

MARCH 2016 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>ADALIMUMAB 40 mg/0.8 mL injection, 2 x 0.8 mL cartridges 40 mg/0.8 mL injection, 2 x 0.8 mL syringes 40 mg/0.8 mL injection, 6 x 0.8 mL cartridges 40 mg/0.8 mL injection, 6 x 0.8 mL syringes</p> <p>Humira®</p> <p>Abbvie Pty Ltd</p> <p>Change to listing (Major Submission)</p>	<p>Hidradenitis suppurativa</p>	<p>Authority Required listing for the treatment of moderate to severe hidradenitis suppurativa.</p>	<p>The PBAC decided not to recommend adalimumab for PBS listing for moderate to severe hidradenitis suppurativa (HS) on the basis that the cost-effectiveness of ongoing treatment with adalimumab was unknown. The submission was based on three head-to-head trials comparing adalimumab to placebo and the primary outcome was hidradenitis suppurativa clinical response (HiSCR) which was defined as a greater than or equal to 50% decrease from baseline in inflammatory abscesses and nodules and no increase in the numbers of abscesses or draining fistulae. The PBAC noted that the pooled result from all three trials indicated that for every 100 patients treated with adalimumab in comparison to placebo, approximately 29 additional patients would have achieved HiSCR over a maximum duration of exposure of 12 weeks.</p> <p>The PBAC considered that the claim of superior comparative effectiveness was adequately supported by the data for the first 12 weeks of treatment. However, the PBAC noted that there was limited comparative data and no clear evidence of a clinically meaningful maintenance of efficacy beyond 12 weeks of therapy. The PBAC considered that the claim of inferior comparative safety was reasonable.</p> <p>The PBAC was concerned the some assumptions and modelling used in the economic analysis were not appropriate to allow the PBAC to assess the cost-effectiveness of adalimumab for use on the PBS for this patient population.</p>
		<p>Sponsor Comment:</p>	<p>AbbVie welcomes the PBAC recognition of the high unmet need and benefits of adalimumab in patients with moderate to severe HS and will continue to work with the PBAC to ensure access to patients in need.</p>

MARCH 2016 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>ADRENALINE 300 microgram/0.3 mL injection, 1 x 0.3 mL syringe 150 microgram/0.3 mL injection, 1 x 0.3 mL syringe</p> <p>EpiPen® EpiPen® Jr.</p> <p>Alphapharm Pty Limited</p> <p>Change to listing (Minor Submission)</p>	<p>Anaphylaxis</p>	<p>To request inclusion on the Prescriber Bag (Emergency Drug Supply) for the treatment of anaphylaxis</p>	<p>The PBAC decided not to recommend the listing of auto-injector adrenaline (EpiPen® and EpiPen® Jr) on the Prescriber Bag section of the PBS. This was on the basis of an unacceptably high cost (at the price requested by the sponsor) compared with the comparator, adrenaline ampoule, and a lack of evidence to support the clinical claim of superior ease of administration and decreased risk of overdosing.</p> <p>The PBAC noted that no clinical trials were presented in the submission, which relied upon supportive correspondence provided by Allergy & Anaphylaxis Australia and the Australasian Society of Clinical Immunology and Allergy.</p> <p>The PBAC considered that the claim of superior ease and timeliness of administration and decreased risk of overdosing compared with adrenaline ampoule to justify a price premium over the comparator was not supported by the evidence provided in the submission.</p> <p>The PBAC noted that the current Approved Ex-Manufacturer Price for EpiPen and EpiPen Jr is approximately forty times greater than the currently listed adrenaline ampoule, and considered that the listing of the auto-injector form would result in a significant cost to the PBS.</p>
		<p>Sponsor Comment:</p>	<p>The incidence of anaphylaxis is growing and the success of first line treatment with adrenaline is inextricably linked with how soon it is administered. It is disappointing that in spite of the strong support of both the representative association of clinicians treating anaphylaxis (ASCIA) and the association representing patients and carers dealing with anaphylaxis (Allergy and Anaphylaxis Australia), the PBAC has rejected this application that would make it more likely that adrenaline would be administered sooner in the case of anaphylaxis. It is regrettable that the imperative of cost is paramount to that of superior patient health care outcomes.</p>

