PHARMACEUTICAL BENEFITS ADVISORY COMMITTEE (PBAC) MEETING OUTCOMES
MARCH 2021 PBAC 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	PBAC RECOMMENDATION
ABEMACICLIB Tablet 150 mg Tablet 100 mg Tablet 50 mg Verzenio® Eli Lilly Australia Pty Ltd Change to PBS listing (Major Submission)	Breast cancer	To request an Authority Required (Telephone/Online) listing for the treatment of hormone receptor positive (HR+) human epidermal growth factor receptor 2 negative (HER2-) inoperable locally advanced or metastatic breast cancer.	Recommended	The PBAC recommended the listing of abemaciclib in combination with fulvestrant, for the treatment of non-premenopausal patients with HR+ and HER2- inoperable locally advanced or metastatic breast cancer. The PBAC considered that abemaciclib + fulvestrant was non-inferior in terms of comparative effectiveness and safety compared with ribociclib + fulvestrant while noting there were differences between the safety profiles of abemaciclib and ribociclib. The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of abemaciclib + fulvestrant would be acceptable if it were cost-minimised to ribociclib + fulvestrant.
ACICLOVIR Eye ointment 30 mg per g, 4.5 g Xorox® Clinect Pty Ltd New PBS listing (Minor Submission)	Herpes simplex keratitis	To request a Restricted Benefit listing for a new brand of aciclovir for the treatment of Herpes simplex keratitis (HSK) under the same conditions as the currently listed aciclovir eye ointment.	Not recommended	The PBAC did not recommend the listing of the Xorox brand of aciclovir 3% eye ointment for the treatment of HSK. The PBAC considered there was an inadequate basis for the requested approved ex-manufacturer price (AEMP), which was higher than the delisted Zovirax and the currently listed Section 19A approved product, AciVision. Sponsor's Comment: Clinect and the Department of Health are working towards an alternative pathway to listing this product.

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AMINO ACID FORMULA WITH FAT, CARBOHYDRATE, VITAMINS, MINERALS, TRACE ELEMENTS AND MEDIUM CHAIN TRYGLYCERIDES Oral powder 800 g Essential Care Jr® Cortex Health Pty Ltd New PBS listing (Minor Submission)	Multiple food allergies and various gastrointestinal disorders and allergic conditions	To request an Authority Required (Telephone) listing for the treatment of a number of different gastrointestinal (GI) intolerance and allergy indications under the same conditions as the currently listed comparator.	Recommended	The PBAC recommended the listing of Essential Care Jr under conditions which are consistent with the PBS-listed Neocate Junior.
ATEZOLIZUMAB Solution concentrate for I.V. infusion 840 mg in 14 mL Tecentriq® Roche Products Pty Ltd Change to PBS listing (Major Submission)	Breast cancer	Resubmission to request a Section 100 (Efficient Funding of Chemotherapy) Authority Required (STREAMLINED) listing for the first-line treatment of metastatic triple negative breast cancer.	Not recommended	The PBAC did not recommend atezolizumab for the first line treatment of patients with metastatic triple-negative breast cancer who are PD-L1 positive. The PBAC acknowledged that there was a high clinical need for effective treatments for these patients. <u>Comparator: nab-paclitaxel</u> The PBAC considered the appropriate comparator was physician choice as nab-paclitaxel is not the only treatment pathway for this population and in some patients, may be an inferior treatment choice. <u>Clinical claim: superiority compared with nab-paclitaxel</u> The PBAC considered the survival benefit claimed was uncertain due to the comparator and because the overall survival benefit was not statistically significant. The PBAC noted that the resubmission provided updated trial data, but considered the additional data did not provide confidence that atezolizumab provided the claimed overall survival benefit. In addition, the PBAC noted that a confirmatory trial in a similar patient group had reported contradictory results. <u>Economic claim: cost-effectiveness compared with nab- paclitaxel</u> The PBAC noted that the incremental cost-effectiveness ratio remained high and modelled assumptions regarding overall survival were not sufficiently supported by the clinical evidence. The PBAC considered that the overall survival extrapolations applied were not appropriately conservative and the

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				proposed caps did not provide confidence in the cost-effectiveness of atezolizumab. Sponsor's Comment: Roche is disappointed with the outcome of this submission. We remain committed to Australian triple negative breast cancer patients and will continue to seek innovative therapeutic developments in this area of clinically unmet need.
AVELUMAB Solution concentrate for I.V. infusion 200 mg in 10 mL Bavencio® Merck Healthcare Pty Ltd Change to PBS listing (Major Submission)	Urothelial carcinoma	To request a Section 100 (Efficient Funding of Chemotherapy) Authority Required (STREAMLINED) listing for the first-line maintenance treatment of locally advanced (Stage III) or metastatic (Stage IV) urothelial carcinoma.	Recommended	The PBAC recommended a Section 100 (Efficient Funding of Chemotherapy) Authority Required (Telephone/Online) listing for avelumab for the maintenance treatment of Stage III or Stage IV urothelial carcinoma in patients whose disease has not progressed following first-line platinum-based chemotherapy. The PBAC considered that the appropriate comparator would be best supportive care with subsequent therapy with pembrolizumab on progression. The PBAC considered that, while the magnitude of the incremental benefit of the use of maintenance avelumab versus initiation of pembrolizumab on disease progression was uncertain, it was likely avelumab in this context would offer benefit to some patients. The PBAC considered that the incremental cost-effectiveness ratio was underestimated due to reliance on optimistic assumptions and inputs in the economic model. The PBAC considered that with the appropriate model inputs the cost-effectiveness of avelumab could be brought into an acceptable range with a price reduction.
AVELUMAB Solution concentrate for I.V. infusion 200 mg in 10 mL Bavencio® Merck Healthcare Pty Ltd Change to PBS listing (Minor Submission)	Renal cell carcinoma (RCC)	Resubmission to request a Section 100 (Efficient Funding of Chemotherapy) Authority Required (STREAMLINED) listing, in combination with axitinib, for the first-line treatment of patients with Stage IV clear cell variant RCC.	Recommended	The PBAC recommended the listing of avelumab in combination with axitinib (AVE + AXI), for the first-line treatment of Stage IV clear cell variant RCC in patients classified as intermediate or poor according to the International Metastatic Renal Cell Carcinoma Database Consortium (IMDC) prognostic criteria. The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of AVE + AXI would be acceptable if it were cost-minimised to nivolumab in combination with ipilimumab (NIVO + IPI). The PBAC considered that the totality of clinical evidence supported a benefit for AVE+AXI compared to sunitinib and non-inferiority compared to NIVO + IPI. The PBAC considered there is a modest clinical need for an alternative treatment for RCC, and that AVE + AXI may benefit patients who may not be suitable for NIVO + IPI.

