NOVEMBER 2017 PBAC OUTCOMES – 1ST TIME DECISIONS NOT TO RECOMMEND

DRUG NAME, FORM(S), STRENGTH(S), SPONSOR, TYPE OF SUBMISSION	DRUG TYPE AND USE	LISTING REQUESTED BY SPONSOR / PURPOSE OF SUBMISSION	PBAC OUTCOME
ALIROCUMAB Injection 75 mg in 1 mL single dose pre-filled pen Injection 150 mg in 1 mL single dose pre-filled pen Praluent® Sanofi-Aventis Australia Pty Ltd New listing (Major Submission)	Familial hypercholesterolaemia and clinical atherosclerotic cardiovascular disease	To request an Authority Required listing for the treatment of patients with familial heterozygous hypercholesterolaemia and clinical atherosclerotic cardiovascular disease.	The PBAC did not recommend alirocumab for patients with familial hypercholesterolaemia (FH) and clinical atherosclerotic cardiovascular disease (ASCVD) on the basis of uncertain cost-effectiveness (the submission presented a very high incremental cost effectiveness ratio) and uncertainty around the size of the patient population and financial estimates. The PBAC also considered that the qualifying level of low-density lipoprotein cholesterol (LDL-c) proposed in the submission was inadequately supported by the evidence presented and that further clarity around the definition of the eligible population was necessary. The PBAC noted that the results of the ongoing ODYSSEY OUTCOMES trial, evaluating major adverse cardiac events (MACE) in individuals with hypercholesterolaemia, are due in early 2018 and will better inform the clinical benefit of alirocumab and economic model.
		Sponsor Comment:	Sanofi will continue to work with the Department of Health and remains committed to securing access to alirocumab in patients with the highest unmet clinical need.
AMINO ACID FORMULA with CARBOHYDRATE, VITAMINS, MINERALS and TRACE ELEMENTS WITHOUT PHENYLALANINE, SUPPLEMENTED WITH DOCOSAHEXAENOIC ACID Sachets containing oral powder 33 g, 30 (PKU Synergy) PKU Synergy® Nutricia Australia Pty Ltd New Listing (Minor Submission)	Phenylketonuria	To request a Restricted Benefit listing of PKU Synergy for the dietary management of patients with phenylketonuria.	The PBAC did not recommend the listing of PKU Synergy® for the dietary management of Phenylketonuria (PKU) or hyperphenylalanaemia in children from 10 years of age on the basis of concerns as to whether the product would provide enough copper and phosphorus for patients on a relaxed diet and that the PBAC considered that there were other products with better nutritional profiles for this patient population. The PBAC advised that a case for the clinical need for this product had not been made.
		Sponsor Comment:	Whilst Nutricia is disappointed in the PBAC outcome, we will continue to work with the PBAC on demonstrating the value of PKU Synergy. Nutricia firmly believes that medical nutrition products are important in the nutritional management of patients with a disease, disorder or medical condition and will continue to seek subsidised access for patients.

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BEZLOTOXUMAB Solution concentrate for I.V. infusion 1000 mg in 40 mL Zinplava® Merck Sharp & Dohme (Australia) Pty Ltd New listing (Major Submission)	Prevention of Clostridium difficile infection (CDI) recurrence	To request a Section 100 (Highly Specialised Drugs Program) Authority Required listing to prevent recurrence of CDI, as an add-on to antibiotic treatment.	The PBAC did not recommend the listing of bezlotoxumab on the PBS for the prevention of recurrence of Clostridium difficile infection (CDI) in patients receiving antibiotic therapy for CDI on the basis of modest comparative effectiveness and uncertain cost-effectiveness in the Australian setting. The PBAC considered that the group at highest risk of recurrence, and therefore most likely to benefit from treatment, was uncertain. The PBAC was also of the view that while there was a statistically significant reduction in the rate of recurrence in patients treated with bezlotoxumab, the magnitude of benefit was marginal. Further, the PBAC considered that the economic model overestimated the mortality benefit of bezlotoxumab treatment and did not account for other potential quality of life and health system benefits.
		Sponsor Comment:	The Sponsor had no comment.

