitaflo Australia Pty Ltd</p> <p>New listing (Minor Submission)</p> | <p>Phenylketonuria</p> | <p>To request a Restricted Benefit listing for the dietary management of patients with phenylketonuria.</p> | <p>The PBAC deferred making a decision on the listing of PKU Start® for the dietary management of Phenylketonuria (PKU) noting that the product provides only 70% of iron requirements for infants aged 7-12 months. The PBAC noted that the sponsor attempted to address this issue in the pre-PBAC response and considered it would be appropriate to seek advice from the PBAC's Nutritional Products Working Party, regarding the matters raised in the response, prior to making its decision.</p> |
| | | <p align="center">Sponsor Comment:</p> | <p>The Sponsor had no comment.</p> |
| <p>APREMILAST</p> <p>Tablet 30 mg Pack containing 4 tablets of 10 mg , 4 tablets of 20 mg and 19 tablets of 30 mg</p> <p>Otezla®</p> <p>Celgene Pty Ltd</p> <p>New listing (Major Submission)</p> | <p>Moderate to severe plaque psoriasis</p> | <p>Resubmission to request a Restricted Benefit listing for treatment of patients with moderate to severe plaque psoriasis.</p> | <p>The PBAC deferred making a recommendation on whether apremilast should be listed on the PBS for the treatment of moderate to severe plaque psoriasis in adults to allow further discussion and modelling to establish a price that could be considered cost effective. The PBAC noted the input received from individuals and health professionals and acknowledged that there was a consumer need for an alternative therapy for psoriasis.</p> <p>In making this decision, the PBAC considered that the monitoring and adverse event cost offsets presented in the submission, which gave apremilast a significant price advantage over cyclosporin, were considerably overestimated. Further, the committee considered there was significant uncertainty in the apremilast utilisation estimates presented. Overall, the PBAC considered that apremilast was not cost-effective at the requested price.</p> <p>Based on the uncertainty in the clinical data available to show that apremilast is not of inferior efficacy to cyclosporin, but taking into account the reduced toxicity of apremilast compared to cyclosporin and the requirement for less monitoring, the PBAC advised the sponsor of a price premium for apremilast that would be likely be acceptably cost-effective for the purposes of the <i>National Health Act 1953</i>.</p> |
| | | <p align="center">Sponsor Comment:</p> | <p>The Sponsor had no comment.</p> |

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| <p>ARGININE</p> <p>Tablet 500 mg</p> <p>Arginine Easy®</p> <p>Orpharma Pty Ltd</p> <p>New listing (Minor Submission)</p> | | <p>Urea cycle disorders (UCD)</p> | <p>The PBAC deferred making a decision on the listing of Arginine Easy® for the dietary management of urea cycle disorders. The PBAC noted there was a lack of clinical justification for the higher amount of protein equivalent in one tablet of Arginine Easy® compared with one sachet of Arginine 500® (0.4 g). The PBAC considered that the higher amount of protein may be detrimental to patients on highly restrictive protein diets. The PBAC also noted that the product may come under the definition of a therapeutic good in the <i>Therapeutic Goods Act 1989</i> and may therefore be required to be registered with the TGA rather than as a food that has medical purposes under <i>The Australia New Zealand Food Standards Code — Standard 2.9.5: Food for Special Medical Purposes..</i> The PBAC noted that the sponsor attempted to address these issues in the pre-PBAC response and considered it would be appropriate to seek advice from the PBAC’s Nutritional Products Working Party, regarding matters raised in the response, prior to making its decision.</p> |
| | | <p align="center">Sponsor Comment:</p> | <p>The Sponsor will continue to work with the PBAC and the Nutritional Products Working Party to address the matters raised in the pre-PBAC advice.</p> |
| <p>BARICITINIB</p> <p>Tablet 2 mg Tablet 4 mg</p> <p>Olumiant®</p> <p>Eli Lilly Australia Pty Ltd</p> <p>New listing (Major Submission)</p> | <p>Severe active rheumatoid arthritis</p> | <p>To request an Authority Required listing for the treatment of severe active rheumatoid arthritis under certain conditions.</p> | <p>The PBAC deferred its discussion of this item pending the receipt of the TGA delegate’s overview, in the context of concerns about the safety profile of baricitinib, particularly in relation to serious adverse events.</p> |
| | | <p align="center">Sponsor Comment:</p> | <p>Eli Lilly looks forward to working with the PBAC and Department to enable access to OLUMIANT for patients with severe active rheumatoid arthritis once a positive outcome from the TGA is known.</p> |