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BEVACIZUMAB Solution for I.V. infusion 100 mg in 4 mL Solution for I.V. infusion 400 mg in 16 mL Mvasi® Amgen Australia Pty Ltd Change to PBS listing (Minor Submission)	Non-small cell lung cancer (NSCLC)	To request changes to the restriction wording for Mvasi for treatment of NSCLC under Section 100 (Efficient Funding of Chemotherapy).	Recommended	The PBAC recommended the listing of bevacizumab under Section 100 (Efficient Funding of Chemotherapy) as an unrestricted benefit. The PBAC considered that changing the current bevacizumab restriction for all currently listed indications to unrestricted would allow access to combination treatment with atezolizumab so that no patients would be disadvantaged. The PBAC noted that an unrestricted listing for bevacizumab would likely increase utilisation of bevacizumab. Therefore, the PBAC considered that for the listing to be cost-effective, a price reduction would be needed to offset the likely increase in utilisation, in addition to the statutory price reduction that would apply when any of the recommended biosimilar brands of bevacizumab is listed on the PBS.
BRENTUXIMAB VEDOTIN Powder for I.V. infusion 50 mg Adcetris® Takeda Pharmaceuticals Australia Pty Ltd Change to PBS listing (Major Submission)	T-cell lymphoma	To request a Section 100 (Efficient Funding of Chemotherapy) Authority Required (STREAMLINED) listing for the first-line treatment of CD30 positive peripheral T-cell lymphoma.	Recommended	The PBAC recommended the listing of brentuximab vedotin (BV), for use in combination with combination with cyclophosphamide, doxorubicin, and prednisone (CHP) for the treatment of patients with previously untreated CD30 positive peripheral T-cell lymphoma. The PBAC accepted that BV+CHP was clinically superior in terms of progression free survival compared to cyclophosphamide, doxorubicin, vincristine and prednisone and that the immature overall survival data also suggested a clinical benefit. The PBAC also accepted that BV+CHP was non-inferior in terms of safety. The PBAC considered the incremental cost-effectiveness ratio was high but acceptable at the proposed price in the context of this rare disease with a high clinical need and the certainty of the estimated ICER.
BROLUCIZUMAB Solution for injection 19.8 mg in 0.165 mL pre-filled syringe Beovu® Novartis Pharmaceuticals Australia Pty Ltd New PBS listing (Major Submission)	Wet age-related macular degeneration (AMD)	To request an Authority Required (Written) listing for the treatment of neovascular (wet) AMD.	Recommended	The PBAC recommended the listing of brolucizumab for the treatment of subfoveal choroidal neovascularisation (CNV) due to AMD in patients who are non-responsive despite first-line anti-vascular endothelial growth factor (VEGF) treatment. The PBAC considered that a second- or subsequent-line treatment option of brolucizumab in CNV due to AMD would be useful for patients who have ongoing exudation/fluid despite first-line anti-VEGF treatment. The PBAC considered the cost-effectiveness of brolucizumab would be acceptable in the later-line setting as it is likely to be equi-effective to currently listed anti-VEGF agents (aflibercept and ranibizumab). The PBAC advised that brolucizumab would be required to join the risk sharing arrangement currently in place for ranibizumab and aflibercept in this indication.

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BUDESONIDE Tablet (orally disintegrating) 1 mg Jorveza® Dr Falk Pharma Australia Pty Ltd New PBS listing (Major Submission)	Eosinophilic Oesophagitis (EoE)	To request an Authority Required (STREAMLINED) listing for the treatment of EoE.	Not recommended	The PBAC did not recommend budesonide orally disintegrating tablets (BOT) for the treatment of EoE. The PBAC considered the clinical claim of superiority of BOT compared to placebo for both induction and maintenance therapy to be well supported by the evidence. However, the PBAC considered PBS listing for use in the maintenance therapy setting is beyond the maximum duration of treatment reflected in the current approved product information. The PBAC considered the cost-effectiveness of induction therapy alone to be uncertain and the incremental cost-effectiveness ratio for both induction and maintenance therapy to be high and uncertain at the proposed price. The PBAC nominated the Early Re-entry resubmission pathway* for this item. <u>Sponsor's Comment:</u> Dr Falk Pharma Australia are disappointed that the Jorveza submission was unsuccessful on this occasion, but will work with the Department to resolve the open issues and resubmit so that this important treatment is made available to patients suffering from this chronic condition.
BUROSUMAB Injection 10 mg in 1 mL Injection 20 mg in 1 mL Injection 30 mg in 1 mL Crysvita® Kyowa Kirin Australia Pty Ltd New PBS listing (Major Submission)	X-linked hypo-phosphataemia (XLH)	To request a Section 100 (Highly Specialised Drugs Program) Authority Required (Written) listing for the treatment of XLH.	Not recommended	The PBAC did not recommend burosumab for the treatment of paediatric patients with XLH. The PBAC considered that there were complex issues relating to the clinical evidence presented and the proposed restriction. In addition, the PBAC considered that the incremental cost effectiveness ratio was high and likely underestimated and that the financial estimates were highly uncertain. <u>Sponsor's Comment:</u> Kyowa Kirin Australia is disappointed by the decision not to recommend the PBS listing of burosumab (Crysvita) for the treatment of children with X-linked hypophosphataemia (XLH). There is a high clinical need for new treatments for this condition and Kyowa Kirin will continue to work towards bringing burosumab to XLH patients in Australia.

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CABAZITAXEL Concentrated injection 60 mg (as acetone solvate) in 1.5 mL, with diluent Cabazitaxel Ever Pharma® Interpharma Pty Ltd Change to PBS listing (Minor Submission)	Prostate cancer	To request a Section 100 (Efficient Funding of Chemotherapy) Authority Required (STREAMLINED) listing for a new brand with a different form for the same conditions as the currently listed cabazitaxel.	Recommended	The PBAC recommended the listing of a new form of cabazitaxel, Cabazitaxel Ever Pharma, for the treatment of patients with castration resistant metastatic carcinoma of the prostate, under the same conditions as Jevtana, the currently listed cabazitaxel brand, under Section 100 (Efficient Funding of Chemotherapy).
CABOTEGRAVIR AND RILPIVIRINE Pack containing 1 injection of cabotegravir 600 mg in 3 mL and 1 injection of rilpivirine 900 mg in 3mL Cabenuva® ViiV Healthcare Pty Ltd New PBS listing (Major Submission)	Human Immuno-deficiency virus (HIV)	To request a Section 100 (Highly Specialised Drugs Program - Community Access) Authority Required (STREAMLINED) listing for the treatment of HIV infection in adults who are virologically suppressed.	Not recommended	The PBAC did not recommend the listing of cabotegravir (CAB) tablets or cabotegravir and rilpivirine long acting injections (CAB LA + RPV LA). In deciding not to recommend the listing, the PBAC considered the presented evidence did not support a conclusion that CAB and CAB LA + RPV LA offered advantages in terms of quality of life, reduced anxiety or worry due associated with daily oral therapy or fear of unintentional disclosure of HIV status. The Committee acknowledged that some people living with HIV feel anxiety and worry with regards to the daily reminder of daily oral therapy and the risk of unwanted disclosure of HIV status, and these issues negatively impact their lives. However, the PBAC was uncertain the availability of a long acting injectable alternative to oral anti-retroviral therapy (ART) would provide tangible improvements in patients' quality of life and further considered the clinical data was of uncertain clinical significance in terms of potential quality of life benefits and the economic analyses presented did not allow an exploration of these issues. The PBAC considered the economic analysis, which relied on a cost benefit analysis (CBA) rather than a formal cost utility analysis (CUA) was uninformative for decision-making as it did not capture or allow exploration of the factors for which advantages over daily oral ART were claimed. The PBAC nominated the Early Re-entry resubmission pathway* for this item.

