NOVEMBER 2020 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
CEMIPLIMAB Solution for IV infusion 350 mg in 7 mL Libtayo® Sanofi-Aventis Australia Pty Ltd New listing (Major Submission)	Squamous cell carcinoma (SCC)	To request Section 100 (Efficient Funding of Chemotherapy) Authority Required (STREAMLINED) listing for the treatment of metastatic or locally advanced cutaneous SCC in patients who are not candidates for curative surgery or curative radiation.	The PBAC did not recommend cemiplimab for the treatment of patients with metastatic or locally advanced cutaneous squamous cell carcinoma (mCSCC or laCSCC) who are not candidates for curative surgery or curative radiation. The PBAC considered that the data presented were insufficient to adequately determine the magnitude of improvement in effectiveness and safety of cemiplimab compared to best supportive care ± chemotherapy (BSC ± CT) with the comparison of single arm studies highly uncertain. The PBAC considered the incremental cost-effectiveness ratio (ICER) uncertain given the limitations with the clinical data, and substantially underestimated. The PBAC considered the financial impact as estimated in the submission was uncertain and potentially very high.
		Sponsor's comment:	Sanofi is disappointed with the outcome. We are committed to supporting timely access in Australia for a cohort of patients with a life limiting and disfiguring condition associated with significant disease burden, and for whom there are no effective alternative treatment options.
DAPAGLIFLOZIN Tablet 10 mg Forxiga® AstraZeneca Pty Ltd Change to listing (Major Submission)	Heart failure	To request an extension of the current Authority Required (STREAMLINED) listing to include the treatment of heart failure in patients with reduced ejection fraction.	The PBAC did not recommend dapagliflozin for the treatment of patients with chronic heart failure with reduced ejection fraction. The PBAC considered that, although dapagliflozin was effective for this indication, its clinical place was unclear and likely to evolve. The selection of sacubitril/valsartan as the main comparator was inappropriate, and hence the economic analysis presented in the submission did not allow for an assessment of cost effectiveness. The PBAC considered the cost-effectiveness of dapagliflozin added to standard care (comprising a beta-blocker plus an angiotensin-converting enzyme (ACE) inhibitor or angiotensin II receptor blocker (ARB) versus standard care alone (comprising a beta-blocker plus an ACE inhibitor or ARB) would need to be established in a future resubmission. An additional cost-effectiveness analysis would also be required for concomitant use of dapagliflozin and sacubitril/valsartan (plus a beta-blocker) compared to sacubitril/valsartan (plus a beta-blocker), which would be allowed under the proposed PBS listing. The PBAC also considered that the financial estimates were likely underestimated, and noted that several Quality Use of Medicines issues would need to be addressed in any resubmission.

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		Sponsor's comment:	The sponsor had no comment.
ECULIZUMAB Solution concentrate for I.V. infusion 300 mg in 30 mL Soliris® Alexion Pharmaceuticals Australasia Pty Ltd Change to listing (Major Submission)	Neuromyelitis optica spectrum disorder (NMOSD)	To request an Authority Required (Written) listing for the treatment of patients with relapsing NMOSD who are anti-aquaporin-4 (AQP4) antibody positive.	The PBAC did not recommend the listing of eculizumab for the treatment of NMOSD. Although the PBAC considered that eculizumab was more effective than best supportive care in reducing relapses, the magnitude of this effect on disability progression and quality of life outcomes was highly uncertain. The PBAC noted that the incremental cost effectiveness ratio (ICER) was exceptionally high and advised that a significant price reduction would aid in achieving an acceptable ICER. The PBAC, noting that eculizumab was proposed as a lifelong prophylactic treatment, considered that, at the proposed price, the cost of listing eculizumab on the PBS was high for the number of patients expected to be treated.
