PHARMACEUTICAL BENEFITS ADVISORY COMMITTEE (PBAC) MEETING OUTCOMES
MAY 2021 PBAC INTRACYCLE MEETING

The PBAC outcomes and recommendations are presented in alphabetical order by drug name.

DRUG NAME, FORM(S), STRENGTH(S), SPONSOR, TYPE OF SUBMISSION	DRUG TYPE AND USE	LISTING REQUESTED BY SPONSOR / PURPOSE OF SUBMISSION	PBAC OUTCOME	
ELEXACAFTOR/ TEZACAFTOR/ IVACAFTOR AND IVACAFTOR Pack containing 56 tablets of elexacaftor 100 mg with tezacaftor 50 mg and ivacaftor 75 mg and 28 tablets of ivacaftor 150 mg Trikafta® Vertex Pharmaceuticals (Australia) Pty Ltd New PBS listing (Matters Outstanding)	Cystic fibrosis (CF)	To request a Section 100 (Highly Specialised Drugs Program) Authority Required (Written) listing for the treatment of CF in patients aged 12 years or older who have at least one F508del mutation on the cystic fibrosis transmembrane conductance regulator (CFTR) gene.	Deferred	The PBAC again deferred making a recommendation regarding the proposed listing of elexacaftor/tezacaftor/ivacaftor and ivacaftor for the treatment of CF patients aged 12 years and older who have at least one F508del mutation in the CFTR gene. It did so because the sponsor's revised proposal did not adequately address the parameters outlined in the minutes of the PBAC's March 2021 meeting. The PBAC noted the revised proposal resulted in a net cost to Government that was higher than the proposal put by the sponsor for consideration at the March 2021 meeting. Although the PBAC accepted to further increase the budget for this listing by 80%, the PBAC considered that the revised proposal was overall not aligned with the PBAC's March 2021 advice as it requested significant deviations with regard to the pricing and financial estimates. Therefore, it deferred completion of its consideration to allow the sponsor to provide further information.
				Sponsor's Comment: Vertex is disappointed that the PBAC has again deferred its decision on the funding of Trikafta (elexacaftor/tezacaftor/ivacaftor), especially given the solutions provided by Vertex to address the points raised in the previous deferral. Vertex welcomes the PBAC's reappraisal of patient numbers, particularly as the initial assessment from the PBAC was not representative of the number of eligible patients. We remain committed to continuing to work collaboratively with the PBAC to ensure all eligible patients, as identified within the Australian Cystic Fibrosis Data Registry, who could benefit from treatment, have government-funded access to Trikafta as quickly as possible.