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				Sponsor's Comment: ViiV Healthcare maintains there is strong evidence to support the claim that CAB LA + RPV LA (Cabenuva) provides additional benefit compared with daily oral therapy for many people living with HIV in terms of quality of life, reducing the burden of the daily reminder of HIV, reduced anxiety or worry associated with adherence to daily oral therapy or fear of unintentional disclosure of HIV status. ViiV will continue to work with the PBAC to ensure this innovative treatment option becomes available to Australians living with HIV.
CICLOSPORIN Eye drops 0.1%, single dose units 0.4 mL, 30 Ikervis® Seqirus (Australia) Pty Ltd New PBS listing (Major Submission)	Dry eye disease in patients with keratitis	To request an Authority Required (STREAMLINED) listing for the treatment of dry eye disease with keratitis.	Recommended	The PBAC recommended the listing of ciclosporin for the treatment of severe keratitis with dry eye disease The PBAC was satisfied that ciclosporin provides, for some patients, a significant improvement in efficacy over best supportive care. The PBAC considered that ciclosporin was cost effective at the price offered in the pre-PBAC response. The PBAC considered that the financial implication estimates were uncertain and recommended that a risk sharing arrangement be implemented.
DAROLUTAMIDE Tablet 300 mg Nubeqa® Bayer Australia Ltd New PBS listing (Major Submission)	Prostate cancer	Resubmission to request an Authority Required (Telephone) listing for the treatment of non-metastatic castration resistant carcinoma of the prostate (m0CRPC).	Not recommended	The PBAC did not recommend the listing of darolutamide for the treatment of patients with m0CRPC who are at high risk of distant metastases. The submission nominated best supportive care as the comparator, consistent with previous PBAC advice; however, the PBAC considered that based on changing clinical practice, abiraterone and enzalutamide were also relevant comparators. The PBAC noted that the resubmission provided revisions to the economic model, but considered that the resultant incremental cost effectiveness ratio (ICER) remained underestimated and high at the proposed price. Further, the PBAC considered that the size of the incremental population relative to the existing market for abiraterone and enzalutamide, and thus the net financial impact of listing darolutamide, was substantially overestimated. The PBAC nominated the Early Re-entry resubmission pathway* for this item. Comparator: watchful waiting (placebo) The PBAC considered watchful waiting (placebo) remains an appropriate comparator. The PBAC considered that changing clinical practices also supported the current treatments for metastatic castration resistant prostate cancer (i.e. abiraterone and enzalutamide) also being relevant comparators.

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				Clinical claims: Darolutamide was superior in terms of effectiveness and inferior in terms of safety compared with placebo. Darolutamide was non-inferior in terms of efficacy and safety compared with apalutamide and enzalutamide. The PBAC considered that the clinical claims versus placebo were reasonable, but that magnitude of the survival benefit was uncertain due to the immaturity of the data. The PBAC considered that the clinical claims versus apalutamide and enzalutamide were reasonable. Economic claim: cost-utility analysis compared with watchful waiting The PBAC noted that the ICER remained high and uncertain. The PBAC considered that the incremental quality adjusted life years (QALYs) gained were overestimated and recommended that a cost minimisation analysis be conducted with abiraterone or enzalutamide. The PBAC noted that the ICER was cost effective if the cost-minimised price was applied in the model with more appropriate assumptions relating to extrapolation and utility values.
				Sponsor's Comment: Bayer is disappointed by the PBAC's decision not to recommend darolutamide for the treatment of castration resistant carcinoma of the prostate. Bayer remains committed to working with the PBAC to find a pathway forward to ensure darolutamide is made available to Australian patients through the PBS.
DECITABINE AND CEDAZURIDINE Tablet containing decitabine 35 mg + cedazuridine 100 mg Inqovi® Otsuka Australia Pharmaceutical Pty Ltd New PBS listing (Major Submission)	Myelodysplastic syndromes (MDS) and chronic myelomonocytic leukaemia (CMML)	To request an Authority Required (Non-immediate/Delayed) - In Writing only/Electronic listing for the treatment of high risk MDS and CMML.	Not recommended	The PBAC did not recommend the listing of decitabine+cedazuridine for the treatment of patients with MDS classified as intermediate-2 or high-risk according to the International Prognostic Scoring System (IPSS) and patients with CMML. The PBAC acknowledged the advantages of decitabine+cedazuridine being an oral treatment, in particular for patients living in rural and remote areas, whereas the current standard of care, azacitidine, is administered subcutaneously or intravenously and requires attendance at an outpatient clinic for seven days each month. However, the PBAC considered the claims of non-inferior effectiveness and safety compared with azacitidine to be uncertain. The PBAC considered that this uncertainty also impacted on the reliability of the cost minimisation analysis presented in the submission. The PBAC nominated the Early Re-entry resubmission pathway* for this item.

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				Sponsor's Comment: Otsuka Australia Pharmaceutical is disappointed that decitabine+cedazuridine has not received a positive recommendation and is committed to working with the PBAC and the Department of Health to find a way to make this important treatment accessible to patients in Australia.
DEUTETRABENAZINE Tablet 6 mg Tablet 9 mg Tablet 12 mg Austedo® Teva Pharma Australia Pty Ltd New PBS listing (Major Submission)	Chorea associated with Huntington's Disease (HD)	To request an Authority Required listing for the treatment of mild, moderate and severe chorea associated with HD.	Not recommended	The PBAC did not recommend the listing of deutetrabenazine for the treatment of chorea associated with HD in patients who have failed prior tetrabenazine treatment due to intolerance or inadequate response. The PBAC considered the proposed clinical place of deutetrabenazine as second line treatment was inappropriate and considered that the most appropriate clinical place for deutetrabenazine was first-line treatment as an alternative to tetrabenazine (irrespective of prior or co-therapy with an antipsychotic). The PBAC further noted the evidence base was primarily as a first-line treatment option and there was no evidence provided to support use in the requested place in therapy. The PBAC also considered the economic model constructed for the proposed place in therapy was unreliable for decision-making. The PBAC acknowledged the devastating impact HD has on patients and their families and considered there was a high clinical need for new therapies to assist patients with the wide range of debilitating physical and mental impacts of this disease and improve quality of life. The Committee considered that whilst deutetrabenazine likely represents an effective treatment option for the treatment of chorea symptoms in people with HD the most appropriate approach for considering its comparative efficacy, safety and cost-effectiveness was to compare it to tetrabenazine, its non-deuterated analogue.
				Sponsor's Comment: Teva is committed to working with the PBAC to achieve a listing for deutetrabenazine.

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ELEXACAFTOR/ TEZACAFTOR/ 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 (Major Submission)	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.	Defer	The PBAC deferred making a recommendation to list elexacaftor/tezacaftor/ivacaftor (ELX/TEZ/IVA) for the treatment of CF patients aged 12 years and older who have at least one F508del mutation in the CFTR gene. The PBAC considered ELX/TEZ/IVA provided a significant benefit for some patients, in particular, patients who are homozygous for the F508del mutation in the CFTR gene and patients who are heterozygous for the F508del mutation in the CFTR gene with a minimal function mutation. The PBAC considered the safety and effectiveness of ELX/TEZ/IVA beyond 48 weeks was uncertain but this could be managed with an appropriate Managed Access Program (MAP), similar to what is in place for the other CFTR modulators. The PBAC deferred making a recommendation in order to allow engagement with the sponsor to align the proposed listing of ELX/TEZ/IVA, and associated costs and financial implications with the MAP and risk share arrangements of the currently listed CFTR modulators, with the cost-effectiveness link with these comparators having not satisfactorily been established by the submission. <u>Sponsor's Comment:</u> Vertex is pleased that the PBAC has acknowledged the significant benefits that Trikafta® (elexacaftor/tezacaftor/ivacaftor) can bring to Cystic Fibrosis (CF) patients. Vertex, along with the CF community, was hopeful for a first time PBAC recommendation for Trikafta, particularly given our involvement in the TGA-PBAC Alignment Pilot, which has the overall objective of aligning the regulation and reimbursement process to ensure patients have access to medicines as soon as possible. However, we are committed to continuing to work collaboratively with the PBAC to ensure all eligible patients (estimated 2,200 patients based on the Australian Cystic Fibrosis Disease Registry Annual Report 2019) who can benefit from treatment have government-funded access to Trikafta as quickly as possible.
ENCORAFENIB Capsule 50 mg Capsule 75 mg Braftovi®	Colorectal cancer	To request an Authority Required (STREAMLINED) listing for the treatment of BRAF V600E-variant metastatic (Stage IV) colorectal cancer (mCRC).	Defer	The PBAC deferred its decision about encorafenib for the 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. The PBAC foreshadowed its support for recommending that the combination of therapies be listed. It 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