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BUDESONIDE Capsule (modified release) 3 mg Entocort® Emerge Health Pty Ltd New listing (Major Submission)	Crohn disease	To request an Authority Required listing for the treatment of patients with mild to moderate Crohn disease (CD) affecting the ileum and/or the ascending colon who meet certain criteria.	The PBAC did not recommend the listing of budesonide controlled release capsules for treatment of mild to moderate CD affecting the ileum and/or the ascending colon on the basis that the nominated comparator (treatment likely to be replaced in practice) was not appropriate, and that cost-effectiveness against the appropriate comparator had not been established. The PBAC noted that evidence on lack of efficacy of aminosalicylate drugs (5-ASAs) in CD had emerged in recent years (Lim 2016 Cochrane review) and that they were not recommended by recent Australian guidelines while oral corticosteroids and budesonide were. Hence, the PBAC considered that the 5-ASA drug mesalazine nominated as the comparator in the submission was not reflective of contemporary practice and that prednisolone (or a similar oral corticosteroid) would be a more appropriate comparator for budesonide as it is the treatment most likely to be replaced in practice. The PBAC considered that in terms of efficacy budesonide may be slightly inferior to prednisolone but that in terms of safety, the trial evidence suggests budesonide to be superior to prednisolone, particularly in terms of glucocorticoid associated adverse events. A cost-minimisation analysis versus prednisolone was conducted during the evaluation. The PBAC considered that a cost-minimisation analysis versus prednisolone conducted during the evaluation highlighted the substantial price difference between budesonide and prednisolone, but noted that offsets related to the superior safety profile of budesonide compared with prednisolone were unable to be factored into the analysis. The PBAC concluded that at the proposed price, a budesonide listing would likely be associated with a significant cost to the PBS rather than the cost saving estimated in the submission.
		Sponsor Comment:	The Sponsor had no comment.

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DARATUMUMAB Solution concentrate for I.V infusion 100 mg in 5 mL Solution concentrate for I.V infusion 400 mg in 20 mL Darzalex® Janssen-Cilag Pty Ltd New listing (Major Submission)	Relapsed/refractory multiple myeloma	To request an Authority Required listing, in combination with bortezomib or lenalidomide, for the treatment of relapsed or refractory multiple myeloma in patients who have progressive disease after at least one prior therapy.	The PBAC did not recommend the listing of daratumumab for use in combination with bortezomib and dexamethasone (DBd) or lenalidomide and dexamethasone (DLd) in relapsed or refractory multiple myeloma due to the very high and uncertain incremental cost-effectiveness ratios (ICERs). The PBAC considered that the proposed clinical place in therapy was appropriate, but that the requested listing for daratumumab in combination with the other drugs excluded a group of patients with a high clinical need who may benefit from daratumumab monotherapy. The PBAC welcomed the comments received via the Consumer Comments facility on the PBS website. The PBAC noted the significant public interest in the listing of daratumumab. The consumer comments that were considered by the Committee included the benefits that daratumumab improved survival, had the potential to improve quality of life, and better tolerability. The PBAC accepted that the proposed comparators were reasonable, but also considered that other potentially relevant comparators had not been considered. The PBAC noted that the financial impact of the proposed listing had a very high opportunity cost to the funding of other therapies through the PBS.
		Sponsor Comment:	Janssen will continue to work with the PBAC to make daratumumab available to patients as soon as practical.