MARCH 2016 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>CETUXIMAB 100 mg/20 mL injection, 1 x 20 mL vial 500 mg/100 mL injection, 1 x 100 mL vial</p> <p>Erbix®</p> <p>Merck Serono Australia Pty Ltd</p> <p>Change to listing (Major Submission)</p>	<p>Recurrent and/or metastatic squamous cell carcinoma of the head and neck</p>	<p>Section 100 (Efficient Funding of Chemotherapy) Authority Required (STREAMLINED) listing for use in combination with platinum-based chemotherapy for the treatment of recurrent and/or metastatic squamous cell carcinoma of the head and neck.</p>	<p>The PBAC decided not to recommend the listing of cetuximab in combination with platinum-based chemotherapy, for the treatment of patients with metastatic and/or recurrent squamous cell carcinoma (SCC) of the oral cavity (SCCOC), on the basis of uncertain magnitude of clinical benefit and likely high and unacceptable cost-effectiveness at the price proposed by the sponsor. The PBAC noted that the TGA-registered indication for cetuximab included a broader listing of all patients with metastatic and/or recurrent SCC of the head and neck (SSCHN). Patients with SCCOC are a subgroup of patients with SSCHN. The clinical evidence provided to the PBAC was a randomised controlled trial of patients with SSCHN and a post hoc subgroup analysis of patients with SCCOC.</p> <p>On the basis of direct evidence presented by the submission in the intention to treat trial population (SCCHN), the comparison of cetuximab plus chemotherapy versus chemotherapy alone resulted in:</p> <ul style="list-style-type: none"> • Approximately 2.7 months difference in median overall survival; and • Approximately 2.3 months difference in median progression-free survival. <p>On the basis of direct evidence presented by the submission, for every 100 patients treated with cetuximab plus chemotherapy in comparison to chemotherapy alone in the intention to treat trial population (SCCHN);</p> <ul style="list-style-type: none"> • Approximately 16 additional patients would have a complete or partial response for at least 4 weeks over a median duration of follow-up of approximately 18.7 months; • Approximately 62 additional patients would experience skin reaction(s) over a median duration of follow-up of approximately 18.7 months; • Approximately 9 additional patients would experience Grade 3 or 4 skin reaction(s) over a median duration of follow-up of approximately 18.7 months; and • Approximately 4 additional sepsis events (including septic shock) over a median duration of follow-up of approximately 18.7 months.
		<p align="center">Sponsor Comment:</p>	<p>The sponsor had no comment</p>

MARCH 2016 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>DENOSUMAB 120 mg/1.7 mL injection, 1 x 1.7 mL vial</p> <p>Xgeva®</p> <p>Amgen Australia Pty Ltd</p> <p>Change to listing</p> <p>(Major Submission)</p>	<p>Hypercalcaemia of malignancy</p>	<p>Authority Required (STREAMLINED) listing for the treatment of hypercalcaemia of malignancy which is refractory to intravenous biphosphonate therapy.</p>	<p>The PBAC did not recommend the PBS listing of denosumab for hypercalcaemia of malignancy on the basis of that the submission's clinical data did not support the claim of superior efficacy, relative to bisphosphonates, and the lack of a clear clinical place for denosumab.</p> <p>The PBAC noted the submission's claim of superior efficacy and non-inferior safety was based on an indirect comparison between a single-arm denosumab observational study and a pooled subgroup analysis of zoledronic acid 8 mg retreatment from two randomised controlled trials.</p> <p>The PBAC considered that the clinical place for denosumab had not been clearly defined, particularly in the context of refractory and relapsed patients. The PBAC considered that although the low quality clinical data suggested that denosumab was likely to be effective, there was substantial uncertainty regarding comparative efficacy and safety relative to bisphosphonates, and did not form an adequate basis to support the clinical claim of superior efficacy. Furthermore, the PBAC considered that the values selected for use in the economic model were not justified as the data did not support superior efficacy for denosumab over zoledronic acid, an assumption on which the modelling based.</p> <p>The PBAC noted that no further head to head trials of denosumab and zoledronic acid were planned. In this context the PBAC considered that a future major submission should include a cost-minimisation analysis between denosumab and bisphosphonates.</p>
		<p>Sponsor Comment:</p>	<p>Amgen is disappointed with the PBACs decision as we believe there is a clinical need for alternative treatments for hypercalcaemia of malignancy that is refractory to bisphosphonate therapy.</p>

MARCH 2016 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>ECULIZUMAB 300 mg/30 mL injection, 1 x 30 mL vial</p> <p>Soliris®</p> <p>Alexion Pharmaceuticals Australasia Pty Ltd</p> <p>Change to recommended listing</p> <p>(Other Submission)</p>	<p>atypical Haemolytic Uraemic Syndrome (aHUS) following kidney transplantation</p>	<p>To provide the PBAC with updated data regarding the use of eculizumab in the context on renal transplant.</p>	<p>The PBAC did not recommend the request to extend the current listing for eculizumab for atypical haemolytic uraemic syndrome (aHUS) to include use in a renal transplant setting. The PBAC noted that the submission provided sparse data in support of the use of eculizumab in a renal transplant setting. No comparative data were available to determine the relative effectiveness of eculizumab compared with supportive care.</p> <p>The PBAC considered that in the context of a condition of the rarity of aHUS the clinical data demonstrated that eculizumab is effective when used at the time of renal allograft. However, the PBAC also considered that the clinical data provided did not permit a confident estimate of the magnitude of the additional benefit over supportive care (ongoing dialysis), prophylactic use versus treatment should recurrence occur, and long-term use versus short term use.</p> <p>With regard to the number of patient numbers, the PBAC noted the submission's projections of the number of additional patients per year accessing eculizumab in a peri-transplant setting. The Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) reported 7 patients whose primary renal disease leading to ESRD was haemolytic uraemic syndrome (table 1.13, 38th Annual ANZDATA Report 2015), although the report did not distinguish typical HUS from atypical HUS.</p> <p>The PBAC also noted a published study using the ANZDATA registry investigating the characteristics and outcomes of patients receiving renal replacement therapy for ESRD secondary to HUS (Tang, et al 2012, BMJ Nephrology, 13:164). This study identified 241 patients in Australia and New Zealand between 1963 and 2010 who had ESRD secondary to HUS. A more contemporary cohort from the 15-year period from 1996 to 2010 identified 148 patients with ESRD secondary to HUS.</p> <p>The PBAC considered that, in light of the natural history and prognosis of atypical HUS, it would be reasonable to conclude that most or all HUS cases leading to ESRD would be the atypical form of the disease. The PBAC therefore did not consider that the submission's estimate of the</p>