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Pierre Fabre Australia Pty Ltd Change to PBS listing (Major Submission)				PBAC considered that the cost-effectiveness and estimated financial impact were acceptable. If MSAC decided to support the MBS listing of BRAF V600 testing in mCRC, PBAC would support an expedited process for reconsideration to align any PBAC recommendation for listing encorafenib with the circumstances supported by MSAC. Sponsor's Comment: Pierre Fabre welcome the opportunity to work with PBAC and MSAC to expedite availability of Braftovi® (encorafenib) in combination with cetuximab for patients with BRAF V600E variant mCRC.
ENZALUTAMIDE; ABIRATERONE ACETATE Capsule 40 mg Tablet 500 mg Tablet 250 mg Xtandi®; Zytiga® Astellas Pharma Australia Pty Ltd; Janssen-Cilag Pty Ltd Change to PBS listing (Other Business Submission)	Prostate cancer	To seek the PBAC's advice on amending the existing listings for enzalutamide and abiraterone to allow their use prior to docetaxel in patients with metastatic castrate-resistant prostate cancer (mCRPC).	Recommended	The PBAC recommended amending the listings of abiraterone and enzalutamide to allow their use in patients with mCRPC without prior use of docetaxel. The PBAC considered that removal of the requirement for patients to have either received prior docetaxel or to have a predicted intolerance to docetaxel would better align the restrictions for abiraterone and enzalutamide with how these drugs are being used in clinical practice and with their TGA indications. The PBAC considered that there would be no financial impact, as amending the restrictions will align them with current clinical practice.
ESLICARBAZEPINE Tablet 800 mg Zebinix® Stada Pharmaceuticals Australia Pty Ltd New PBS listing (Major Submission)	Epilepsy	To request an Authority Required (STREAMLINED) listing for the treatment of epilepsy in patients aged 16 years or older with partial onset seizures with or without secondary generalisation.	Not recommended	The PBAC did not recommend the listing of eslicarbazepine (ESL) for the treatment of intractable partial epileptic seizures, with or without secondary generalised seizures. The PBAC considered that the efficacy of ESL compared to placebo, and the claim of non-inferior effectiveness and safety of ESL compared with lacosamide, was not supported by the clinical data and indirect treatment comparison. The PBAC also considered that the economic analysis was problematic with respect to the estimation of equi-effective doses. Sponsor's Comment: STADA is disappointed with the outcome. STADA is committed to work collaboratively with the Department of Health to review our progress. This aligns with STADA's mission to care for people's health and we will still work towards the opportunity to provide patients with refractory epilepsy in Australia to access eslicarbazepine acetate through the PBAC.

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EVOLOCUMAB Injection 420 mg in 3.5 mL single use pre-filled cartridge Repatha® Amgen Australia Pty Ltd Change to PBS listing (Minor Submission)	Familial heterozygous hyper-cholesterolaemia; Non-familial hyper-cholesterolaemia; Familial homozygous hyper-cholesterolaemia	To request an Authority Required listing for a new form of evolocumab under the same conditions as the already listed evolocumab 420 mg/3.5 mL pre-filled pen.	Recommended	The PBAC held no objections to the planned discontinuation of the existing evolocumab 420 mg/3.5 mL injection (cartridge presentation) and its replacement with an updated product whereby the modified automated mini-doser will shorten the injection time from 9 minutes to 5 minutes. The PBAC noted there have been no changes to the drug or cartridge container with the design change, and that the current PBS listings of evolocumab 420 mg/3.5 mL do not require any amendments.
FILGOTINIB Tablet 100 mg Tablet 200 mg Jyseleca® Gilead Sciences Pty Ltd New PBS listing (Major Submission)	Rheumatoid arthritis	To request an Authority Required (Written) listing for the treatment of severe active rheumatoid arthritis.	Not Applicable	This submission was withdrawn
GEMTUZUMAB OZOGAMICIN Powder for injection 5 mg Mylotarg® Pfizer Australia Pty Ltd New PBS listing (Major Submission)	Acute myeloid leukaemia (AML)	To request Section 100 (Efficient Funding of Chemotherapy) Authority Required (Telephone) listing for the treatment of de novo CD33-positive AML.	Not recommended	The PBAC did not recommend gemtuzumab ozogamicin for the treatment of de novo CD33-positive AML patients, except acute promyelocytic leukaemia, who do not have an unfavourable cytogenetic profile. The PBAC considered, based on the clinical evidence presented, that the magnitude of the overall survival benefit over current standard of care in the proposed PBS population was difficult to determine. The PBAC noted that the economic model was complex and difficult to assess and considered the incremental cost effectiveness ratio highly uncertain. <u>Sponsor's Comment:</u> Pfizer looks forward to continuing to work with the PBAC and the Department of Health to provide access to gemtuzumab ozogamicin for de novo CD33-positive AML patients.

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GLATIRAMER Injection containing glatiramer acetate 20 mg in 1 mL single dose pre-filled syringe Injection containing glatiramer acetate 40 mg in 1 mL single dose pre-filled syringe Glatira® Juno Pharmaceuticals Pty Ltd New PBS listing (Minor Submission)	Multiple sclerosis	To request an Authority Required (STREAMLINED) listing of a new brand with two different strengths under the same conditions as the currently listed glatiramer pre-filled syringe.	Recommended	The PBAC recommended the listing of a new brand of glatiramer, Glatira 40 mg/mL injection, and the listing of Glatira 20 mg/mL injection, on the PBS for the treatment of multiple sclerosis. The PBAC recommended the listings on a cost-minimisation basis to the Copaxone brand of glatiramer. The PBAC noted that the TGA considered Glatira and Copaxone to be therapeutically equivalent. The PBAC advised, under Section 101 (4AACD) of the *National Health Act 1953*, that Glatira 40 mg/mL injection and Copaxone 40 mg/mL injection should be considered equivalent for the purposes of substitution.
GUSELKUMAB Injection 100 mg in 1 mL single use pre-filled pen Tremfya® Janssen-Cilag Pty Ltd Change to PBS listing (Minor Submission)	Severe chronic plaque psoriasis (CPP)	Resubmission to request an Authority Required (Written) listing for a new form for the treatment of severe CPP under the same conditions as the currently listed guselkumab injection syringe.	Not recommended	The PBAC reaffirmed its recommendation from July 2020 that guselkumab 100 mg pre-filled pen be listed, under the same arrangements as the currently listed guselkumab pre-filled syringe, on a cost-minimisation basis against the lowest cost PBS-listed biological disease-modifying antirheumatic drugs (bDMARDs) for the treatment of severe CPP. The PBAC considered that guselkumab pre-filled pen did not satisfy the criteria for a price higher than the lowest cost of other available PBS-listed bDMARDs for the treatment of severe CPP. <u>Sponsor's Comment:</u> Janssen considers that the guselkumab pre-filled pen (PFP) will only replace the pre-filled syringe (PFS) form of guselkumab currently listed on the PBS and as such, should not be cost-minimised to the lowest cost biological disease-modifying antirheumatic drugs (bDMARDs) for severe CPP. Janssen is unable to move forward with this recommendation as we believe that the introduction of patient-centric innovations, like the PFP, should not be disincentivised.

