MARCH 2019 PBAC OUTCOMES – OTHER MATTERS

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Post-market Review of Pulmonary Arterial Hypertension (PAH) Medicines AMBRISENTAN BOSENTAN MACITENTAN EPOPROSTENOL ILOPROST SILDENAFIL (20mg, 90 tablets) TADALAFIL (20mg, 56 tablets) RIOCIGUAT (All forms, strengths and listed brands)	Medicines specifically used to treat PAH	Matters relating to the PBAC consideration of the Post-market Review of PAH Medicines report in November 2018.	In November 2018, the PBAC noted that guidelines for the management of PAH generally recommend treatment of World Health Organisation (WHO) Functional Class (FC) II patients and that nonsubsidised therapy appears to be prevalent. The PBAC considered and accepted that the estimated cost of extending PBS subsidised monotherapy with endothelin receptor antagonists (ERAs) (bosentan, ambrisentan and macitentan) and phosphodiesterase-5 (PDE-5) inhibitors (sildenafil and tadalafil) to patients presenting with WHO FC II PAH symptoms ranges from approximately $2.7 million in 2019 to $3.5 million in 2023. The underlying assumptions used in the modelling for the cost estimates were considered reasonable. The PBAC noted the estimated annual cost to the PBS was acceptable given the high clinical need and the evidence that ERAs and PDE-5 inhibitors are effective in patients presenting with WHO FC ll symptoms and may delay patients deteriorating to WHO FC lll/lV. The PBAC reviewed and accepted the revised PBS restrictions to extend subsidy to patients in WHO FC II PAH for monotherapy with ERAs and PDE-5 inhibitors medicines, the amendment to the PBS restriction definition for PAH as proposed by the Reference Group, and the other changes made to PBS restrictions for PAH medicines as recommended at the November 2018 meeting. The PBAC considered the pre-PBAC responses from sponsors, and noted that GSK requested extension of PBS subsidy of epoprostenol to first line treatment for patients with WHO FC III PAH symptoms at high risk of deterioration. The PBAC also noted that the Department intends to progress a stakeholder meeting to discuss potential dual combination (initial and/or sequential combination) PBS subsidised therapy with ERAs and PDE-5 inhibitor medicines for patients with WHO FC III/IV PAH symptoms with increased risk factors or evidence of rapid deterioration in their condition. PBS subsidy would be dependent on achievement of an acceptable price. Sponsors had previously supported a stakeholder meeting to address this.

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			The meeting may also be used to progress the request for extension of PBS subsidy of epoprostenol to first line treatment. The PBAC noted Department advice that a review of the PAH Designated Prescribing Centre guidelines had commenced.
Drugs for the treatment of hepatitis C (all listed forms and brands)	Hepatitis C	To seek PBAC's advice on changes to the listings of direct-acting antiviral (DAA) regimens and the associated General Statement for drugs used for the treatment of hepatitis C, raised at the Hepatitis C clinical stakeholder meeting on 13 December 2018	The PBAC considered a number of issues raised in the Hepatitis C stakeholder meeting held on 13 December 2018 and provided the following advice: • Recommend the removal of age restrictions from all PBS listings of DAA regimens in the current General Statement for Drugs Used for the Treatment of Hepatitis C on the basis that requirements for various regimens were adequately outlined in the approved Product Information documents; • Recommend the removal of the remaining peg-interferon alfa-2a containing regimen options on the basis that interferon-free options are available for all genotypes; and • Request the Department investigate the feasibility of a number of other significant changes to hepatitis C listings and provide advice for consideration at a future meeting.
PEMBROLIZUMAB Solution concentrate for I.V. infusion 100 mg in 4 mL Keytruda® Merck Sharp and Dohme (Australia) Pty Ltd	First-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) expressing PD-L1 TPS>50%.	The Department sought the advice of the PBAC on the clinical and economic analyses for pembrolizumab when used for the first line treatment of patients with metastatic NSCLC expressing PD-L1 TPS > 50% as recommended for PBS listing in July 2018 in light of the availability of new clinical trial data.	The PBAC emphasised the critical importance of having all potentially relevant results at the time it considers a listing application in order to ensure evidence based decision making particularly when newly emerging data show differing benefits. The PBAC requested that the Department work to implement new guidance and processes to ensure all available data is provided to PBAC in listing submissions and, where data becomes available following a PBAC recommendation for listing, there are processes to ensure those data are rapidly reviewed in the context of the value proposition on which the listing recommendation was based. The PBAC recalled it had recommended pembrolizumab monotherapy for listing for NSCLC in July 2018 on the basis of interim study results for