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GOLIMUMAB Injection 50 mg in 0.5 mL single use pre-filled syringe Simponi® Janssen-Cilag Pty Ltd Change to listing (Major Submission)	Active non-radiographic axial spondyloarthritis (nr-axSpA)	To request an Authority Required listing for the treatment of active nr-axSpA.	The PBAC did not recommend the listing of golimumab for nr-axSpA on the basis an uncertain incremental cost-effectiveness ratio (ICER) and the significant opportunity cost of the proposed listing in the context of a poorly defined patient population. The PBAC considered that there is a clinical need for effective subsidised therapy for nr-axSpA but considered that treatment should be targeted to those patients who would benefit the most from biologic therapy. The PBAC also considered that the long-term incremental outcomes were uncertain, in the context of a chronic therapy. The PBAC indicated it would welcome a submission for a bDMARD for this condition that restricted use to those patients with the highest clinical need who are most likely to benefit from biological therapy, proposed a lower cost per patient in the context of the lack of long-term outcome data, and addressed the uncertainty in the cost-effectiveness and potential for use beyond the restriction.
		Sponsor Comment:	Janssen will continue to work with the PBAC to make golimumab available to patients as soon as practical.
IBRUTINIB Capsule 140 mg Imbruvica® Janssen-Cilag Pty Ltd Change to recommended listing (Major Submission)	Chronic lymphocytic leukaemia (CLL)/small lymphocytic lymphoma (SLL)	To request an Authority Required listing for the first line treatment of patients with CLL or SLL who meet certain criteria.	The PBAC did not recommend the Authority Required listing for ibrutinib for patients with previously untreated chronic lymphocytic leukaemia (CLL) or small lymphocytic leukaemia (SLL) who are unsuitable for treatment with a fludarabine-based chemoimmunotherapy. The PBAC noted the current availability of a number of effective first-line therapies for this population on the PBS. Although the PBAC accepted there is a clinical benefit in progression-free survival (PFS) and overall survival (OS) for ibrutinib when compared to chlorambucil in combination with either rituximab or ofatumumab, the benefit over chlorambucil in combination with obinutuzumab was not supported. The incremental cost-effectiveness ratio presented using the blended comparator of chlorambucil in combination with rituximab, ofatumumab and obinutuzumab was considered high and overly optimistic. The PBAC also noted that the net cost of listing ibrutinib in the first-line setting would have a significant financial impact, leading to a significant opportunity cost to the Commonwealth in funding other therapies.

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		Sponsor Comment:	Janssen will continue to work with the PBAC to make ibrutinib available to patients as soon as practical.
INSULIN DEGLUDEC WITH INSULIN ASPART Injections, cartridges, 70 units-30 units per mL, 3 mL, 5 Injections, pre-filled pen, 70 units-30 units per mL, 3 mL, 5 Ryzodeg FlexTouch® Ryzodeg Penfill® Novo Nordisk Pharmaceuticals Pty Ltd New listing (Major Submission)	Diabetes mellitus	To request an unrestricted listing to improve glycaemic control in adult patients with diabetes mellitus where basal and prandial insulin treatment is necessary.	The PBAC did not recommend insulin degludec with insulin aspart (IDegAsp) for treatment of adult patients with diabetes mellitus where insulin treatment is necessary on the basis that the cost effectiveness of the drug treating patients with type 2 diabetes mellitus (T2DM) was not established at the proposed price, and because the clinical place for use in patients with type 1 diabetes mellitus (T1DM) was not established by the submission. The PBAC accepted biphasic insulin aspart 30 (BIAsp 30) as the appropriate comparator for IDegAsp in T2DM. However in T1DM, the submission nominated insulin detemir (IDet) as the main comparator and the PBAC noted that pre-mixed insulins are not typically used in this population and considered that it was not clear what role IDegAsp would have in T1DM if listed. Therefore, the PBAC considered that the comparison of IDegAsp against IDet in T1DM to be of limited value for decision making, as this drug is unlikely to be replaced by IDegAsp in clinical practice in this population. The PBAC considered that the claim of non-inferior comparative effectiveness was reasonably supported by the data for T2DM, based on three head-to-head trials comparing IDegAsp to BIAsp 30. However, the PBAC considered that the claim of superior comparative safety was not adequately supported by the data given. The PBAC noted that although there was a slight reduction in hypoglycaemic events per patient year, no improvement in severe hypoglycaemic events was demonstrated. The PBAC considered that due to issues with the safety claim, there was a high degree of uncertainty around the cost effectiveness and financial impact of listing IDegAsp.
		Sponsor Comment:	Novo Nordisk looks forward to working with the PBAC to determine the best approach to make Ryzodeg® 70/30 available for Australians with diabetes mellitus who would benefit from this product.