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HIGH FAT FORMULA WITH VITAMINS, MINERALS AND TRACE ELEMENTS AND LOW IN PROTEIN AND CARBOHYDRATE Oral semi-solid, 100 g, 36 K.Yo® Vitaflo Australia Pty Ltd Change to PBS listing (Minor Submission)	Dietary management of conditions requiring a ketogenic diet	To request a Restricted Benefit listing of a new brand with a different pack size and formulation.	Recommended	The PBAC recommended the listing of K.Yo to replace the PBS-listed brand Keyo.
HIGH FAT FORMULA WITH VITAMINS, MINERALS AND TRACE ELEMENTS AND LOW IN PROTEIN AND CARBOHYDRATE Oral powder 300 g KetoCal 3:1® KetoCal 4:1® Nutricia Australia Pty Ltd Change to PBS listing (Minor Submission)	Ketogenic Diet	To request approval for changing the nutrient composition for the already listed KetoCal 3:1 and KetoCal 4:1.	Recommended	The PBAC recommended continuing the Restricted Benefit listing of KetoCal 3:1 and KetoCal 4:1 with new formulations under their existing conditions.

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LACOSAMIDE Tablet 50 mg Tablet 100 mg Tablet 150 mg Tablet 200 mg Oral solution 10 mg per mL, 200 mL Vimpat® UCB Australia Proprietary Ltd Change to PBS listing (Major Submission)	Epilepsy	To request an Authority Required (STREAMLINED) listing for the treatment of idiopathic generalised epilepsy with primary generalised tonic-clonic seizures.	Recommended	The PBAC recommended the listing of lacosamide for the treatment of patients with idiopathic generalised epilepsy with primary generalised tonic-clonic seizures on a cost minimisation basis to perampanel. The PBAC advised the equi-effective doses have a daily dose relativity of lacosamide to perampanel of 50:1, where twice-a-day dosing of lacosamide 50 mg, 100 mg, 150 mg and 200 mg is equal to once daily dosing of perampanel 2 mg, 4 mg, 6 mg and 8 mg, 10 mg, 12 mg, respectively.
MELATONIN Tablet 1 mg Tablet 5 mg Slenyto® Aspen Pharmacare Australia Pty Ltd New PBS listing (Major Submission)	Insomnia	To request an Authority Required (Telephone) listing for the treatment of insomnia in patients aged between the ages of 2 to 18 with Autism Spectrum Disorder (ASD) and/or Smith-Magenis syndrome (SMS).	Not recommended	The PBAC did not recommend the listing of melatonin for the treatment of insomnia in children aged 2-18 years with ASD and/or SMS where sleep hygiene measures have been insufficient. In deciding not to recommend melatonin for the requested populations, the PBAC considered the evidence presented indicated that while melatonin may be effective at increasing total sleep time (TST) per night for some patients, the effect was highly variable and of uncertain and likely modest clinical benefit. The PBAC considered the cost effectiveness of melatonin at the price requested in the submission could not reliably be assessed with the economic model provided. The PBAC considered the estimated number of patients likely to be treated with melatonin was poorly supported and the financial estimates were high and uncertain. Given the very high need for effective treatments in the SMS population, the PBAC considered prolonged release melatonin may be acceptably cost-effective for this small, well-defined population at a price consistent with that of extemporaneously compounded melatonin. The PBAC nominated the Early Re-entry resubmission pathway* for the SMS population if outstanding issues were addressed. <u>Sponsor's Comment:</u> Aspen is pleased that the PBAC has recognised a place for Slenyto PR in the SMS population. Aspen is looking forward to addressing the outstanding issues for the early re-entry resubmission pathway for this patient group, and working with the PBAC to potentially expand the listing to include ASD patients in the future.

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NINTEDANIB Capsule 100 mg Capsule 150 mg Ofev® Boehringer Ingelheim Pty Ltd Change to PBS listing (Major Submission)	Progressive fibrosing interstitial lung disease (PF-ILD)	To request an Authority Required (Written) listing for the treatment of PF-ILD.	Not recommended	The PBAC did not recommend the listing of nintedanib for the treatment of patients with PF-ILD. The PBAC considered that the available data indicated a benefit in terms of slowing decline in lung function compared with best supportive care (BSC); however, the PBAC considered that although an overall survival benefit was plausible, the magnitude of any such benefit was uncertain. The PBAC considered the incremental cost-effectiveness ratio (ICER) was uncertain and likely underestimated, primarily due to the uncertainty around the modelled overall survival benefit. The PBAC advised that a price reduction would be required to address this uncertainty and to achieve an acceptable ICER. The PBAC considered the financial impact was overestimated in the submission due to the prevalence of PF-ILD used, the assumed uptake rates and underestimating the extent of dose reductions. The PBAC nominated the Early Resolution resubmission pathway* for this item. Sponsor's Comment: The sponsor had no comment.
NIRAPARIB Capsule 100 mg Zejula® GlaxoSmithKline Australia Pty Ltd New PBS listing (Major Submission)	Ovarian, fallopian tube, or primary peritoneal cancer	To request an Authority Required (Telephone) listing for the treatment of platinum-sensitive, relapsed, high grade serous ovarian, fallopian tube or primary peritoneal cancer.	Not recommended	The PBAC did not recommend niraparib, for platinum-sensitive, relapsed, high grade serous ovarian, fallopian tube, or primary peritoneal cancer. The PBAC considered that for patients with BRCA1/2 pathogenic gene variants the most appropriate treatment is in the first line maintenance setting so the proposed second line listing would have diminishing clinical relevance over time. More importantly, the PBAC considered that the claim of non-inferior efficacy and safety compared with olaparib was not supported by the data presented, for the 300 mg TGA-approved dose. The PBAC considered that for patients without a BRCA1/2 pathogenic variant, the PFS benefit over standard medical management was difficult to interpret, given the missing long-term data on overall survival in the pivotal NOVA trial. The cost utility model claimed a benefit on overall survival which was not established by the final data cut-off (1 Oct 2020) for NOVA on either the unadjusted or the adjusted analysis (adjusted for subsequent poly ADP ribose polymerase inhibitor (PARPi) use in the control group). Sponsor's Comment: GSK is disappointed by the PBAC's decision to not recommend niraparib (Zejula), for platinum-sensitive relapsed, high grade serous ovarian, fallopian tube, or primary peritoneal cancer in which there are limited maintenance treatment options. However, we remain committed to working with the PBAC to ensure Australian women with ovarian cancer have timely access to Zejula.