MARCH 2016 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>number of additional patients per year was reasonable or adequately justified.</p> <p>With regard to the transplantation rate, the PBAC noted that the risk of graft loss due to aHUS recurrence following allografting represented a contraindication to transplant in many circumstances. The PBAC considered it possible that the availability of eculizumab for aHUS patients in ESRD would contribute to a higher transplantation rate than estimated in the submission.</p> <p>The PBAC noted that there is no consensus on the ideal duration of treatment following transplant among treating clinicians. The PBAC considered that clarifying the appropriate duration of treatment was an important element in any future resubmission of eculizumab for this indication.</p> <p>The PBAC requested that the Department engage with clinical stakeholders to clarify the likely number of patients who would use eculizumab in a renal transplant setting, and to determine the most appropriate duration of treatment following transplant.</p> <p>The PBAC noted the submission's request for pre-approval of eculizumab at the time a patient is activated on the deceased kidney donor list or once a living kidney donor transplantation is scheduled. The PBAC considered that responsibility for subsidising eculizumab during hospital inpatient treatment would be a matter for the treating hospital. The PBAC noted that PBS subsidy would commence once a patient is discharged from hospital and once PBS eligibility is established as defined by the restriction criteria.</p> <p>The PBAC noted the submission's request for sustained treatment with eculizumab following transplant. The PBAC considered that the submission had not established an evidence base for ongoing treatment for patients following transplant. The PBAC considered that following consultation with clinical experts about treatment duration, patients who experience a recurrence of aHUS will be able to access PBS-subsidised eculizumab</p>

MARCH 2016 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>under the existing restrictions.</p> <p>The PBAC noted the United Kingdom's Renal Association Guidelines, which specify that treatment with eculizumab should continue unless withdrawn with close monitoring as part of a clinical study. The PBAC noted that eligibility for PBS subsidy could not be made available in the context of a clinical study. However, the PBAC considered that in view of the lack of ongoing research into withdrawal of eculizumab treatment, the concept did bear some merit under the circumstances.</p>
		Sponsor Comment:	<p>While Alexion is disappointed with the PBAC's recommendation not to extend the current listing for eculizumab for aHUS, Alexion notes the PBAC's acknowledgement that the clinical data demonstrates that eculizumab is effective for aHUS when used at the time of renal allograft. The PBAC also acknowledges in its commentary that the risk of graft loss due to aHUS recurrence following allograft represents a contraindication to transplant and restricts patients' opportunity for transplantation. Alexion therefore intends to continue to engage with the PBAC and the clinical and patient communities to address the issues raised and to assist in securing much needed access to eculizumab for aHUS patients in the renal transplant setting where no treatment alternative exists.</p>

MARCH 2016 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>GONADOTROPHIN gonadotrophin-menopausal human 600 units injection [1 vial] (&) inert substance diluent [1 mL syringe], 1 pack</p> <p>Menopur®</p> <p>Ferring Pharmaceuticals Pty Ltd</p> <p>Change to Listing</p> <p>(Major Submission)</p>	<p>Anovulatory infertility</p>	<p>Restricted benefit listing for anovulatory infertility.</p> <p>Sponsor Comment:</p>	<p>The PBAC decided not to recommend that the PBS listing for human menopausal gonadotrophin (hMG) be extended to include treatment of anovulatory infertility. In making its recommendation, the PBAC considered that the evidence presented in the submission did not adequately support a claim of having same clinical effect as the comparator, follitropin alfa. The PBAC further considered that extending the current listing of human menopausal gonadotrophin would not address any unmet clinical need.</p> <p>The submission was based on one head-to-head trial comparing highly purified hMG to follitropin alfa.</p> <p>Ferring is disappointed with the outcome and will continue to work constructively with the PBAC towards the listing of MENOPUR for patients with anovulatory infertility.</p>
<p>LENVATINIB</p> <p>4 mg capsule, 30</p> <p>10 mg capsule, 30</p> <p>Lenvima®</p> <p>Eisai Australia Pty Ltd</p> <p>New listing</p> <p>(Minor Submission)</p>	<p>Differentiated thyroid cancer</p>	<p>Re-submission for Authority Required listing for the treatment of radioactive iodine refractory differentiated thyroid cancer (RR-DTC)</p> <p>Sponsor Comment:</p>	<p>The PBAC decided not to recommend lenvatinib for the treatment of radioactive iodine refractory differentiated thyroid carcinoma (RAI-R DTC) on the basis that the incremental cost-effectiveness ratio (ICER) was too high at the price requested and the eligible population was sub-optimally defined. The PBAC recalled that it had deferred a submission for lenvatinib in November 2015 and advised an ICER range where lenvatinib would be considered cost-effective, however the resubmission did not meet the PBAC's request.</p> <p>The sponsor had no comment</p>