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LENVATINIB Capsule 10 mg (as mesilate) Capsule 4 mg (as mesilate) Lenvima® Eisai Australia Pty Ltd Change to listing (Major Submission)	Advanced renal cell carcinoma (RCC)	To request an Authority Required (STREAMLINED) listing for the treatment of patients with advanced renal cell carcinoma following treatment with at least one anti-angiogenic therapy.	The PBAC did not recommend the listing of lenvatinib in combination with everolimus for advanced RCC on the basis that the clinical need and the clinical place in therapy of lenvatinib were not adequately established. In addition, the PBAC considered that the magnitude of the clinical benefit was uncertain. The PBAC noted that the submission nominated everolimus as the main comparator and nivolumab as a secondary comparator, with axitinib and cabozantinib as supplementary comparators. The PBAC considered that concerns regarding the magnitude of clinical benefit and the toxicity profile of lenvatinib in combination with everolimus when compared to established treatments (both everolimus and nivolumab) meant that its clinical place in therapy was unclear. The PBAC considered that until the clinical place in therapy is established, an appropriate comparator for lenvatinib in combination with everolimus cannot be determined. The PBAC considered the claim of superior efficacy for lenvatinib in combination with everolimus over everolimus monotherapy in terms of progression-free survival (PFS) and overall survival (OS) was not well supported by the data, as Study 205 was a small and underpowered phase II trial which was subject to bias due to its open-label design and use of investigator assessment for disease progression. The PBAC considered that the toxicity associated with the combination of lenvatinib in combination with everolimus was not insignificant, with serious adverse events of Grade 3 or 4 occurring more frequently in patients receiving this treatment regimen. The PBAC advised that the appropriate comparator for the cost-utility analysis was unclear, and considered the proposed incremental cost-effectiveness ratio (ICER) presented in the submission to be high and uncertain due to the sensitivity of the model to the estimate of OS improvement.
		Sponsor Comment:	The Sponsor had no comment.

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MEDIUM CHAIN TRIGLYCERIDES 2) TRIGLYCERIDES LONG CHAIN 1) Oral liquid 225 mL (betaquik) 2) Oral liquid 225 mL (carbzero) 1) Betaquik 2) Carbzero Vitaflo Australia Pty Ltd Change to listing (Minor Submission)	1) Ketogenic diet; dietary management of conditions requiring a source of medium chain triglycerides 2) Ketogenic diet	To advise the PBAC of a change to the formulation and request a change in the pack size and maximum quantity of Betaquik and Carbzero.	The PBAC did not recommend amending the maximum quantity of cartons per script from two to three of both Betaquik® and Carbzero®, for the dietary management of conditions requiring a source of medium chain triglyceride and for patients who require a ketogenic diet respectively. The PBAC considered that the increase in volume per script would result in a higher dispensed maximum quantity per script, and potentially higher costs to the PBS. The PBAC also noted the change to container size for Betaquik® and Carbzero® from 250 mL to 225 mL, and the change in number of containers per carton from 18 to 15.
		Sponsor Comment:	The Sponsor had no comment.

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MIDOSTAURIN Capsule 25 mg Rydapt® Novartis Pharmaceuticals Australia Pty Ltd New listing (Major Submission)	Acute myeloid leukaemia (AML)	To request a Section 100 (Highly Specialised Drugs Program) Authority Required listing of midostaurin for the treatment of patients with newly diagnosed FMS-like tyrosine kinase 3 (FLT3) mutation positive AML.	The PBAC did not recommend midostaurin for the treatment of FLT3 mutation positive acute myeloid leukaemia (AML). In reaching this outcome, the PBAC acknowledged the high unmet clinical need in this population and demonstrated increase in overall survival in the clinical trial. However, it noted that TGA input was required regarding the role of midostaurin as maintenance therapy and considered that, at the price proposed by the submission, the cost effectiveness of midostaurin was uncertain and unacceptable, particularly in the population over the age of sixty years. The PBAC acknowledged that there was an unmet clinical need for new effective therapies for AML. The PBAC considered that the pivotal trial, RATIFY, demonstrated that midostaurin improved overall survival versus placebo in patients aged under 60 years. The PBAC noted that the RATIFY trial only enrolled patients aged ≤59 years, and that the only evidence presented to support midostaurin's effectiveness in the aged ≥60 years was from the the single arm AMLSG 16-10 study. The PBAC considered that while it was biologically plausible for older patients to respond to midostaurin, it was not convinced of the magnitude of incremental benefit in the older patient population due to the absence of a placebo comparison and information about background mortality (e.g. transplant-related or from causes unrelated to AML) in the older population. While the PBAC advised against restricting the use of midostaurin based on age and considered the effect of age on treatment eligibility would be best regulated if left to the discretion of the prescriber, the Committee advised that the impact of lower comparative effectiveness in the older age group should be adequately incorporated in the economic model. The PBAC considered that midostaurin was inferior in safety compared with placebo, but considered that in the context of chemotherapy-induced morbidity and mortality, the additional toxicity with midostaurin treatment is relatively minor. The PBAC identified a number of issues with the economic model that would need be addressed in a future major resubmission.