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NIVOLUMAB Injection concentrate for I.V. infusion 40 mg in 4 mL Injection concentrate for I.V. infusion 100 mg in 10 mL Opdivo® Bristol-Myers Squibb Australia Pty Ltd Change to PBS listing (Minor Submission)	Non-small cell lung cancer (NSCLC)	Resubmission to address the PBAC's concerns about the incremental effectiveness of nivolumab in patients 75 years or older.	Not recommended	The PBAC advised against the removal of the rebate for patients initiating treatment at the age of 75 years or older in the Deed of Agreement for nivolumab for the treatment of NSCLC (as second-line drug therapy). The PBAC considered that, while the submission presented some evidence to support similar overall survival benefit in patients aged 75 years and older compared with those under 75 years, any amendment to the risk sharing arrangements (RSA) for nivolumab should be considered with regard to its overall cost-effectiveness and in the broader context of the RSA subsidisation caps and the total cost per patient. <u>Sponsor's Comment:</u> The sponsor had no comment.
NIVOLUMAB IPILIMUMAB Nivolumab: Injection concentrate for I.V. infusion 40 mg in 4 mL Injection concentrate for I.V. infusion 100 mg in 10 mL Opdivo® Ipilimumab: Injection concentrate for I.V. infusion 50 mg in 10 mL Yervoy® Bristol-Myers Squibb Australia Pty Ltd Change to PBS listing (Major Submission)	Malignant pleural mesothelioma (MPM)	To request a Section 100 (Efficient Funding of Chemotherapy) Authority Required (STREAMLINED) listing for the use of nivolumab in combination with ipilimumab for the treatment of MPM.	Recommended	The PBAC recommended the Section 100 (Efficient Funding of Chemotherapy – Public and Private Hospital) Authority Required (Streamlined) listing of nivolumab in combination with ipilimumab (NIVO+IPI), for the treatment of MPM. The PBAC considered that there was a high clinical need for effective therapies for MPM and NIVO+IPI provided a substantial clinical benefit compared to pemetrexed-based chemotherapy. The PBAC considered it would be appropriate for the listing of NIVO+IPI to allow use in the first-and second-line treatment setting and in the small number of patients with non-pleural mesothelioma. The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of NIVO+IPI could be brought into an acceptable range with a price reduction. The PBAC considered a risk sharing arrangement would be required to manage the uncertainty associated with the number of patients that would be treated.

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OBETICHOLIC ACID Tablet 5 mg Tablet 10 mg Ocaliva® Chiesi Australia Pty Ltd New PBS listing (Minor Submission)	Primary biliary cholangitis (PBC)	To request an Authority Required (Written) listing for the treatment of PBC.	Recommended	The PBAC recommended the listing of obeticholic acid (OCA) for the treatment of PBC in combination with ursodeoxycholic acid (UDCA) in UDCA inadequate responders and as monotherapy in patients intolerant to UDCA. The PBAC was satisfied that OCA provides, for some patients, an improvement in efficacy compared to UDCA monotherapy in UDCA inadequate responders and placebo in UDCA intolerant patients. The PBAC considered that the estimated incremental cost effective ratio was acceptable when considered in conjunction with the estimated financial impact and proposed risk-sharing arrangement.
OFATUMUMAB Injection 20 mg in 0.4 mL single use pre-filled pen Kesimpta® Novartis Pharmaceuticals Australia Pty Ltd New PBS listing (Major Submission)	Multiple Sclerosis (MS)	To request an Authority Required (STREAMLINED) listing for the treatment of MS.	Recommended	The PBAC recommended the Authority Required (STREAMLINED) listing of ofatumumab for the treatment or relapsing-remitting multiple sclerosis (RRMS). The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of ofatumumab would be acceptable if it were cost minimised to the least costly of fingolimod, natalizumab, alemtuzumab, ocrelizumab, cladribine and ozanimod. The PBAC considered that while there were uncertainties with the multi-step indirect comparison of ofatumumab to the nominated alternative therapies which were further compounded by risk of bias issues with key bridging studies in the analysis, that overall the plurality of analyses and included network meta-analysis supported a conclusion that ofatumumab is of non-inferior comparative efficacy to these therapies. The Committee noted that safety comparisons between ofatumumab and other RRMS therapies were challenging, however considered that based on the evidence presented that there were no specific signals that would indicate ofatumumab has a worse safety profile than the nominated alternatives.
OLAPARIB Tablet 150 mg Tablet 100 mg Lynparza®	Prostate cancer	To request an Authority Required (Telephone/Electronic) listing for the treatment of metastatic castration resistant carcinoma of the prostate (mCRPC).	Not recommended	The PBAC did not recommend olaparib for the treatment of mCRPC in patients with pathogenic or likely pathogenic BRCA1/2 gene variants. The PBAC considered that although olaparib demonstrated clinical benefit in patients with BRCA1/2 gene variants, the nominated comparator did not reflect current Australian clinical practice which meant that the economic evaluation was highly uncertain.

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AstraZeneca Pty Ltd Change to PBS listing (Major Submission)				Sponsor's Comment: The sponsor had no comment.
PEMBROLIZUMAB Solution concentrate for I.V. infusion 100 mg in 4 mL Keytruda® Merck Sharp & Dohme (Australia) Pty Ltd Change to PBS listing (Major Submission)	Colorectal cancer	To request a Section 100 (Efficient Funding of Chemotherapy) Authority Required (STREAMLINED) listing for the treatment of metastatic (Stage IV) mismatch repair deficient (dMMR) colorectal cancer (mCRC).	Recommended	The PBAC recommended the Section 100 (Efficient Funding of Chemotherapy – Public and Private Hospital) Authority Required (Telephone) listing of pembrolizumab for the first line treatment of unresectable and metastatic (Stage IV) dMMR mCRC. The PBAC considered a revision to the time horizon used in the economic model was required to account for the uncertain gain in overall survival, and that with the revised model pembrolizumab would be cost effective with an incremental cost-effectiveness ratio closer to what was presented as the base case in the submission. The PBAC considered a risk sharing arrangement was required to manage the uncertainty associated with the overall cost to the PBS.
RIPRETINIB Tablet 50 mg Qinlock® Specialised Therapeutics Pm Pty Ltd New PBS listing (Major Submission)	Gastrointestinal stromal tumour (GIST)	To request an Authority Required (Written) listing for the treatment of metastatic or unresectable malignant GIST.	Not recommended	The PBAC did not recommend ripretinib for treatment of advanced GIST. The PBAC considered the claim of superior efficacy compared to best supportive care was reasonable based on improvements in progression free survival with the magnitude of gain in overall survival uncertain but clinically meaningful in the context of metastatic or unresectable GIST being a rare cancer with an unmet need for effective third line treatment. In addition, the PBAC considered the evidence presented indicated ripretinib had an acceptable safety profile. However, the PBAC considered the incremental cost-effectiveness ratio was very high and uncertain at the proposed price. Furthermore, the PBAC considered the proposed number of patients to be treated with ripretinib was likely overestimated. The PBAC nominated the Early Re-entry resubmission pathway* for this item.
				Sponsor's Comment: Specialised Therapeutics will continue to work with the PBAC to hopefully achieve a positive outcome enabling rapid access for Australian patients with this rare cancer (Gastrointestinal Stromal Tumours).

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RISDIPLAM Powder for oral solution 0.75 mg per 1 mL, 80 mL Evrysdi® Roche Products Pty Ltd New PBS listing (Major Submission)	Spinal Muscular Atrophy (SMA)	To request a Section 100 (Highly Specialised Drugs Program) Authority Required (Written) listing for the treatment of SMA.	Recommended	The PBAC recommended the listing of risdiplam for patients with SMA Types 1, 2 or 3a who are aged 18 years or under at treatment initiation, on the basis that it should be available only under special arrangements under Section 100. The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of risdiplam would be acceptable if it were cost-minimised against nusinersen. The PBAC did not recommend the listing of risdiplam for: patients with Type 3b SMA aged 18 years or under at treatment initiation (population 2); or for patients with SMA Types 1, 2 or 3 aged over 18 years at treatment initiation (population 3). The PBAC acknowledged the clinical need for effective treatments in the adult patient population with SMA. The PBAC considered that the submission did not provide evidence demonstrating a clinical benefit for risdiplam in population 2 and the evidence for population 3 did not demonstrate that risdiplam delays or prevents progression in these patients. Therefore the cost-effectiveness of risdiplam compared with best supportive care in these populations could not be determined.
ROXADUSTAT Tablet 20 mg Tablet 50 mg Tablet 70 mg Tablet 100 mg Evrenzo® AstraZeneca Pty Ltd New PBS listing (Major Submission)	Anaemia of chronic kidney disease	To request an Authority Required (STREAMLINED) listing for the treatment of anaemia associated with chronic kidney disease.	Not Applicable	This submission is to be considered at future PBAC meeting.