MARCH 2016 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>LUMACAFITOR + IVACAFITOR lumacaftor 200 mg + ivacaftor 125 mg tablet, 4 x 28</p> <p>Orkambi®</p> <p>Vertex Pharmaceuticals (Australia) Pty Ltd</p> <p>New listing</p> <p>(Major Submission)</p>	<p>Cystic Fibrosis</p>	<p>Authority Required listing for the treatment of cystic fibrosis in patients aged 12 years and older who are homozygous for the F508del mutation in the CFTR gene.</p>	<p>The PBAC decided to not recommend lumacaftor with ivacaftor for PBS listing based on an unacceptably high and uncertain incremental cost-effectiveness ratio at the requested price by the sponsor, and uncertainty around the impact of ivacaftor/lumacaftor on long-term improvements in lung function and survival.</p> <p>The PBAC recognised the potential clinical value of lumacaftor/ivacaftor in the treatment of cystic fibrosis in patients aged 12 years or older who are homozygous for the F508deletion mutation (F508del/ F508del).</p> <p>The PBAC acknowledged the many consumer comments received in relation to the submission, both from people living with the condition and on behalf of patients and their carers. The PBAC also acknowledged the correspondence from the Thoracic Society of Australia and New Zealand, and Cystic Fibrosis Australia (and state based equivalents). In addition, representatives of the PBAC met with Cystic Fibrosis Australia prior to the PBAC meeting to discuss the clinical place, benefits and side effects of lumacaftor/ivacaftor for the requested patient population. The Committee recognised the strong support for subsidised access to lumacaftor/ivacaftor.</p> <p>The PBAC noted that, based on two head-to-head trials comparing lumacaftor/ivacaftor to placebo, lumacaftor/ivacaftor resulted in a 2.81% increase in absolute ppFEV1 over a median duration of follow-up of 24 weeks. The PBAC considered that it was uncertain whether this observed improvement in ppFEV1 represented a clinically significant difference, noting that this was considerably smaller than the improvement of 10.58% demonstrated for ivacaftor monotherapy.</p> <p>The PBAC noted the statistically significant reductions in the number of pulmonary exacerbations (including exacerbations requiring hospitalisation and/or intravenous antibiotics) and statistically significant improvement in weight gain, associated with treatment with lumacaftor/ivacaftor through to week 24. However, the PBAC noted that there was no statistically significant difference in the quality of life measure (CFQ-R). Furthermore, the PBAC considered that the extrapolation of short-term results to longer</p>

MARCH 2016 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>term efficacy was uncertain.</p> <p>The PBAC considered that, at the requested price, the requested listing for lumacaftor/ivacaftor was not sufficiently cost-effective to enable PBAC recommendation for PBS listing. Additionally, the PBAC considered that the estimated incremental cost-effectiveness ratio per quality-adjusted life year (QALY) was likely to be underestimated. The PBAC considered that, given the more modest clinical benefit, the price of lumacaftor/ivacaftor was too high to result in acceptable cost-effectiveness, even if it was recommended in conjunction with risk-sharing and pay-for-performance arrangements.</p> <p>The PBAC noted that the net cost of lumacaftor/ivacaftor to government was more than \$100 million in each of the first five years of listing.</p>
		Sponsor Comment:	The sponsor had no comment