		Sponsor's comment:	Alexion is disappointed with the PBAC's decision not to recommend eculizumab for NMOSD. We appreciate there is a high threshold of evidence required to establish the value of a new treatment, which can be even more challenging in rare diseases, however, adult patients with NMOSD in Australia will greatly benefit from access to eculizumab – the first approved treatment for NMOSD. As such, we will continue to work with the PBAC and the Department of Health to reach an agreement that ensures long term, sustainable access for people living with this devastating disease.
ELOTUZUMAB Powder for IV infusion 300 mg Powder for IV infusion 400 mg Empliciti® Bristol-Myers Squibb Australia Pty Ltd New listing (Major Submission)	Multiple myeloma	To request Section 100 (Efficient Funding of Chemotherapy) Authority Required (Telephone) listing in combination with lenalidomide and dexamethasone for the treatment of patients with relapsed or refractory multiple myeloma.	The PBAC did not recommend the listing of elotuzumab, in combination with lenalidomide and dexamethasone (ELd), for the treatment of patients with relapsed and/or refractory multiple myeloma. The PBAC considered that, due to the nature of the indirect treatment comparison (ITC) and differences between the key trials, the results of the ITC were difficult to interpret and did not adequately demonstrate non-inferiority between ELd and the nominated comparator, carfilzomib plus dexamethasone, in terms of efficacy or safety. The PBAC therefore considered that the presentation of a cost minimisation analysis was not appropriate.
		Sponsor's comment:	The sponsor had no comment.

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EVOLOCUMAB Injection 140 mg in 1 mL single use pre-filled pen Injection 420 mg in 3.5 mL single use pre-filled cartridge Repatha® Amgen Australia Pty Limited Change to listing (Minor Submission)	Familial heterozygous hypercholesterolaemia; Non-familial hypercholesterolaemia; Familial homozygous hypercholesterolaemia	To request an amendment to the Authority Required listing to allow general practitioners to initiate treatment in consultation with a specialist.	The PBAC did not recommend amending the Authority Required listings of evolocumab for all indications to allow GPs to initiate treatment after having consulted a specialist. Consistent with its previous advice, the PBAC advised that "Must be treated by a specialist physician" should remain a requirement for initiation of treatment for all indications. The PBAC considered that it was too early to assess the financial impact of the evolocumab listings and that it would be appropriate to review the utilisation data after at least 18 months from the date evolocumab's listing was extended to include non-familial hypercholesterolaemia (1 May 2020).
		Sponsor's comments:	Amgen will continue to work with the PBAC on this matter so Australians have equitable access to evolocumab.
FLUOCINOLONE ACETONIDE Intravitreal injection 190 micrograms Iluvien® Specialised Therapeutics Alim Pty Ltd New listing (Minor Submission)	Diabetic macular oedema	Resubmission to request an amendment to the PBAC's previously recommended equi-effective doses for fluocinolone acetonide and dexamethasone.	The PBAC reaffirmed its previous recommendation from March 2020 for the listing of fluocinolone acetonide (FA) for the treatment of diabetic macular oedema in patients who are unsuitable for, contraindicated to, or have failed treatment with vascular endothelial growth factor (VEGF) inhibitors. The PBAC made this recommendation on a cost minimisation basis against dexamethasone (DEX), using a trial-based dose relativity of 1.3 FA versus 4.11 DEX administrations over 36 months. The PBAC reiterated its recommendation from March 2020 that the cost minimisation analysis should only include the cost of drug and the cost of administering the implants, and that the listing of FA should be cost neutral to Government.
		Sponsor's comment:	It is very disappointing that the original PBAC conditional recommendation, and subsequent minor application, has been unsuccessful in achieving a price that is similar to reimbursed prices in Europe and the UK. While the proposed Risk Share terms were acceptable, the ex-manufacture net price offered is less than half the global average reimbursed price for Iluvien. Given the acquisition cost from the drug developer Alimera is greater than the proposed PBS price, and the impact such a low price, if accepted, would have on Alimera's existing reimbursed global pricing, Specialised Therapeutics cannot proceed with Iluvien's listing on the PBS.