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SEMAGLUTIDE Solution for injection 2 mg in 1.5 mL pre-filled pen Solution for injection 4 mg in 3 mL pre-filled pen Ozempic® Novo Nordisk Pharmaceuticals Pty Ltd Change to PBS listing (Major Submission)	Type 2 diabetes mellitus (T2DM)	To request an Authority Required (STREAMLINED) listing for the treatment of T2DM.	Recommended	The PBAC recommended extending the existing listing of semaglutide to include the treatment of T2DM in combination with insulin and metformin unless contraindicated or not tolerated. The PBAC's recommendation for listing was based on, among other matters, its assessment, that the cost-effectiveness of semaglutide (both 0.5 mg and 1.0 mg) once weekly under the requested restriction would be acceptable if it were cost-minimised against dulaglutide 1.5 mg once weekly.
TAFAMIDIS Capsule 61 mg Vyndamax® Pfizer Australia Pty Ltd New PBS listing (Major Submission)	Transthyretin cardiac amyloidosis	Resubmission to request an Authority Required (Written) listing for the treatment of transthyretin cardiac amyloidosis.	Not recommended	The PBAC did not recommend again the listing of tafamidis for the treatment of amyloid transthyretin cardiomyopathy (ATTR-CM). The PBAC acknowledged again the clinical need for treatments for this condition, and recognised that the resubmission had partially addressed a number of the PBAC's previous concerns. However, it considered that a further price reduction would be needed to reach an acceptable incremental cost-effectiveness ratio (ICER), and a risk sharing arrangement was needed to manage the high risk of use above the submission's estimates. The PBAC nominated the Early Resolution resubmission pathway* for this item <u>Comparator: Best supportive care</u> The comparator was unchanged from the previous submission, and remained appropriate. <u>Clinical claim: Superior in terms of effectiveness and inferior in terms of safety, compared to best supportive care</u> The PBAC considered that the claims were reasonable, however, a moderate level of uncertainty remained with respect to the magnitude of the benefit. <u>Economic claim: Cost-utility analysis compared with best supportive care</u> Overall, the PBAC considered that the resubmission's model results were more reliable than those from the previous model, but that the ICER produced under the most realistic scenario presented ($155,000 to <$255,000 per QALY) remained excessively high.

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				Sponsor's Comment: Pfizer welcomes the PBAC's acknowledgement of the high unmet clinical need for effective therapies for ATTR-CM and acceptance of the superiority of tafamidis over standard management. Pfizer will continue to work collaboratively with the PBAC to deliver access to tafamidis for patients with this debilitating and life-threatening condition.
TEDUGLUTIDE Powder for injection 5 mg with diluent Revestive® Takeda Pharmaceuticals Australia Pty Ltd Change to PBS listing (Minor Submission)	Short bowel syndrome (SBS)	To extend the Section 100 (Highly Specialised Drugs Program) Authority Required (Written) listing to include paediatric patients with SBS.	Recommended	The PBAC recommended amending the Section 100 (Highly Specialised Drugs Program) Authority required listing of teduglutide for the treatment of paediatric patients with Type III (chronic) SBS with intestinal failure to include specific response criteria for paediatric patients. The PBAC acknowledged that, as children's nutritional requirements continue to increase with continued body growth, it may not always be possible to demonstrate a benefit in terms of a reduction in days of parenteral support (PS) within the specified timeframes of the current restriction. The PBAC considered that the proposed response criterion for patients aged less than 18 years, of a reduction in the mean weekly PS volume of at least 20% (mL per kg of body weight) relative to baseline, was clinically appropriate.
TERIPARATIDE Injection 250 micrograms per mL, 2.4 mL in multi-dose pre-filled cartridge Terrosa® Gedeon Richter Australia Pty Ltd Change to PBS listing (Minor Submission)	Severe established osteoporosis	To request Authority Required (STREAMLINED) listing of teriparatide biosimilar under the same conditions as its reference biologic.	Recommended	The PBAC recommended the listing of biosimilar brand of teriparatide (Terrosa) as an Authority Required (STREAMLINED) listing for the same indications as the reference brand Forteo. The PBAC recommended listing Terrosa on a cost-minimisation basis to Forteo. The PBAC advised that, under Section 101(4AACD) of the *National Health Act 1953*, in the Schedule of Pharmaceutical Benefits, Terrosa and Forteo should be treated as equivalent ('a' flagged) to each other. The PBAC recommended the addition of an administrative note to encourage the uptake of biosimilar prescribing for treatment naïve patients, in accordance with the Australian Government's Biosimilar Uptake Driver policy.
TESTOSTERONE Transdermal cream 50 mg per mL, 50 mL AndroForte 5®	Testosterone deficiency	To request a change in the number of repeats for the currently listed testosterone cream.	Recommended	The PBAC recommended amending the listing of AndroForte 5 to reduce the number of repeats from six to one and recommended an increase to the unit price which should not result in additional cost to the PBS. The PBAC's recommendation was based on the TGA approval for scrotal application that reduces the dose from 100 mg to 25 mg daily, and increases the number of treatments per tube from 25 to 100.

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Lawley Pharmaceuticals Pty Ltd Change to PBS listing (Minor Submission)				
TETRACOSACTIDE Compound depot injection 1 mg in 1 mL Synacthen® Clinect Pty Ltd Change to PBS listing (Minor Submission)	Hypsarrhythmia and/or infantile spasms	To request a change in restriction level from Restricted Benefit to Unrestricted Benefit listing.	Defer	The PBAC deferred the consideration of derestricting the listing to an unrestricted benefit, pending further consultation with the Australian and New Zealand Child Neurology Society. Sponsor's Comment: The sponsor had no comment.
TUCATINIB Tablet 150 mg Tablet 50 mg Tukysa® Lucid Health Consulting Pty Ltd New PBS listing (Major Submission)	Breast cancer	To request an Authority Required (telephone) listing for the treatment of metastatic (Stage IV) human epidermal growth factor receptor 2 (HER2) positive breast cancer.	Not recommended	The PBAC did not recommend tucatinib, in combination with trastuzumab and capecitabine, for the management of HER2-positive metastatic breast cancer, including patients with brain metastases. The PBAC noted that tucatinib provided a clinical benefit in terms of progression free survival and overall survival and acknowledged the high clinical need, especially in the subgroup of patients with brain metastases. However, the PBAC considered that the incremental cost effectiveness ratio was unacceptably high at the proposed price. The PBAC also considered that the number of treated patients was likely overestimated. The PBAC recommended the Early Re-Entry resubmission pathway* for this item. Sponsor's Comment: The sponsor had no comment.
UPADACITINIB Tablet 15 mg Rinvoq® Abbvie Pty Ltd	Ankylosing spondylitis (AS)	To request an Authority Required (Written) listing for the treatment of AS.	Recommended	The PBAC recommended the Authority Required listing of upadacitinib for the treatment of AS. The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of upadacitinib would be acceptable if it were cost minimised to the lowest cost biologic disease modifying anti-rheumatic drug (bDMARD) for this indication.