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		Sponsor Comment:	Novartis are pleased with the PBAC's acknowledgement of the high clinical need for an effective treatment in this patient population. Novartis are committed to working with the PBAC to achieve agreement on sustainable PBS listing conditions for midostaurin at the earliest opportunity.
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 listing (Major Submission)	Squamous cell carcinoma for the head and neck (SCCHN)	To request a Section 100 (Efficient Funding of Chemotherapy) Authority Required (STREAMLINED) listing for the treatment of patients with squamous cell carcinoma of the head and neck (SCCHN) that progresses within 6 months following platinum-based therapy.	The PBAC did not recommend the Section 100 (Efficient Funding of Chemotherapy - Public and Private Hospital) Authority Required (STREAMLINED) listing of nivolumab for the treatment of squamous cell carcinoma of the head and neck (SCCHN). The PBAC advised that there was uncertainty in the nature and magnitude of its incremental clinical benefit in Australian clinical practice, and that the estimated incremental cost effectiveness ratio was high and overoptimistic at the price proposed by the submission. The PBAC acknowledged that SCCHN is a particularly debilitating malignancy, and advised that there was a trend to slower deterioration in quality of life after starting nivolumab treatment compared to chemotherapy. Further, the PBAC considered that several assumptions in the financial estimates resulted in significant budgetary uncertainty for the Commonwealth.
		Sponsor Comment:	While the sponsor is disappointed with the PBAC outcome, it is committed to working with the PBAC to ensure earliest possible PBS access for nivolumab to treat Australian patients with squamous cell carcinoma of the head and neck.

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NUSINERSEN Solution for injection 12 mg in 5 mL Spinraza™ Biogen Australia Pty Ltd New listing (Major Submission)	Spinal muscular atrophy (SMA)	To request a Section 100 (High Specialised Drugs Program) Authority Required listing for treatment of patients with infantile-onset (Type I) and childhood-onset (Types II and III) SMA.	The PBAC did not recommend the Section 100 (Highly Specialised Drugs Program) listing of nusinersen for the treatment of patients with Infantile-onset (Type I) and childhood-onset (Types II & III) spinal muscular atrophy (SMA) due to uncertainty about the clinical effectiveness of nusinersen in terms of the extent and durability of response across the spectrum of SMA for which subsidy was sought. Overall, the submission contained insufficient information for the PBAC to form a view on the cost-effectiveness of treatment with nusinersen across the spectrum of SMA. The PBAC acknowledged that there is a high and urgent clinical need for treatments for SMA, particularly for the most severe forms of the condition and noted that the consumer input was strongly supportive of a broad PBS listing across all forms of SMA, including adult onset disease. The PBAC considered that while the available evidence suggests patients may receive some benefit from nusinersen, the benefit needed to be better quantified. The PBAC formed the view that the Pharmaceutical Benefits Scheme (PBS) is the most appropriate mechanism for subsidising nusinersen for Australian patients. The PBAC considered that further information on the cost-effectiveness of treatment with nusinersen is necessary in order for it to be able to form a view on the appropriate PBS subsidy price, but that based on the information already available it is likely that a substantial reduction in the proposed price will be required.
		Sponsor Comment:	Biogen is disappointed by the PBAC's decision as this will delay the SMA community's access to SPINRAZA when there are currently no other disease-modifying medicines available to treat this devastating disease. Biogen is confident in the clinical evidence supporting SPINRAZA for the treatment of SMA. Following discussions at the post-PBAC meeting we have identified next steps and are determined to meet the needs of the PBAC and the SMA community to make SPINRAZA available as soon as possible.