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			KN024. The PBAC noted that at the time it had not been provided with data from a planned analysis of a clinical trial which was relevant to the PBAC's considerations, and that the top-line results of this analysis had been released publicly a month before the PBAC meeting. The PBAC further noted that these results were not provided to the Department in the context of the subsequent price negotiations for pembrolizumab monotherapy. The PBAC noted that not providing relevant information is contrary to the spirit of the submission guidelines with potential to undermine the integrity of its evidence based decision making processes. The PBAC requested that the submission guidelines should be amended to make it clear how such incidences should be managed in future. Overall, on consideration of all the information provided to it, the PBAC advised that it remains confident that the overall clinical claim of superior efficacy remains supported and unchanged for pembrolizumab monotherapy in the PD-L1≥50% population from its prior July 2018 consideration. However, in light of the KN042 data, the PBAC considered that there is increased uncertainty regarding the cost-effectiveness of pembrolizumab monotherapy for this indication. The PBAC applied revised inputs to the economic model, based on the new information available to it, and recommended the Department pursue a price reduction to the effective price of pembrolizumab monotherapy for non-small cell lung cancer to re-establish certainty of cost-effectiveness of pembrolizumab monotherapy in NSCLC and take account of the evidence from both KN024 and KN042. Should MSD not offer a revised price, the PBAC considered options proposed by the Minister's delegate and advised there was no reason the Minister (delegate) should not amend the circumstances for pembrolizumab to telephone authority, if required (from the current streamlined authority), with prescribers being asked to verbally confirm that the patient meets each aspect of the restriction requirement. The PBAC further advised if an alternative first line immunotherapy regimen, whether it be monotherapy or combination therapy becomes available on the PBS, it would be ready to re-consider the future place of pembrolizumab in the therapy of NSCLC. Potential options would include limiting access to pembrolizumab subsidy to only include patients for whom

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			no other first line immunotherapy based option for NSCLC is available on the PBS.
SOMATROPIN Powder for injection 5 mg (15 i.u.) with diluent in pre-filled pen (with preservative) Powder for injection 12 mg (36 i.u.) with diluent in pre-filled pen (with preservative) Genotropin GoQuick Pfizer Australia Pty Ltd Solution for injection 10 mg (30 i.u.) in 2 mL cartridge (with preservative) NutropinAq Ipsen Pty Ltd (Correspondence from the Endocrine Society of Australia)	Severe growth hormone deficiency	To seek advice from the PBAC on the requirement for prescribers to use the Quality of Life Assessment of Growth Hormone Deficiency in Adults (QoL-AGHDA) questionnaire in order to assess whether patients meet the eligibility criteria for the Section 100 (Growth Hormone) Authority Required listing of somatropin for the treatment of adults with severe growth hormone deficiency.	The PBAC recommended the removal of the requirement for prescribers to use the QoL-AGHDA questionnaire from the current somatropin restrictions for the treatment of severe growth hormone deficiency. In making its recommendation, the PBAC noted that not all endocrinologists in Australia have access to the questionnaire as it is privately owned. Further, the PBAC considered there was some uncertainty in the validity and reliability of the questionnaire given it comprises of a set of self-administered binary (yes/no) questions.
Take home Naloxone Pilot Program (All listed brands and forms)	Opiate dependence	To: • Inform the PBAC of a pilot to test the feasibility of a national roll out for a PBS	The PBAC noted the Take Home Naloxone pilot program announced by the Hon. Minister Hunt on 27 February 2019 and the potential impact the pilot program will have on potential future naloxone PBS listings.