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ENCORAFENIB Capsule 50 mg Capsule 75 mg Braftovi® Pierre Fabre Australia Pty Ltd Change to PBS listing (Matters Outstanding)	Colorectal cancer	To request an Authority Required (STREAMLINED) listing for the treatment of BRAF V600E-variant metastatic (Stage IV) colorectal cancer (mCRC).	Recommended	At its March 2021 PBAC meeting, the PBAC deferred its consideration of encorafenib in combination with cetuximab for the targeted treatment of patients with BRAF V600E-variant mCRC who have received prior systemic therapy pending support from MSAC on the funding of the co-dependent BRAF V600 testing. At its 31 March – 1 April 2021 meeting, the MSAC supported an amendment to the descriptor for MBS item 73338 to include BRAF V600 testing. Following this, in May 2021, the PBAC recommended the listing of encorafenib in combination with cetuximab for the treatment of these patients. The PBAC again acknowledged the high clinical need in a patient population with poor prognosis, considered that the clinical benefit was meaningful, and the economic model was reliable for decision making. The PBAC considered that the cost-effectiveness and estimated financial impact were acceptable.
ONASEMNOGENE ABEPARVOVEC Solution for injection, customised based on patient weight Zolgensma® Novartis Pharmaceuticals Australia Pty Ltd New PBS listing (Matters Outstanding)	Spinal muscular atrophy (SMA)	To request an Authority Required (Written) listing for the treatment of paediatric patients with Type 1 SMA.	Deferred	The PBAC maintained its deferral from the November 2020 meeting for PBS listing of onasemnogene abeparvovec (ONA) for SMA as a number of concerns with the subsidy proposal remained. The PBAC noted the proposed population was revised to patients aged less than 9 months (from patients less than 2 years of age), with 1-3 copies of the SMN2 gene, although patients with 3 copies of SMN2 are currently not eligible for treatment with nusinersen (NUSI). The PBAC considered the request for inclusion of patients with 3 copies of SMN2 was not adequately supported, and at the requested price ONA was unlikely to be cost-effective in these patients. The PBAC considered that the cost-minimisation analysis for ONA versus NUSI should be revised to take into account discounting of costs in the forward years, and an analysis versus risdiplam (as a near market comparator) should also be presented. The PBAC considered that the proposal, which was conditional on an upfront payment with no outcomes-based measures, did not adequately address the uncertainties with the clinical evidence and associated cost-effectiveness.
				Sponsor's Comment: Novartis is disappointed at another deferral. Novartis has worked to find a resolution, meeting all requests made at the post-PBAC meeting around the comparator and offering a substantially discounted price package to balance the continued uncertainty felt by the PBAC. We remain committed to bringing Zolgensma to Australian babies with SMA and working with DOH and members of the PBAC to clarify further comparator, pricing and risk share arrangement concerns.

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TETRACOSACTIDE Compound depot injection 1 mg in 1 mL Synacthen® Clinect Pty Ltd Change to PBS listing (Matters Outstanding)	Hypsarrhythmia and/or infantile spasms	To request a change in restriction level from Restricted Benefit to Unrestricted Benefit listing.	Advice given	The PBAC advised that the delisting of tetracosactide would result in an unmet clinical need for patients with hypsarrhythmia and/or infantile spasms. The PBAC noted that there is no clinical need for tetracosactide in the treatment of multiple sclerosis and considered that the current restriction for the treatment of hypsarrhythmia and/or infantile spasms should remain unchanged.
				Sponsor's Comment: The sponsor had no comment.

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INFLIXIMAB 100 mg powder for injection Inflectra® Pfizer Australia Pty Ltd Remicade® Janssen-Cilag Pty Ltd Renflexis® Organon Pharma Pty Ltd	Ulcerative colitis	To consider correspondence from Services Australia regarding whether patients treated under the acute severe restriction could transition to treatment under the moderate to severe restriction without having to first trial and fail other treatments.	The PBAC considered a request from treating physicians (via Services Australia) to allow patients treated with PBS-subsidised infliximab under the acute severe ulcerative colitis (ASUC) listing to subsequently transition to PBS-subsidised infliximab for the treatment of moderate to severe ulcerative colitis (MSUC) without having to demonstrate prior failure to alternative treatments. The PBAC noted a 'Review article: acute severe ulcerative colitis – evidence based consensus statements' (J.-H Chen, et al.) from the Australian Inflammatory Bowel Disease Consensus Working Group (2016); and a 'British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults' in Gut (2019), and considered that although there is limited evidence of efficacy of subsequent treatment of infliximab following ASUC, infliximab is generally better tolerated than thiopurines. The PBAC also noted an advice from the Drug Utilisation Sub-Committee (DUSC) that around 15 per cent of patients that initiated PBS-subsidised infliximab in 2018 for ASUC went on to receive PBS-subsidised infliximab for MSUC at the time of analysis on 31 March 2021. The PBAC considered it is reasonable that ASUC patients who responded to PBS-subsidised infliximab for the treatment of ASUC in the 4 months prior to transition to PBS-subsidised infliximab for MSUC not having to demonstrate failure with pre-treatment with a 5-aminosalicylate oral preparation and one of azathioprine, 6-mercaptopurine or oral steroids. The PBAC also considered that the eligibility of ongoing PBS-subsidised treatment with infliximab for this patient cohort requires to be assessed under the continuing restriction for the MSUC setting.
Systematic Review of treatments for Spinal Muscular Atrophy (SMA)	SMA	To request that the PBAC consider the Review and any comments from relevant Sponsors.	The PBAC considered a systematic literature review on current and emerging treatments for SMA and the stakeholder comments received. The PBAC noted the review focused on the SMA treatments of nusinersen, branaplam, risdiplam and onasemnogene abeparvovec, and provided a summary of published data for these treatments as of January 2021. The PBAC acknowledged that Biogen was the only sponsor company thus far to consider a "whole of disease approach" to SMA treatment. The PBAC noted that since the review was restricted to publically available information, the committee had considered the majority of the included clinical

