NOVEMBER 2020 PBAC OUTCOMES – SUBSEQUENT DECISIONS NOT TO RECOMMEND

DRUG NAME, FORM(S), STRENGTH(S), SPONSOR, TYPE OF SUBMISSION	TGA INDICATION	CURRENT PBS LISTING	LISTING REQUESTED BY SPONSOR / PURPOSE OF SUBMISSION	PBAC OUTCOME
APALUTAMIDE Tablet 60 mg Erlyand® Janssen-Cilag Pty Ltd New listing (Major Submission)	Treatment of patients with non-metastatic, castration-resistant prostate cancer.	Apalutamide is currently not PBS listed.	Resubmission to request an Authority Required (Telephone) listing for the treatment of castration resistant prostate cancer with no distant metastasis on conventional imaging.	The PBAC did not recommend the listing of apalutamide for the treatment of patients with non-metastatic castration-resistant prostate cancer (m0CRPC) who are at high risk of distant metastases. The PBAC considered that apalutamide provided a substantial benefit to some patients in delaying metastases; however, they considered that the magnitude of the survival benefit was modest. The PBAC noted that not all of the requested changes to the economic model were implemented in the resubmission and that the incremental cost-effectiveness ratio (ICER) remained high and uncertain, and that a price reduction would be required to bring the ICER into an acceptable range. The PBAC also considered that the estimated financial impact of listing apalutamide on the PBS remained high.
			Comparator: Watchful waiting (placebo)	The PBAC considered watchful waiting (placebo) remains the appropriate comparator.
			Clinical claim: A statistically significant and clinically important improvement in survival compared with watchful waiting.	Based on the updated data provided, the PBAC considered that apalutamide provides an overall survival benefit; however, the magnitude of this benefit was modest.
			Economic claim: Cost-utility analysis compared with watchful waiting	The PBAC noted that not all of the requested changes to the economic model were implemented in the resubmission and considered that the ICER remained high and uncertain. The PBAC considered that a price reduction would bring the ICER into an acceptable range.
			Sponsor's comment:	Janssen is disappointed with the PBAC's decision not to recommend the PBS listing of ERYLAND® (apalutamide) for the treatment of patients with high-risk castration-resistant prostate cancer with no distant metastases. Given the strength and maturity of the clinical data. Janssen does not agree with the PBAC that apalutamide only provides modest survival benefit and this is supported

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				by significant support from the clinical and patient communities that identified ERYLAND as being a high priority for PBS listing.
CRISABOROLE Ointment 2%, 30 g; Ointment 2%, 60 g Staquis® Pfizer Australia Pty Ltd New listing (Major Submission)	Crisaborole is indicated for the treatment of mild to moderate atopic dermatitis in patients aged 2 years and older.	Crisaborole is not currently PBS listed.	Resubmission to request an Authority Required (STREAMLINED) listing for the treatment of mild to moderate atopic dermatitis.	The PBAC did not recommend crisaborole for mild to moderate atopic dermatitis in patients who have failed to achieve satisfactory disease control with, are contraindicated to, or are intolerant to topical corticosteroids (TCS). The PBAC considered TCS are effective in patients with mild to moderate disease when used appropriately, and hence there is a low clinical need for crisaborole. The PBAC considered that the cost-effectiveness of crisaborole remained highly uncertain. The PBAC considered that the intended population was likely to be relatively small, however there was a high risk of use in a broader population, resulting in increased financial cost.
			Comparator: Pimecrolimus for face and eyelids, standard care for the rest of the body.	The PBAC previously accepted pimecrolimus was the appropriate comparator for the face and eyelids and standard care was the appropriate comparator for the rest of the body. The PBAC considered that despite the intention of the resubmission and the proposed restriction, there is a substantial risk that prescribers and patients will perceive crisaborole as a steroid sparer/alternative. When used in this way, topical corticosteroids would also be a relevant comparator.
			Clinical claim: Superior effectiveness and inferior safety compared with standard care, non-inferior effectiveness and safety compared with pimecrolimus.	The PBAC previously considered that overall the claim of superior effectiveness compared with standard management was not adequately supported by the data. The PBAC considered that the additional analyses presented did not substantially change the conclusion regarding efficacy. The PBAC considered that the claim of inferior comparative safety was reasonable. The PBAC considered that the changes in the indirect comparison with pimecrolimus did not substantially impact the overall