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OBINUTUZUMAB Solution for I.V. infusion 1000 mg in 40 mL Gazyva® Roche Products Pty Ltd Change to listing (Major Submission)	CD20 positive follicular lymphoma	To request an Authority Required (STREAMLINED) listing for untreated patients with Stage II bulky or Stage III/IV CD20 positive follicular lymphoma.	The PBAC did not recommend the listing of obinutuzumab on the PBS for treatment of previously untreated advanced follicular lymphoma (stage II bulky or stage III/IV), as, the clinical benefits of obinutuzumab over rituximab were uncertain, with no demonstrated improvement in quality of life or overall survival, and an inferior comparative safety profile particularly in the elderly. Further, the PBAC considered the cost-effectiveness against rituximab to be highly uncertain and that the clinical need for an additional first-line therapy was not clear. The PBAC considered that, given the prognosis of the disease and its high response to rituximab, the clinical need for obinutuzumab in the first-line setting may be limited to a yet unidentified subgroup of patients destined to progress on rituximab who were able to tolerate its increased toxicity. The PBAC considered that the claim of superior effectiveness in terms of progression free survival (PFS) compared with rituximab was not adequately supported by the data. The PBAC reiterated that it considered PFS to be a potentially important outcome in indolent diseases such as follicular lymphoma. However, for this submission the PBAC was concerned that the modest gain in PFS over rituximab may be offset by increases in serious adverse events. In addition, the PBAC noted that no difference in overall survival (OS) or health-related quality of life measures was demonstrated between treatment arms. In the context of its concerns around the uncertainty of the incremental cost effectiveness ratio (ICER) presented in the submission's base case, which it considered to be underestimated, the PBAC was concerned that financial impact of obinutuzumab was uncertain, and the uptake rate would be higher than proposed.
		Sponsor Comment:	There remains an unmet need for a novel treatment alternative to rituximab that can prolong progression free survival for all previously untreated patients with advanced stage follicular lymphoma. Roche is committed to working with the Department of Health and the PBAC to enable access to obinutuzumab for people with advanced follicular lymphoma.

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OCRELIZUMAB Solution concentrate for I.V. infusion 300 mg in 10 mL Ocrevus® Roche Products Pty Ltd Change to recommended listing (Major Submission)	Primary progressive multiple sclerosis (PPMS)	To request an Authority Required (STREAMLINED) listing for the treatment of adult patients with PPMS	The PBAC did not recommend the listing of ocrelizumab for the treatment of patients with primary progressive multiple sclerosis (PPMS), on the basis of a modest clinical benefit and the resulting high and uncertain incremental cost-effectiveness ratio (ICER). The PBAC was concerned about the applicability of trial results to the potential PBS population, and that the base case ICER per quality adjusted life year (QALY) gained presented by the submission may be underestimated as ocrelizumab is likely to be less effective in the PBS population than observed in the ORATORIO trial. The PBAC was also concerned about the uncertain utilisation estimates due to issues with defining the target PBS population, and the high and likely underestimated financial impact. The PBAC accepted best supportive care (BSC) as the appropriate main comparator. Although the PBAC noted the statistically significant results of ocrelizumab over placebo in the ORATORIO trial, the PBAC considered that the treatment effect was modest and that the clinical significance of the trial outcomes was uncertain. The PBAC accepted the claim of inferior comparative safety of ocrelizumab over BSC, however, did not accept the claim that ocrelizumab has an acceptable safety profile that is comparable with placebo. The PBAC noted that the base case ICER (>$200,000) was based on the secondary outcome from the ORATORIO extension period, rather than on the primary endpoint of the trial and that using the results of the primary endpoint further increased the ICER. The PBAC noted that even when the most optimistic point estimate was applied in the economic model, using the lower bound of the 95% confidence interval for the primary endpoint, the ICER gained was in the range of $105,000 - $200,000, well above what is normally considered cost effective. The PBAC noted the consumer comments and the submission's arguments for "unmeasured value" and considered that this did not justify the high ICER gained of ocrelizumab in PPMS.
		Sponsor Comment:	Roche remains committed to working with the PBAC to enable access to ocrelizumab for people with primary progressive multiple sclerosis.