MARCH 2016 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>MEPOLIZUMAB 100 mg/10 mL vial, powder for injection, 1</p> <p>Nucala®</p> <p>GlaxoSmithKline Australia Pty Ltd</p> <p>New listing</p> <p>(Major Submission)</p>	<p>Severe eosinophilic asthma</p>	<p>Section 100 (Highly Specialised Drugs Program) Authority Required listing for the treatment of severe eosinophilic asthma.</p>	<p>The PBAC did not recommend the listing of mepolizumab on the basis of high and uncertain cost-effectiveness in the comparison with standard of care (SOC), at the price proposed by the sponsor, and inappropriate equi-effective doses proposed in the cost-minimisation analysis against omalizumab.</p> <p>The PBAC accepted that mepolizumab had a clinical place in the treatment of eosinophilic asthma, noting advice received from the Thoracic Society of Australia and New Zealand clarifying that there is sufficient distinction to allow recognition and application of different therapies to this distinct type of asthma.</p> <p>The clinical evidence provided in the submission included 3 randomised controlled trials of mepolizumab against placebo and an indirect comparison against 3 randomised controlled trials of omalizumab against placebo.</p> <p>The PBAC considered that several assumptions and inputs into the economic model highly favoured mepolizumab versus SOC. The PBAC noted that when errors in the model were corrected during the consideration of the submission, the incremental cost-effectiveness ratio was \$45,000 – \$75,000/QALY.</p> <p>The PBAC did not agree with the submission’s method of estimating the equi-effective doses for mepolizumab and omalizumab, which derived the omalizumab dose from utilisation data rather than using the trial based doses.</p> <p>On the basis of the direct comparison evidence presented by the submission, for every 100 patients treated with mepolizumab in comparison to standard of care:</p> <ul style="list-style-type: none"> • Approximately 22 fewer patients would have a clinically significant exacerbation over a maximum duration of exposure of 32 weeks. • There are no differences in adverse events.

MARCH 2016 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
		Sponsor Comment:	GSK is disappointed with the outcome and is reviewing the PBAC recommendation to inform a resubmission. GSK is committed to working with the PBAC and the Department to ensure severe asthma patients can gain the benefit of mepolizumab through the PBS.

MARCH 2016 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>METHOTREXATE solution for injection, 7.5 mg/0.15 mL solution for injection, 10 mg/0.2 mL solution for injection, 15 mg/0.3 mL solution for injection, 20 mg/0.4 mL solution for injection, 25 mg/0.5 mL</p> <p>Trexject®</p> <p>Link Medical Products Pty Ltd</p> <p>New listing</p> <p>(Minor Submission)</p>	<p>Rheumatoid arthritis or psoriasis</p>	<p>Restricted Benefit listing for the treatment of rheumatoid arthritis or psoriasis for use in patients where the oral tablet form of methotrexate is unsuitable.</p>	<p>The PBAC did not recommend the PBS listing of methotrexate pre-filled syringe for the treatment of rheumatoid arthritis or psoriasis when methotrexate oral tablets are unsuitable. The PBAC considered that while a clinical need existed for pre-filled syringes, uncertainty remained around key inputs into the cost-minimisation analysis.</p> <p>The PBAC noted that the submission's claim of bioequivalence was based on a bioequivalence study and an observational study. Based on this evidence, the PBAC accepted that the pre-filled syringe subcutaneous injection was bioequivalent to the intramuscular injection. The PBAC also noted that there may be potential safety concerns with self-administration of injectable methotrexate outside the clinic setting.</p> <p>The PBAC considered that the estimated proportion of patients who would self-inject may be overestimated and considered that a future submission would need to provide clarity around the proportion of patients likely to self-administer with the associated decrease in GP visits, and should also address the health and safety concerns associated with self-administration. The PBAC also considered that a risk share arrangement would be needed to mitigate the costs to government in the context of leakage to unrequested indications. PBAC considered that the outstanding data requests could only be met in the form of a Major submission to the PBAC.</p>

MARCH 2016 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
		Sponsor Comment:	<p>Link Medical Products Pty Ltd (Link) is disappointed with the PBAC outcome. Link is committed to providing access for patients to this much needed clinical alternative where no current TGA-approved alternatives exist.</p> <p>The product is designed for self-administration and this is reflected in the TGA-approved Product Information.</p> <p>Link have launched a patient support initiative D.Y.T.A. (Dispose of your Trexject Appropriately) and is featured in health care professionals (HCP) and patient's education materials to support safe disposal of used Trexject syringes. Link offers a complimentary cytotoxic sharps container to patients who are prescribed Trexject.</p> <p>Link will continue to work with interested HCP to better understand the role of Trexject in the Australian clinical setting.</p>