			evidence as part of its previous considerations of nusinersen, risdiplam and onasemnogene abeparvovec. The PBAC considered there were limitations with the review in terms of types of publications included, noting non peer reviewed publications (for e.g. abstracts and company press releases) were included while reviews and indirect comparisons were excluded. While the PBAC noted indirect comparisons and reviews were excluded due to potential methodological issues with these types of analyses, it considered that an assessment of findings from these analyses and their limitations may have been informative. Overall, the PBAC considered that the findings from the review contributed little to the Committee's existing knowledge around SMA treatments, though the PBAC considered that the information provided about emerging longer term data for nusinersen and onasemnogene abeparvovec in paediatric patients was informative. The PBAC noted that the clinical management of SMA was changing, increasingly based around SMN2 copy number(s) rather than just a focus on age of symptom onset or SMA type classification. The PBAC noted that this was a result of the changing SMA diagnostic and testing landscape. The PBAC considered that this may have implications for existing and future listings for SMA treatments, for which consideration may need to be given regarding consistency with current clinical practice.

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Resubmission pathways

*There are four different resubmission pathways available to applicants following a 'not recommended' PBAC outcome. Resubmission pathways are not available for submissions that receive a positive recommendation from the PBAC. The resubmission pathways are classified into the following categories:	
Standard re-entry	The Standard Re-entry Pathway is the default pathway for resubmissions and also applies where: • an applicant chooses not to accept the PBAC nominated resubmission pathway; or • an Early Re-entry or Early Resolution Pathway has been nominated by the PBAC and an applicant decides to address issues other than those identified by the PBAC (including a subset of issues); or • an applicant decides to lodge later than the allowable timelines for the other pathways.
Early re-entry pathway	An Early Re-entry Pathway may be nominated by the PBAC where the PBAC considers that the remaining issues could be easily resolved and the medicine or vaccine does not represent HATV for the proposed population. Applicants who accept this pathway are eligible for PBAC consideration at the immediate next meeting.
Early resolution pathway	For medicines or vaccines deemed by the PBAC to represent High Added Therapeutic Value (HATV) AND where the PBAC considers that the remaining issues could be easily resolved, including when: • new clinical study data requiring evaluation is not considered necessary by the PBAC to support new clinical claims to be made in the resubmission; and • a revised model structure or input variable changes (beyond those specified by the PBAC) are not necessary to support any new economic claims, or to estimate the utilisation and financial impacts to be made in the resubmission. Applicants who accept this pathway are eligible for PBAC consideration out-of-session (before the main meeting), unless the department, in consultation with the PBAC Chair, identifies an unexpected issue such that the resubmission needs consideration at the next main PBAC meeting.
Facilitated resolution pathway	A Facilitated Resolution Pathway may be nominated by the PBAC where the PBAC considers the issues for resolution could be explored through a workshop AND where the medicine or vaccine meets the HATV criteria. Applicants who accept this pathway are eligible for a solution-focussed workshop with one or more members of the PBAC. The workshop agenda will be based on the issues for resolution outlined in the PBAC Minutes. This can be further clarified during the post-PBAC meeting with the Chair.