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| <p>CRIZOTINIB</p> <p>Capsule 200 mg</p> <p>Capsule 250 mg</p> <p>Xalkori®</p> <p>Pfizer Australia Pty Ltd</p> <p>Change to listing (Major Submission)</p> | <p>Stage IIIB (locally advanced) or Stage IV (metastatic) non-small cell lung cancer (NSCLC) with a ROS1 gene rearrangement confirmed by fluorescent in situ hybridisation (FISH) testing</p> | <p>To request an Authority Required listing for the treatment of patients with Stage IIIB (locally advanced) or Stage IV (metastatic) NSCLC with a ROS1 gene rearrangement confirmed by FISH testing, in patients who have failed at least one treatment with platinum-based chemotherapy.</p> | <p>The PBAC deferred its decision about whether to recommend listing crizotinib for the treatment of ROS1-positive non-small cell lung cancer (NSCLC), requesting that the sponsor develop an appropriate pricing strategy in response to the Committee's concerns. In deciding to defer, the PBAC noted that the codependent test for ROS1 mutations would be considered by the Medical Benefits Advisory Committee (MSAC) in late November 2017. The PBAC acknowledged that there is a high unmet clinical need in the small proposed population, and advised that crizotinib's effectiveness and safety profile in the ROS1-positive NSCLC population was similar to that in the ALK-positive NSCLC population, for which it is already PBS listed.</p> |
| | | <p align="center">Sponsor Comment:</p> | <p>The Sponsor is committed to working with the PBAC and the Department of Health to make crizotinib available for the treatment of advanced ROS1-positive non-small cell lung cancer; a rare disease with high unmet clinical need.</p> |

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| <p>EVOLOCUMAB</p> <p>Injection 420 mg in 3.5 mL single use pre-filled cartridge Injection 140 mg in 1 mL single use pre-filled pen</p> <p>Repatha®</p> <p>Amgen Australia Pty Ltd</p> <p>Change to listing (Major Submission)</p> | <p>Familial hypercholesterolaemia (FH)/ hypercholesterolaemia with symptomatic atherosclerotic cardiovascular disease (ASCVD) who do not have underlying FH</p> | <p>Resubmission to request an Authority Required listing for treatment of patients with FH and patients with non-familial hypercholesterolaemia who have symptomatic ASCVD.</p> | <p>The PBAC deferred its decision as to whether to make a recommendation to extend the PBS listing of evolocumab for patients with familial hypercholesterolaemia in order to for its residual concerns with the economic model to be addressed. The PBAC acknowledged the positive cardiovascular outcomes data from the FOURIER trial addressed previous PBAC concerns regarding the lack of cardiovascular (CV) event data for evolocumab. The PBAC also noted that, while the trial did not demonstrate a reduction in mortality with evolocumab compared to placebo, the effect on all other cardiovascular outcomes was robust and consistent with the extensive body of knowledge of the benefits of LDL-c lowering. However, the PBAC noted that any benefits on mortality would not be realised immediately and the economic model needed to reflect this. The PBAC also felt that the definition of statin intolerance in the proposed PBS listing should be revised to ensure that evolocumab is used in the most appropriate population.</p> <p>The PBAC did not recommend the listing of evolocumab for patients with non-familial hypercholesterolaemia with atherosclerotic disease on the basis of a high incremental cost effectiveness ratio (ICER) and high and uncertain patient population numbers. The PBAC considered this population required more refined eligibility criteria in the proposed PBS listing given the very high financial estimates. The PBAC also considered use of the CV outcomes data from the FOURIER trial would better inform the economic model.</p> |
| | | <p align="center">Sponsor Comment:</p> | <p>Amgen is pleased that the PBAC has acknowledged the positive cardiovascular outcomes achieved in the FOURIER trial. Patients with familial hypercholesterolaemia are at very high CV risk and require access to effective therapy to achieve meaningful reductions in LDL-C. Amgen intends to work with PBAC to adjust the economic model to address the residual concerns as an immediate priority with the aim to extend the current PBS listing to include these patients. Amgen will continue to work with PBAC towards achieving reimbursement for all patients in whom there is a clinical need.</p> |