MARCH 2016 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>NIVOLUMAB 40mg in 4ml (10mg/mL concentrate for IV infusion) 100mg in 10mL (10mg/mL concentrate for IV infusion)</p> <p>Opdivo®</p> <p>Bristol-Myers Squibb Australia Pty Ltd</p> <p>New listing (Major Submission)</p>	<p>Squamous non-small cell lung cancer</p>	<p>Section 100 (Efficient Funding of Chemotherapy) Authority Required (STREAMLINED) listing for the treatment of locally advanced or metastatic squamous non-small cell lung cancer with progression on or after prior chemotherapy.</p>	<p>The PBAC decided not to recommend that nivolumab be listed in the PBS for the treatment of squamous non-small cell lung cancer (NSCLC) on the basis that acceptable cost-effectiveness had not been adequately demonstrated. The PBAC considered that the economic model presented in the submission included numerous assumptions that favoured nivolumab, and that the resulting incremental cost-effectiveness ratio, in the range of \$45,000 – \$75,000 per quality-adjusted life-year gained, was too high at the price proposed in the submission and likely to be significantly underestimated.</p> <p>The submission was based on one open-label head-to-head randomised controlled trial comparing nivolumab with docetaxel in previously treated patients with locally advanced or metastatic squamous NSCLC.</p> <p>On the basis of the direct evidence presented by the submission, for every 100 squamous NSCLC patients treated with nivolumab in comparison to docetaxel:</p> <ul style="list-style-type: none"> • Approximately 15 additional patients would be expected to be alive at 18 months. There was a 3.2 month difference in median overall survival time favouring patients treated with nivolumab over those treated with docetaxel; • Approximately 17 fewer patients would experience a drug-related Grade 3 or 4 serious adverse event and 29 fewer patients would experience drug-related Grade ≥3 neutropenia, but 5 more patients would experience endocrine-related adverse events.
		<p>Sponsor comment</p>	<p>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>

MARCH 2016 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>NIVOLUMAB 40mg in 4ml (10mg/mL concentrate for IV infusion) 100mg in 10mL (10mg/mL concentrate for IV infusion)</p> <p>Opdivo®</p> <p>Bristol-Myers Squibb Australia Pty Ltd</p> <p>New listing (Major Submission)</p>	<p>Non-squamous non-small cell lung cancer</p>	<p>Section 100 (Efficient Funding of Chemotherapy) Authority Required (STREAMLINED) listing for the treatment of locally advanced or metastatic non-squamous non-small cell lung cancer with progression on or after prior chemotherapy.</p>	<p>The PBAC decided not to recommend that nivolumab be listed in the PBS for the treatment of non-squamous non-small cell lung cancer (NSCLC) on the basis that the cost-effectiveness against pemetrexed, which the PBAC considered to be a relevant main comparator, could not be determined because an economic comparison was not presented, and that acceptable cost-effectiveness against the submission's nominated main comparator, docetaxel, had not been adequately demonstrated. The PBAC considered that the economic model presented in the submission included numerous assumptions that favoured nivolumab, and that the resulting incremental cost-effectiveness ratio, in the range of \$45,000 – \$75,000 per quality-adjusted life-year gained, was high at the price proposed in the submission and likely to be significantly underestimated.</p> <p>The submission was based on one open-label head-to-head randomised controlled trial comparing nivolumab with docetaxel in previously treated patients with metastatic non-squamous NSCLC. An indirect comparison with pemetrexed using docetaxel as the common reference was also conducted based on main trial and a retrospective non-squamous subgroup analysis (Scagliotti (2009)) of a trial which compared pemetrexed with docetaxel in NSCLC (Hanna et al (2004)).</p> <p>On the basis of the direct evidence presented by the submission, for every 100 non-squamous NSCLC patients (unselected for expression of the cell surface protein PD-L1) treated with nivolumab in comparison to docetaxel:</p> <ul style="list-style-type: none"> • Approximately 16 additional patients would be expected to be alive at 18 months. However, whilst nivolumab doubled median overall survival compared to docetaxel in PD-L1 positive patients, there was no meaningful median overall survival difference between nivolumab and docetaxel in PD-L1 negative patients; • Approximately 43 fewer patients would experience a drug-related Grade 3 or 4 adverse event, 27 fewer patients would experience drug-related neutropenia, but an additional 9 patients would experience a Grade 3 or 4 endocrine adverse event. These differences would be expected to be fairly similar for both PD-L1 positive and negative patients.

MARCH 2016 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
		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>PEMBROLIZUMAB 50mg injection: powder for, 1 vial</p> <p>Keytruda®</p> <p>Merck Sharp and Dohme (Australia) Pty Limited</p> <p>Change to listing (Major Submission)</p>	Melanoma	To seek PBAC reconsideration of the cost-effectiveness of pembrolizumab for the treatment of unresectable stage III or stage IV metastatic melanoma and to fulfil the requirements of the Managed Entry Scheme.	The PBAC decided not to recommend that there be any change to the circumstances under which pembrolizumab is made available as a pharmaceutical benefit. This decision was based on the assessment of new data from a previously submitted randomised, open-label trial comparing pembrolizumab and ipilimumab and an associated new economic evaluation which were not considered to provide sufficient basis to justify a change in the initial managed entry scheme conditions or risk share arrangements or an increase in price over that of the comparator ipilimumab. Listing nivolumab for malignant melanoma as recommended recently by the PBAC would also mean that nivolumab would become a comparator for pembrolizumab with consequences for pricing and risk share arrangements.
		Sponsor Comment:	The PBAC has already accepted pembrolizumab's superior efficacy over ipilimumab, and this submission provided an economic comparison to translate this into a change in conditions as stipulated in the deed of agreement. MSD finds the conclusion that the submission did not provide sufficient basis to justify any change in the conditions over ipilimumab difficult to understand. In addition, the assertion that the listing of nivolumab means that nivolumab would become a comparator for pembrolizumab is inconsistent with our deed and contravenes the managed entry scheme provision that a second entrant does not affect the QALY gained of the original drug over its original comparator. MSD will work with the PBAC to ensure that the survival gains that pembrolizumab delivers over ipilimumab are appropriately recognised.