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		Subsidised Take Home Naloxone Program. • Seek advice from the PBAC regarding dual list of naloxone products under Section 100 for the purposes of the pilot.	The PBAC considered it would be appropriate to have a dual listing across Section 85 and Section 100 for existing forms of naloxone to enable their inclusion within the pilot program.
TENOFOVIR WITH EMBTRICITABINE AND EFAVIRENZ Tablet containing tenofovir disoproxil fumarate 300 mg with emtricitabine 200 mg and efavirenz 600 mg Atripla® TENOFOVIR WITH EMBTRICITABINE AND RILPIVIRINE Tablet containing tenofovir disoproxil fumarate 300 mg with emtricitabine 200 mg and rilpivirine 25 mg (as hydrochloride) Eviplera® TENOFOVIR WITH EMBTRICITABINE, ELVITAGREVIR AND COBICISTAT	Human immunodeficiency virus (HIV) infection	To seek advice from the PBAC in relation to the removal of tenofovir with embtricitabine containing medicines from the PBS.	Advice from the PBAC was sought on whether the following medicines should be removed from the PBS schedule: tenofovir with embtricitabine and efavirenz (Atripla®); tenofovir with embtricitabine and rilpivirine (Eviplera®); and/or tenofovir with emtricitabine, elvitagrevir and cobicistat (Stribild®). This advice was sought because prices consistent with the current price of the component drug tenofovir with emtricitabine (Truvada®) could not be agreed as required due to price disclosure price reductions to all PBS-listed brands of tenofovir with emtricitabine. The PBAC advised that there were no reasons why these medicines should remain on the PBS, however recommended that Atripla, Eviplera and Stribild should remain listed on the PBS for six months, subject to consultation with clinical and community peak bodies.

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Tablet containing tenofovir disoproxil fumarate 300 mg with emtricitabine 200 mg, elvitegravir 150 mg and cobicistat 150 mg Stribild® Gilead Sciences Pty Ltd			
Cost-effectiveness review of pneumococcal vaccines for the National Immunisation Program (NIP). Pneumovax 23® Seqirus Australia Pty Ltd Prevenar 13® Pfizer Australia Pty Ltd	Vaccines for the prevention of pneumococcal disease	To consider the eligible populations for vaccination with 23vPPV and or 13vPCV via the National Immunisation Program (NIP).	The PBAC deferred making a recommendation about the populations eligible for pneumococcal vaccines via NIP schedule where cost-effectiveness could be considered acceptable to seek further input to inform its advice. In July 2016, the PBAC recommended Prevenar 13® (a 13-valent pneumococcal conjugate vaccine (13vPCV)) to replace the first dose of Pneumovax 23® (a 23-valent pneumococcal polysaccharide vaccine (23vPPV)) for older adults on the basis of cost effectiveness over the 23vPPV. At that time the PBAC noted that the cost-effectiveness of 23vPPV had not been previously reviewed and requested advice from the Australian Technical Advisory Group on Immunisation (ATAGI) on the clinical place and effectiveness of 23vPPV on the NIP with a view to potentially informing a review of the cost-effectiveness of 23vPPV. The PBAC noted that any outcomes of the review of 23vPPV may have implications for the 13vPCV listing. In July 2017, the PBAC considered the advice of the ATAGI and recommended a cost effectiveness review (CER) of 23vPPV compared to no vaccine in the current NIP-funded indications for: • Non-Indigenous adults aged ≥65 years, with and without risk factors; and • Aboriginal and Torres Strait Islander adults aged ≥50 years, with and without risk factors. Given the high and disproportionate burden of invasive pneumococcal disease (IPD) in Aboriginal and Torres Strait Islander adults, the PBAC also