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GALCANEZUMAB Injection 120 mg in 1 mL pre-filled pen Emgality® Eli Lilly Australia Pty Ltd New listing (Major Submission)	Episodic migraine	To request an Authority Required (STREAMLINED) listing for the treatment of adult patients with treatment-resistant episodic migraine.	The PBAC did not recommend the listing of galcanezumab for the treatment of episodic migraine in patients who have experienced an adequate response, intolerance, or a contraindication to at least three prophylactic migraine medications. The PBAC considered the magnitude of benefit in this population was uncertain and galcanezumab was not cost-effective at the price requested in the submission. The PBAC considered there is not a clear distinction between treatment-resistant chronic and episodic migraine with patients moving between these diagnoses. The PBAC considered a listing for treatment-resistant migraine would be appropriate and that any resubmission would need to address offsets for patients that might otherwise be attributed for in the chronic migraine population.
		Sponsor's comment:	Lilly is committed to working with all stakeholders to address the significant unmet medical needs of Australians living with episodic migraine and our efforts to secure a PBS listing for these Australians will continue.
IXAZOMIB Capsule 2.3 mg Capsule 3 mg Capsule 4 mg Ninlaro® Takeda Pharmaceuticals Australia Pty Ltd New listing (Major Submission)	Multiple myeloma	To request Section 100 (Highly Specialised Drugs Program) Authority Required (Telephone) listing in combination with lenalidomide and dexamethasone for patients with relapsed or refractory multiple myeloma.	The PBAC did not recommend the listing of ixazomib, in combination with lenalidomide and dexamethasone (ILd), for the treatment of patients with relapsed and/or refractory multiple myeloma. The PBAC considered that, due to the nature of the naïve indirect treatment comparison (ITC) and differences between the key trials, the results of the naïve ITC were difficult to interpret and did not adequately demonstrate non-inferiority between ILd and the nominated comparator, carfilzomib plus dexamethasone, in terms of efficacy or safety. The PBAC therefore considered that the presentation of a cost minimisation analysis was not appropriate.
		Sponsor's comment:	Takeda Australia wishes to thank the patients, clinicians, and organisations who took time to provide their experience of ixazomib during the PBAC process. Takeda believes ixazomib can be a valuable part of the management of multiple myeloma. We will continue to work with the Department of Health and the PBAC so that Australian patients may soon access ixazomib through the PBS.

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PEMBROLIZUMAB Solution concentrate for I.V. infusion 100 mg in 4 mL Keytruda® Merck Sharp & Dohme (Australia) Pty Ltd Change to listing (Major Submission)	Squamous cell carcinoma of the head and neck (SCCHN)	To request Section 100 (Efficient Funding of Chemotherapy) Authority Required (STREAMLINED) listing for the first line treatment of recurrent or metastatic SCCHN.	The PBAC decided not to recommend the listing of pembrolizumab for first-line treatment of recurrent or metastatic SCCHN in patients with programmed death ligand 1 (PD-L1) combined positive score (CPS) score ≥1. The PBAC considered that pembrolizumab plus chemotherapy (but not pembrolizumab monotherapy) was clinically superior to first-line chemotherapy alone in terms of overall survival. However, the magnitude of clinical benefit over current standard of care, which includes second-line nivolumab, was uncertain, and the evidence supporting a PD-L1-based eligibility criterion was not convincing. The PBAC considered that there were a number of modelling assumptions which resulted in the incremental cost-effectiveness ratio being uncertain and substantially underestimated.