MARCH 2016 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>POMALIDOMIDE 3 mg capsule, 21 4 mg capsule, 21</p> <p>Pomalyst®</p> <p>Celgene Pty Ltd</p> <p>Change to listing (Minor Submission)</p>	<p>Multiple myeloma</p>	<p>To request a change to the current PBS restriction for pomalidomide in order to allow access for patients experiencing disease progression more than 6 months after cessation of lenalidomide and/or bortezomib.</p> <p>Sponsor Comment:</p>	<p>The PBAC rejected the application to change the restriction for pomalidomide in order to allow access for patients with multiple myeloma experiencing disease progression more than 6 months after cessation of lenalidomide and/or bortezomib. At the current price paid by the Government, the Committee did not know whether pomalidomide in this requested treatment setting was cost-effective. The minor submission included a request to change the lenalidomide restriction to enable re-treatment with lenalidomide after a “treatment holiday”. The PBAC recalled views previously expressed by the Myeloma Foundation and HSANZ in support of such a change, and considered it would be reasonable to make the following changes to the listing for lenalidomide:</p> <ul style="list-style-type: none"> • That the listing allow for re-use of lenalidomide in patients who have not previously failed lenalidomide treatment, since there are situations where it may be clinically appropriate to allow patients to take a ‘drug holiday’ and then recommence treatment. • That the need to try thalidomide treatment prior to accessing lenalidomide, upon relapsing after bortezomib treatment be removed. <p>Celgene will continue to work with the Department of Health to ensure appropriate access to Pomalidomide.</p>
<p>PROGESTERONE 200 mg capsule, 42</p> <p>Utrogestan®</p> <p>Besins Healthcare</p> <p>New listing (Major Submission)</p>	<p>Assisted reproduction</p>	<p>Section 100 (IVF) Authority Required (STREAMLINED) listing for luteal phase support as part of an assisted reproductive technology treatment cycle for infertile women.</p>	<p>The PBAC decided not to recommend progesterone 200 mg capsule (Utrogestan) for PBS listing on the basis that the cost-minimisation analysis was not conducted against the appropriate comparator. The PBAC considered that any form of progesterone currently listed on the PBS for ART could be an appropriate comparator. At the time of PBAC consideration, progesterone pessary and progesterone 8% vaginal gel were listed on the PBS. The PBAC noted that progesterone pessary was the lowest priced of these comparators. As the submission did not provide evidence that progesterone 200 mg capsule provides a significant improvement in efficacy or reduction of toxicity over progesterone pessary for some patients, the PBAC considered there was no basis for progesterone to have a price advantage over progesterone pessary for an equivalent treatment period.</p>

MARCH 2016 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
		Sponsor Comment:	The sponsor is disappointed by this decision but will continue to work with the PBAC and Department to address the matters raised.
<p>SACUBITRIL + VALSARTAN sacubitril 24 mg + valsartan 26 mg tablet, 56 sacubitril 49 mg + valsartan 51 mg, tablet, 56 sacubitril 97 mg + valsartan 103 mg, tablet, 56</p> <p>Entresto®</p> <p>Novartis Pharmaceuticals Australia Pty Ltd</p> <p>New listing</p> <p>(Major Submission)</p>	Chronic heart failure	<p>Authority Required (STREAMLINED) listing for the treatment of chronic heart failure with reduced ejection fraction.</p>	<p>The PBAC did not recommend the listing of sacubitril with valsartan on the basis of uncertain cost-effectiveness and high predicted financial impact. The PBAC considered that the clinical claim of superior comparative effectiveness compared to enalapril was reasonable, but that the size of this benefit was uncertain due to issues with the design of the key study (a randomised controlled trial), and early stopping of this trial. The uncertainty around the treatment effect size, along with the failure of the model to reflect the progression of patients through heart failure, meant that the incremental cost-effectiveness ratio (ICER) estimated by the submission was not reliable and the cost-effectiveness of treatment remained unknown.</p> <p>On the basis of direct evidence presented by the submission, for every 100 patients with chronic cardiac failure and systolic dysfunction, and who are able to tolerate the target drugs, treated with sacubitril/valsartan, in comparison with enalapril, at doses that may not be equivalent, over a median follow-up of 27.1 months:</p> <ul style="list-style-type: none"> • Approximately 3 fewer patients would experience cardiovascular death; • Approximately 5 fewer patients would experience a serious adverse event; • Approximately 3 more patients would experience hypotension.
		Sponsor Comment:	<p>Novartis will continue to work collaboratively with the PBAC, the Department of Health and Federal Government to ensure that Australians with systolic heart failure receive access to Entresto® (sacubitril/valsartan) through the Pharmaceutical Benefits Scheme (PBS) at the earliest possible opportunity.</p>