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			recommended a review of a stepped economic analysis and financial impact of providing 13vPCV, with or without 1 or 2 doses of 23vPPV, to Aboriginal and Torres Strait Islander people ≥50yrs not previously vaccinated with 7vPCV or 13vPCV. The PBAC first considered the CER report in December 2018 and sought further advice from the ATAGI on a proposed pneumococcal NIP schedule for individuals aged 12 months and older at high-risk of pneumococcal disease, where use of 13vPCV and 23vPPV could be considered cost-effective. At its March 2019 meeting, the PBAC considered updated ATAGI advice. The PBAC accepted ATAGI's advice and considered it would be appropriate to fund one dose of 13vPCV and two doses of 23vPPV for those aged 12-59 months with the at-risk conditions ATAGI had identified (which included patients with asplenia, immunocompromised conditions, chronic respiratory or renal disease, cerebrospinal fluid leak, cochlear implants, intracranial shunts or previous episodes of invasive pneumococcal disease). The PBAC also revisited its consideration of the CER and affirmed the findings, which supported routine vaccination with 13vPCV in older, healthy adults ≥75 years, based on acceptable cost-effectiveness. The PBAC also affirmed its view that one dose of the 13vPCV plus two subsequent doses of the 23vPPV in the Indigenous population ≥50 years could be included on the NIP, based on high but acceptable cost-effectiveness in this population. However the PBAC considered the enhanced immunisation schedule for at-risk groups aged ≥ 5years as identified by the ATAGI required further consideration before it would be in a position to make a recommendation and requested the ATAGI provide advice on additional at-risk conditions which may be appropriate for NIP- funding, taking into consideration: a. conditions associated with a high incidence of IPD and small patient numbers, such as persistent nephrotic syndrome; and b. conditions where the risk of IPD is likely to be very high but difficult to accurately quantify because of small patient numbers.

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			The PBAC also noted the feedback from the sponsors of both vaccines and two other stakeholders requesting the opportunity for wider stakeholder input to the CER of 23vPPV. Therefore the PBAC deferred making a recommendation about the populations eligible for the pneumococcal NIP schedule where cost-effectiveness could be considered acceptable so that targeted consultation with relevant stakeholders could be undertaken and to provide an opportunity for the ATAGI to provide further advice on additional at-risk conditions it considers appropriate for inclusion in a pneumococcal NIP.
Mesalazine Sulfasalazine Balsalazide Olsalazine (all listed brands and strengths for oral use, including generic versions)	5-aminosalicylic acid (5-ASA) medicines for ulcerative colitis and Crohn disease	PBAC advice	In March 2019, the PBAC considered a literature review and utilisation analysis of oral 5-ASA medicines and feedback from sponsors. The PBAC also recalled that it considered the DUSC reports on ulcerative colitis medicines (June 2017) and 5-ASA medicines (September 2017). The PBAC noted advice from sponsors and clinicians that oral mesalazine may be preferred to sulfasalazine in certain circumstances, including because it is better tolerated, requires less intensive monitoring, and has a lower pill burden. However, the PBAC recalled this was not the indicated population for whom mesalazine was deemed cost-effective when listed on the PBS. The PBAC re-affirmed its previous advice that subsidised use of oral formulations of mesalazine are no longer cost-effective due to the high proportion of patients who appear to be initiating mesalazine outside of the PBS restrictions i.e. patients who are not hypersensitive or intolerant to sulfasalazine. The PBAC, in reviewing the information provided in past DUSC reports and the literature review, concluded that over 50% of mesalazine use appears to be outside the current PBS restriction due to the high proportion of use in the first line setting. The PBAC also noted that the daily dose appears higher now than when first PBS-listed.

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			The PBAC advised it was willing to broaden the restrictions to allow oral mesalazine to be used in the same setting as sulfasalazine in patients with ulcerative colitis and/or Crohn disease. The PBAC recommended the clinical criteria “Patient must have had a documented hypersensitivity reaction to a sulphonamide; OR Patient must be intolerant to sulfasalazine” be removed, but only if a price-reduction was applied to ensure cost-effectiveness in this setting.