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				assessment of the comparison compared with the November 2018 submission. The PBAC considered that the claim of non-inferior comparative effectiveness compared with pimecrolimus was not adequately supported by the data. The PBAC considered that the claim of non-inferior comparative safety was reasonable.
			Economic claim: Cost-minimisation versus pimecrolimus and cost-effectiveness analysis versus standard care.	The PBAC noted the modelled cost-effectiveness analysis versus standard management, although substantially revised compared with that included in the November 2018 submission, resulted in ICERs that were highly uncertain. The PBAC considered the cost-minimisation analysis versus pimecrolimus may not be reasonable given the clinical claim of non-inferiority was inadequately supported.
			Sponsor's comment:	Pfizer is surprised at the PBAC's most recent view that there is a low clinical need for therapies to treat mild to moderate atopic dermatitis in patients who have failed to achieve satisfactory disease control with, are contraindicated to, or are intolerant to TCS. Such a view is not consistent with advice Pfizer received from clinicians and patients. There is currently no PBS-subsidised treatment available for this population, other than for patients whose face is affected. Pfizer disagrees that TCS are the appropriate comparator for a population whose clinical need is for an alternative to TCS. Pfizer believes that an appropriate risk sharing arrangement could be implemented, to manage the risk of use in a broader population than intended.

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MOGAMULIZUMAB Solution concentrate for I.V. infusion 20 mg in 5 mL Poteligeo® Kyowa Kirin Australia Pty Ltd New listing (Minor Submission)	The proposed TGA indication is the treatment of adult patients with mycosis fungoides (MF) or Sezary syndrome (SS) who have received at least one prior systemic therapy.	Mogamulizumab is not currently PBS listed.	Resubmission to request a Section 100 (Efficient Funding of Chemotherapy) Authority Required (Written) listing for patients with relapsed or refractory cutaneous T-cell lymphoma (CTCL) who have previously been treated with at least one prior systemic therapy.	The PBAC did not recommend the listing of mogamulizumab for the treatment of patients with relapsed or refractory CTCL. The PBAC considered the outcome on which the economic analysis was based, overall response, was variable across trials and had an unclear impact on final patient outcomes. In addition, the PBAC considered that mogamulizumab was not cost-effective at the price proposed in the submission on the basis that the incremental cost per responder (ORR) was unacceptably high and uncertain.
			Comparator: Vorinostat as the main comparator and brentuximab vedotin as the secondary comparator	The PBAC accepted the nomination of vorinostat as the main comparator and brentuximab vedotin as the secondary comparator.
			Clinical claim: Superior effectiveness with non-inferior safety to the main comparator vorinostat. No formal claim made for brentuximab vedotin.	No additional clinical trial data were presented to inform the clinical claims of the minor submission. As such, the PBAC reaffirmed its July 2020 advice, that while the claim of non-inferior comparative safety was reasonable the Committee did not consider the claim of superior comparative effectiveness to be adequately supported (paragraphs 7.7 and 7.8, mogamulizumab PBAC Minutes, July 2020 PBAC Meeting).
			Economic claim: Cost per responder (ORR) versus vorinostat	The PBAC considered that the ICER presented was unacceptably high based on previous PBAC decisions, even in the context of difficult to treat and relatively rare diseases. The PBAC considered that a considerable price reduction would be required in any future resubmission in order to show that mogamulizumab is cost-effective compared with vorinostat.
			Sponsor's comment:	The sponsor had no comment.

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NUSINERSEN Solution for injection 12 mg in 5 mL Spinraza® Biogen Australia Pty Ltd Change to listing (Major Submission)	Nusinersen is indicated for the treatment of 5q Spinal Muscular Atrophy (SMA)	At the time of PBAC consideration, nusinersen was PBS listed for use in patients with Type I, II or IIIa SMA with symptom onset prior to 3 years of age. Treatment must be initiated in patients 18 years of age or under.	Resubmission to request an extension to the current Section 100 (Highly Specialised Drugs Program) Authority Required (Written) listing to include the treatment of adults with SMA.	The PBAC did not recommend extending the listing of nusinersen to include the treatment of SMA in patients with symptom onset prior to 19 years of age, and removal of the age limit of 18 years for initiation of treatment. The PBAC recognised the high clinical need for effective treatments for adults with SMA. However, the PBAC considered that the resubmission had not adequately defined the appropriate adult population for nusinersen and proposed convening a consultation with experts in the clinical management of adult SMA to help resolve the specific issues associated with use of nusinersen in adult patients. The PBAC considered the magnitude and durability of benefit claimed in the submission was difficult to quantify based on the data presented. The PBAC noted that the sponsor had intended to submit additional clinical data, but this was unavailable at the time of PBAC consideration. As such, the PBAC noted that further data may become available in the near future which may help address some of the limitations of the clinical evidence. The PBAC considered that the incremental cost effectiveness ratio (ICER) was >$200,000 per quality adjusted life year (QALY) and likely underestimated. In addition to the aforementioned specific issues regarding the current subsidy proposal for nusinersen, the PBAC considered there was a need for stakeholders to work together to develop an overall and holistic approach to the treatment pathway and clinical evidence for SMA that takes into account the new treatment options that have become available over the past five years as well as developments in newborn screening and pre-conception and early pregnancy testing.