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| <p>LANREOTIDE</p> <p>Injection 120 mg (as acetate) in single dose pre-filled syringe</p> <p>Somatuline® Autogel®</p> <p>Ipsen Pty Ltd</p> <p>Change to listing (Minor Submission)</p> | <p>Non-functional gastroentero-pancreatic neuroendocrine tumours (GEP-NETs)</p> | <p>Resubmission to request a Section 100 (Highly Specialised Drugs Program) Authority Required (STREAMLINED) listing for the treatment of non-functional GEP-NETs in adult patients with un-resectable locally advanced or metastatic disease.</p> | <p>The PBAC deferred its decision on listing lanreotide on the PBS for the treatment of non-functional GEP-NETs on the basis that the cost-effectiveness of the proposed listing was uncertain. The PBAC advised that further negotiations between the Department and sponsor would be required to establish a price of lanreotide and Risk Sharing Arrangement which would adequately offset the uncertainty around cost-effectiveness.</p> <p>While the PBAC noted that the submission had not provided a new economic model to address its previous concerns regarding the applied post-disease progression treatment sequences, costs and durations, it considered that a substantial price reduction in conjunction with a Risk Sharing Arrangement would be adequate to address the uncertainty around cost-effectiveness.</p> |
| | | <p align="center">Sponsor Comment:</p> | <p>The Sponsor had no comment.</p> |

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| <p>PEMBROLIZUMAB</p> <p>Powder for injection 50 mg Solution concentrate for I.V. infusion 100 mg in 4 mL</p> <p>Keytruda®</p> <p>Merck Sharp & Dohme (Australia) Pty Ltd</p> <p>Change to listing (Major Submission)</p> | <p>First-line treatment of patients with metastatic non-small cell lung cancer (NSCLC)</p> | <p>Resubmission to request a Section 100 (Efficient Funding of Chemotherapy) Authority Required (STREAMLINED) listing as first line monotherapy in patients expressing PD-L1 for NSCLC.</p> | <p>The PBAC deferred its decision as to whether to make a recommendation to list pembrolizumab for the first-line treatment of patients with metastatic (Stage IV) NSCLC, who do not have an activating epidermal growth factor receptor (<i>EGFR</i>) gene mutation or an anaplastic lymphoma kinase (<i>ALK</i>) gene rearrangement in tumour material, and whose tumours express high levels of programmed cell death ligand 1 (PD-L1), defined as a tumour proportion score (TPS) of $\geq 50\%$. In deciding to defer its decision, the PBAC advised that a further price reduction would be required for acceptable cost-effectiveness once necessary changes are made to the economic model, and that negotiations with the sponsor are required to determine the best approach for a Risk Sharing Agreement (RSA) in the context of the existing RSA for nivolumab which is PBS listed for NSCLC. The PBAC also noted that updated advice is needed from the Medical Advisory Services Committee (MSAC, meeting in late November 2017) in relation to the codependent the PD-L1 test. The PBAC advised that, if MSAC subsequently decided to support the MBS listing for PD-L1, it would support the listing of pembrolizumab according to the circumstances supported by MSAC, once the PBAC's other concerns were resolved.</p> <p>The PBAC agreed with the submission's nomination of platinum-based doublet chemotherapy as the main comparator for pembrolizumab in the proposed population. However, the PBAC also considered that pembrolizumab may displace rather than replace platinum-based doublet chemotherapy use.</p> <p>The PBAC considered that the claims of superior comparative effectiveness (in terms of both progression-free survival and overall survival) and superior comparative safety were both reasonable.</p> <p>The PBAC considered the key issues with the economic model was the approach taken to extrapolate from the trial data, and the extent of cost offsets estimated for second-line nivolumab.</p> |

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| | | Sponsor Comment: | MSD is disappointed that access to Keytruda has not yet been achieved for 1L NSCLC patients in Australia. MSD will continue to work with the Department to make this therapy available as soon as possible, so that Australian patients have comparable access to innovative NSCLC therapies as patients in other countries. |
| Evaluation of Post market review Salbutamol Terbutaline Ipratropium Beclomethasone Fluticasone Budesonide Ciclesonide Sodium cromoglycate Nedocromil sodium Montelukast Salmeterol Eformoterol Fluticasone with Salmeterol Fluticasone with Eformoterol Fluticasone with Vilanterol Budesonide with Eformoterol Oral glucocorticoids, plain (all listed brands) | Asthma | To consider the findings from the evaluation of the 2014 Post market review of PBS medicines used to treat asthma in children. | The PBAC deferred consideration of this item until a later date. |