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Change to PBS listing (Major Submission)				
UPADACITINIB Tablet 15 mg Rinvoq® Abbvie Pty Ltd Change to PBS listing (Major Submission)	Severe psoriatic arthritis (PsA)	To request an Authority Required (Written) listing for the treatment of PsA.	Recommended	The PBAC recommended the Authority Required listing of upadacitinib for the treatment of PsA. The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of upadacitinib would be acceptable if it were cost minimised to the lowest cost biologic disease modifying anti-rheumatic drug (bDMARD) for this indication.
USTEKINUMAB Injection 45 mg in 0.5 mL Stelara® Janssen-Cilag Pty Ltd Change to PBS listing (Major Submission)	Plaque psoriasis	To request an Authority Required (Written) listing for the treatment of paediatric severe chronic plaque psoriasis.	Recommended	The PBAC recommended the listing of ustekinumab for the treatment of paediatric patients with severe chronic plaque psoriasis, and was satisfied that ustekinumab provides, for some patients, a significant improvement in efficacy over etanercept. Whilst there were limitations to the clinical comparison, the PBAC considered a claim of clinically meaningful superiority was reasonable in the context of an unmet clinical need for an alternative to etanercept, which is limited to 24 weeks duration of therapy. The PBAC considered that ustekinumab would be cost-effective in paediatric patients at a price no greater than the price for adults in the same indication.
VENETOCLAX Tablet 100 mg Venclexta® Abbvie Pty Ltd Change to PBS listing (Major Submission)	Acute Myeloid Leukemia	To request an Authority Required (Telephone/Online) listing for the treatment of acute myeloid leukaemia.	Not recommended	The PBAC did not recommend venetoclax for the treatment of patients with previously untreated acute myeloid leukaemia who are ineligible for standard intensive remission induction chemotherapy. The submission nominated azacitidine monotherapy as the main comparator, and low-dose cytarabine (LoDAC) as a secondary comparator. The PBAC considered that the combination of venetoclax with azacitidine offered a meaningful clinical improvement, but that the incremental cost-effectiveness ratio was high, and for the comparison with low-dose cytarabine uncertain, and that a price reduction would be needed to achieve a cost-effective listing. In addition, the PBAC considered that patients whose eligibility for a standard intensive remission induction chemotherapy regimen was currently "borderline" would likely seek treatment with venetoclax once listed on the PBS. The PBAC considered that a Risk Sharing Arrangement would be necessary to manage the risk of uptake in these patients in which cost-effectiveness has not been established.

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				The PBAC nominated the Early Re-entry resubmission pathway* for this item.
				Sponsor's Comment: AbbVie welcomes the PBAC's acknowledgement that venetoclax + azacitidine provides a meaningful clinical improvement for patients with AML. AbbVie will continue to work collaboratively with the PBAC to seek access for patients in this area of high unmet need.

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MARCH 2021 PBAC MEETING

DRUG NAME, FORM(S), STRENGTH(S), SPONSOR, TYPE OF SUBMISSION	DRUG TYPE AND USE	LISTING REQUESTED BY SPONSOR / PURPOSE OF SUBMISSION	PBAC RECOMMENDATION
Review of PBS Authority Required (Written) listings – Tranche 2 1. imatinib, sunitinib 2. vismodegib, sonidegib 3. lapatinib, pertuzumab, trastuzumab emtansine 4. azacitidine, lenalidomide 5. ruxolitinib 6. crizotinib, osimertinib 7. idelalisib, ibrutinib, venetoclax (Other matters)	Medicines for the treatment of cancer 1. Gastro-intestinal stromal tumour 2. Basal cell carcinoma 3. Metastatic breast cancer 4. Myelo-dysplastic syndrome 5. Myelofibrosis 6. Non-small cell lung cancer (NSCLC) 7. Chronic lymphocytic leukaemia and small lymphocytic lymphoma CLL/SLL	To request that PBAC consider the Authority Required (Written) restriction level for PBS-listed medicines (Tranche 2) and recommend any required amendments.	The PBAC noted the key Review findings from the PBS Authority Required (Written) listings report, which included an analysis of PBS utilisation data for Tranche 2 medicines. The PBAC also noted the input provided by sponsors through submission of Pre-Sub-Committee Responses (PSCRs) on the written authority level of their Tranche 2 medicine(s). The PBAC applied the following key criteria to assist in determining the requirement to maintain a written Authority level of restriction: (1) Potential for use in a population in which the medicine is not cost-effective or where the PBAC has not determined the comparative effectiveness and cost; and (2) Potential for high cost per patient or high total cost to the health system and the government's budget. The PBAC also considered the following factors: quality use of medicines (QUM), safety, and administrative burden. Overall, the PBAC accepted the DUSC February 2021 advice on the need to amend or maintain the current written Authority level of each medicine and made the following recommendations: 1. <u>Gastrointestinal stromal tumour:</u> The PBAC did not recommend an amendment to the authority requirements for imatinib or sunitinib, noting that the recent increase in imatinib patient numbers demonstrated that the market was not yet stable. The PBAC recommended that DUSC review utilisation of the entire GIST market in 12 months' time. Utilisation data for the adjuvant GIST indication and metastatic GIST indication should be analysed separately. 2. <u>Basal cell carcinoma:</u> The PBAC did not recommend an amendment to the authority requirements for vismodegib and sonidegib given the risk of use outside the current PBS restricted population, the comparatively high cost of these medicines and the financial implications to government. 3. <u>Metastatic breast cancer:</u> The PBAC agreed with DUSC advice and did not recommend an amendment to the authority requirements for lapatinib.

			The PBAC recommended that the authority requirements for pertuzumab and trastuzumab emtansine be amended from Authority Required (Written) to Authority Required (Telephone) to ease the administrative burden for prescribers. The PBAC recommended that DUSC review utilisation in 12 months' time. 4. Myelodysplastic syndrome (MDS): The PBAC agreed with DUSC that lowering the level of initial authority for lenalidomide may increase the risk of leakage to use in other indications (particularly multiple myeloma) which require written authorities and have large market costs. The PBAC did not recommend an amendment to the authority requirements for lenalidomide. The PBAC recommended that initial treatment authority requirements for azacitidine be amended from Authority Required (Written) to Authority Required (Telephone) for consistency with the PBAC November 2020 recommendation for azacitidine use in the acute myeloid leukaemia indication. The PBAC recommended that an utilisation analysis be undertaken for these medicines in 12 months. 5. Myelofibrosis: The PBAC agreed with DUSC that the myelofibrosis market is small but costly, with a stable incident and growing prevalent population. Any market growth would significantly increase expenditure, noting that PBS/RPBS expenditure had increased over each of the financial years 2015/16 to 2019/20. The PBAC did not recommend an amendment to the authority requirements for ruxolitinib due to the potential risk of use in other dermatological indications and graft- versus- host disease (GVHD). 6. Non-small cell lung cancer (NSCLC): The PBAC did not recommend an amendment to the authority requirements for osimertinib or crizotinib, due to recent changes to the osimertinib restrictions in January 2021. In addition, the number of incident patients treated with crizotinib is small and the associated administrative burden for prescribers low. 7. Chronic lymphocytic leukaemia and small lymphocytic lymphoma (CLL/SLL): The PBAC did not recommend an amendment to the authority requirements for, ibrutinib or venetoclax, noting that the market for this indication is large and still growing. The PBAC noted the immaturity of the venetoclax market due to its recent PBS listing.

			The PBAC recommended the initial therapy authority requirements for idelasilib be amended from Authority Required (Written) to Authority Required (Telephone) to align with its November 2020 recommendation for refractory follicular B-cell non-Hodgkin's lymphoma. The PBAC noted that idelalisib is a last-line therapy for this indication and the market is small and declining, largely due to safety concerns.

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.