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				The PBAC noted that it first considered a subsidy proposal for the nusinersen in 2017-2018. Prior to that time, there were no direct treatments for SMA. However, since that time, PBAC has considered six more SMA subsidy proposals, including the two considered at this meeting. Further subsidy proposals are expected in the near future. The new subsidy proposals coming to PBAC are both for different groups of SMA patients, including pre-symptomatic and older patients, and for new treatments. The PBAC noted that other potential treatments for SMA include onasemnogene abeparvovec and branaplam (both Novartis products) and risdiplam (Roche). In light of these rapid developments in treatment and diagnosis, the PBAC considered it was in the interests of patients and families, prescribers and payers for a decision support analysis for SMA treatment that takes into account all the currently available clinical data and informs a broader "whole of disease" economic and financial analyses. The PBAC requested the Department convene a stakeholder meeting in the very near future including clinical experts, consumer representatives and relevant sponsors with the intention of progressing work on this decision support analysis.
			Comparator: Placebo/standard of care (SOC)	The PBAC accepted that SOC was an appropriate comparator
			Clinical claim: Superior effectiveness and non-inferior safety compared with SOC	The PBAC considered that, while the claim of superior comparative effectiveness was reasonable, the magnitude and durability of benefit was not able to be quantified based on the data presented.

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				The PBAC considered that the claim of non-inferior comparative safety was not adequately supported by the data, noting that there may be long term implications from repeated lumbar puncture administrations.
			Economic claim: Cost-utility analysis compared with SOC	The PBAC considered the incremental cost effectiveness ratio (ICER) was >$200,000 per QALY and likely underestimated. The PBAC considered that the transition probabilities were unreliable, the expected duration of benefit of nusinersen was not adequately substantiated, and the utility values were unlikely to capture the health-related quality of life of the patient population.
			Sponsor's comment:	Biogen welcomes the PBAC acknowledgement of the high clinical need for adults with SMA. Our submission for SPINRAZA treatment in adults living with SMA has shown clinically meaningful benefit for these individuals. Biogen will work as swiftly as possible to address the PBAC questions on the submission to try and enable access to this deserving population. We understand the PBAC proposal for a whole of disease review and recognise the diversity of the SMA patient population. We hope this review does not further delay access to SPINRAZA for adults living with SMA.

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PATIROMER Sachet, 8.4 g powder for oral liquid Sachet, 16.8 g powder for oral liquid Veltassa® Vifor Pharma Pty Ltd New listing (Major Submission)	Patiromer is indicated for the treatment of hyperkalaemia in adults.	Patiromer is not currently PBS listed.	Resubmission requested an Authority Required (Telephone) listing for patiromer for the initial treatment of patients with chronic kidney disease (CKD) Stage 3 or 4 and chronic hyperkalaemia who are receiving or indicated for renin angiotensin aldosterone system inhibitor (RAASi) therapy. The resubmission requested an Authority Required (STREAMLINED) listing for continuing treatment.	The PBAC did not recommend the listing of patiromer (Veltassa®) for the treatment of hyperkalaemia in patients with CKD Stage 3 or 4 and chronic hyperkalaemia who are receiving or indicated for RAASi therapy. The PBAC considered that the benefit in terms of patient-relevant outcomes in the Australian setting was uncertain, the resubmission had not adequately accounted for sodium polystyrene sulfonate (SPS) or calcium polystyrene sulfonate (CPS) resins as comparators, the estimated ICER was uncertain and significantly underestimated, and the total financial impact was high and uncertain.
			Comparator: Standard care (including low potassium diet and modification of concomitant medications such as RAASi therapy)	The PBAC accepted that standard care was an appropriate comparator, however, the PBAC maintained that intermittent use of SPS/CPS resins were also relevant comparators.
			Clinical claim: Superior efficacy compared to standard care alone. Inferior safety compared to standard care alone.	The PBAC considered that the claim of superior comparative effectiveness was adequately supported for the outcome of potassium lowering, however it was not supported for patient-relevant outcomes such as maintenance or optimisation of RAASi therapy and long-term cardiovascular and renal outcomes. The PBAC considered that the claim of inferior comparative safety was reasonable noting the potential for hypokalaemia and hypomagnesaemia
			Economic claim: Cost-effectiveness analysis versus standard care (placebo).	The PBAC considered the economic model was unreliable and that many of the assumptions lacked face validity. In particular, the PBAC noted that the economic model assumed a median duration of patiromer treatment of 3 months. The PBAC considered it was highly implausible that short-term patiromer treatment would lead to patients

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				remaining on full RAASi therapy for a prolonged period and gaining long-term cardiovascular and renal benefits.
			Sponsor's comment:	Vifor Pharma is disappointed by the PBAC's decision not to recommend Veltassa® (patiromer). Vifor Pharma remains committed to ensuring that this continuous treatment option for the management of chronic hyperkalaemia is made available to Australian patients.