		Sponsor's comment:	MSD is disappointed that the PBAC has decided not to recommend pembrolizumab for recurrent or metastatic SCCHN. This is a debilitating cancer where the side effects of treatment are often visible and can result in severe facial disfigurement impacting a patient's ability to see, swallow speak and breathe. This decision has denied patients the opportunity to have a treatment option that has demonstrated, survival benefits, durable response rates and a reduction in treatment burden. While MSD agrees with the PBAC that pembrolizumab plus chemotherapy is clinically superior to first-line chemotherapy, we disagree that pembrolizumab monotherapy is not clinically superior to first-line chemotherapy, as the data demonstrates that pembrolizumab monotherapy is efficacious for patients with a CPS score ≥1. MSD will work to ensure patients with recurrent or metastatic SCCHN will be able to access pembrolizumab as soon as possible on the PBS.

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SACUBITRIL with VALSARTAN Tablet containing sacubitril 24.3 mg + valsartan 25.7 mg Tablet containing sacubitril 48.6 mg + valsartan 51.4 mg Tablet containing sacubitril 97.2 mg + valsartan 102.8 mg Entresto® Novartis Pharmaceuticals Australia Pty Ltd Change to listing (Major Submission)	Heart failure	To request changes to the current Authority Required (STREAMLINED) listing for patients with chronic heart failure with reduced ejection fraction (HF-rEF) to include a broader population of patients.	The PBAC considered a request to expand the population eligible for PBS subsidised treatment sacubitril with valsartan (SAC/VAL). The submission did not include some of the standard information expected in a major submission and this hindered the Committee's ability to consider the request. The two core requests in the submission were to expand the listing to allow patients with a left ventricular ejection fraction (LVEF) of between 41% and 49% inclusive (from the current ≤40% requirement) and to allow use of SAC/VAL in patients who have not previously been treated with an angiotensin II converting enzyme (ACE) inhibitor, angiotensin II receptor blocker (ARB) or a beta blocker (i.e. first line use). The submission also requested a change to nurse practitioner prescribing arrangements to allow prescribing under a shared care model (from current continuing therapy only arrangements). The PBAC provided four outcomes for these requests: • The PBAC did not recommend expanding the population eligible for SAC/VAL to patients with an LVEF of between 41% and 49% inclusive, as no comparative data or economic analysis was provided to consider the cost effectiveness in this population. The Committee considered arguments in the submission that SAC/VAL would be of similar cost effectiveness in the current LVEF ≤40% population and the expanded population were implausible, as these patients had less severe disease and likely better prognostic outcomes. Therefore, the PBAC considered a formal economic analysis would be required to consider expanding this listing to include these patients. • The PBAC did not recommend expanding the population eligible for SAC/VAL to allow use in patients who have not previously been treated with an ACE inhibitor or ARB. While the Committee considered the evidence presented indicated SAC/VAL may be of similar effectiveness when used in first or second line setting, some patients with heart failure would be adequately treated with ACE inhibitors or ARBs and therefore SAC/VAL would not provide better outcomes in these patients. Given the magnitude

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			of price difference between current first line agents and SAC/VAL, the PBAC considered use in such patients would not be cost effective and considered that a formal economic analysis would be required to consider expanding this listing to include these patients. • The PBAC recommended amendments to beta blocker requirements in the SAC/VAL restriction to be more consistent with clinical guidelines and allow greater flexibility for clinical decision making. The PBAC recommended the current restriction, which requires patients to be on the maximally tolerated dose of a beta blocker, be amended to state that patients prior treatments 'should include' a beta blocker, unless contraindicated or not tolerated. • The PBAC recommended clarification to the nurse practitioner arrangements. The PBAC was of a view that dose titration constitutes continuing therapy (therefore maintaining current continuing therapy nurse practitioner arrangements is appropriate), but that initiating treatment with SAC/VAL should remain restricted to medical practitioners
		Sponsor's comment:	Novartis is disappointed that the PBAC did not recommend changes to the PBS listing to include a broader patient population with HF. Novartis welcomes the amendments to the beta blocker requirements in the restriction to be more consistent with clinical guidelines and allow greater flexibility for clinical decision making.