MARCH 2016 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>SELEXIPAG 200 microgram tablet, 140 200 microgram tablet, 60 400 microgram tablet, 60 600 microgram tablet, 60 800 microgram tablet, 60 1000 microgram tablet, 60 1200 microgram tablet, 60 1400 microgram tablet, 60 1600 microgram tablet, 60</p> <p>Upravi®</p> <p>Actelion Pharmaceuticals Australia Pty Ltd</p> <p>New listing</p> <p>(Major Submission)</p>	<p>Pulmonary arterial hypertension</p>	<p>Section 100 (Highly Specialised Drug Program) Authority Required listing for use as an add-on therapy to endothelin receptor antagonists (ambrisentan, bosentan or macitentan) or to phosphodiesterase type 5 inhibitors (sildenafil and tadalafil) for the treatment of pulmonary arterial hypertension.</p>	<p>The PBAC did not recommend the listing of selexipag on the PBS for pulmonary arterial hypertension (PAH). In reaching this conclusion, the PBAC considered that the magnitude of clinical benefit was unclear, and that the estimate of cost-effectiveness as presented in the submission was difficult to interpret. The PBAC considered that the ICER presented in the submission was high, especially in the context of an outcome of unclear clinical importance (MM events avoided).</p> <p>The PBAC acknowledged the difficulty in assessing the cost-effectiveness of selexipag as add-on to combination therapy in the context of combination therapy being broadly accepted as best clinical practice but not currently being subsidised under the PBS.</p> <p>The PBAC agreed that treatment with selexipag was likely to be superior to placebo, but that the magnitude, and clinical relevance, of any benefit remained unclear.</p> <p>Overall, the PBAC considered that the trial based analysis presented in the submission did not reflect life-long nature of the condition and did not give a reliable estimate of cost-effectiveness. The ICER was difficult to interpret but appeared high, particularly in the context of an outcome of uncertain clinical significance</p> <p>On the basis of direct evidence presented by the submission, for every 100 patients treated with selexipag ± BGT in comparison to placebo ± BGT;</p> <ul style="list-style-type: none"> • Approximately 15 less patients would have experienced a MM event in the first 64 weeks of treatment; • Approximately 7 additional patients would discontinue treatment due to an AE not classified as PAH progression over a median duration of exposure of 64 - 71 weeks; • Approximately 8 additional patients would discontinue treatment due to a prostacyclin-associated AE over a median duration of exposure of 64 - 71 weeks.

MARCH 2016 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
		Sponsor Comment:	Actelion Pharmaceuticals Ltd will consider the comments made by the PBAC when lodging a re-submission requesting PBS listing of selezipag for patients with PAH.
<p>THYROXINE SODIUM 25 microgram tablet, 200</p> <p>Eltroxin®</p> <p>Aspen Pharmacare Australia Pty Ltd</p> <p>New listing (Minor Submission)</p>	<p>Thyroid hormone deficiency thyroid stimulating hormone-responsive tumours of the thyroid</p>	<p>Re-submission to request an Unrestricted benefit listing for thyroxine sodium 25 micrograms.</p>	<p>The PBAC decided not to recommend thyroxine (as sodium) 25 microgram for PBS-listing. In making its recommendation, the PBAC considered that thyroxine 25 microgram tablets would not be cost-effective at the price proposed by the submission, noting that there were several strengths of thyroxine already listed or recommended for listing on the PBS (including 50, 75, 100, 125 and 200 micrograms). The PBAC did not accept that there was an unmet clinical need for this new presentation.</p>
		Sponsor Comment:	<p>Aspen is disappointed that the PBAC has not recommended listing of Eltroxin (thyroxine) 25 mcg tablets. Aspen has received feedback from Endocrinologists that there is a clinical need for thyroxine 25 mcg tablets for dose-adjustment flexibility. Eltroxin tablets in doses of 50 mcg and higher are not scored, the tablets are recommended to be taken whole and not cut into halves to reduce the risk of inaccurate dosing.</p> <p>Eltroxin 25 mcg is the only tablet that is scored and has a break-line. TGA have reviewed the uniformity of content and dissolution data and it was accepted that 25 mcg tablets break in an acceptable manner and a half tablet can deliver 12.5 mcg dose. A dose of 25 mcg or 12.5 mcg is recommended as an initiation dose for elderly patients, for those patients with ischaemic heart disease, during pregnancy, and for children. It is recognized that an accurate dose is important to reduce the risk of unacceptable adverse effects. Such an accurate dose was not available to Australian patients since Oroxine brand (thyroxine) was launched > 50 years ago. Aspen's view is that 25 mcg tablets plays an important role in the management of demonstrated thyroid hormone deficiency for all patients.</p>