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OSIMERTINIB Tablet 40 mg Tablet 80 mg Tagrisso® AstraZeneca Pty Ltd New listing (Major Submission)	Locally advanced (Stage III) or metastatic (Stage IV) epidermal growth factor receptor (EGFR) T790M mutation positive non-small cell lung cancer (NSCLC)	To request an Authority Required (STREAMLINED) listing for the treatment of patients with locally advanced or metastatic EGFR T790M mutation positive NSCLC who have progressed on or after prior treatment with an EGFR tyrosine kinase inhibitor (TKI).	The PBAC did not recommend osimertinib for the treatment of EGFR T790M mutation positive non-small cell lung cancer. Although accepting that osimertinib is more effective than standard chemotherapy, the PBAC advised that the magnitude of incremental overall survival benefit was difficult to determine from the evidence presented in the submission, and this was an important driver of the economic evaluation. Additionally, the PBAC had concerns with other aspects of the economic model, which resulted in a high and overly optimistic estimated incremental cost-effectiveness ratio at the price requested by the submission. The PBAC also noted that the co-dependent test for EGFR T790M mutations would be considered by the Medical Services Advisory Committee (MSAC) in late November 2017, and considered that MSAC's advice would be informative on whether plasma or rebiopsy of tumour tissue would be the most appropriate source of biological material to inform EGFR T790M mutation status in this context.
		Sponsor Comment:	The Sponsor had no comment.
PEMBROLIZUMAB Powder for injection 50 mg Solution concentrate for I.V. infusion 100 mg in 4 mL Keytruda® Merck Sharp & Dohme (Australia) Pty Ltd Change to listing (Major Submission)	Locally advanced or metastatic urothelial cancer (LA or mUC)	To request a Section 100 (Efficient Funding of Chemotherapy) Authority Required (STREAMLINED) listing for the treatment of LA or mUC after the failure of a prior platinum-containing regimen.	The PBAC did not recommend pembrolizumab for the treatment of patients with locally advanced (LA) or metastatic urothelial cancer (mUC) after failure of a platinum containing regimen on the basis that the incremental cost-effectiveness ratio compared to standard of care (SOC) was highly uncertain and likely an underestimate, and the financial implications were considerable and uncertain. However, the PBAC acknowledged the high clinical need and the evidence of positive overall survival benefit and reduced toxicity in this population.
		Sponsor Comment:	MSD is pleased that the PBAC is supportive of the clinical benefit that pembrolizumab offers over current standard of care for patients with second line locally advanced or metastatic urothelial cancer and that there is an unmet clinical need for new therapies. The company is committed to working with the government to make pembrolizumab available to these patients as soon as possible.

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SODIUM PHENYLBUTYRATE Granules for oral suspension 483 mg (as sodium) per g, 174 g Pheburane® Orpharma Pty Ltd New listing (Major Submission)	Urea cycle disorder (UCD)	To request an Authority Required listing for the treatment of patients with UCD.	The PBAC decided not to recommend the listing of a sugar-coated granule formulation of sodium phenylbutyrate (referred to as coated NaPb) on the basis of an unclear incremental clinical benefit and high incremental cost compared with other ammonia scavenger formulations. In particular, the PBAC considered that the clinical evidence was insufficient to support a claim of superior efficacy versus other ammonia scavenger formulations. The PBAC considered that ammonia scavengers have an important clinical place in the treatment of urea cycle disorders. The PBAC was of the view that there was a need to ensure the continuing availability of ammonia scavengers. The PBAC considered that a claim of non-inferior comparative efficacy and safety compared with other ammonia scavenger formulations would have been appropriate given the clinical evidence available. Therefore, the PBAC considered that a cost-minimisation analysis against other ammonia scavengers would have been appropriate.
		Sponsor Comment:	The Sponsor intends to work with the PBAC to make this vital medication available to those in need. It should be noted that Urea Cycle Disorder is a rare disease and the level of evidence is limited.

NOVEMBER 2017 PBAC OUTCOMES – 1ST TIME DECISIONS NOT TO RECOMMEND

DRUG NAME, FORM(S), STRENGTH(S), SPONSOR, TYPE OF SUBMISSION	DRUG TYPE AND USE	LISTING REQUESTED BY SPONSOR / PURPOSE OF SUBMISSION	PBAC OUTCOME
TEDUGLUTIDE Powder for injection 5 mg with solvent Revestive® Shire Australia Pty Ltd New listing (Major Submission)	Short Bowel Syndrome (SBS)	To request a Section 100 (Highly Specialised Drugs Program) Authority Required listing for the treatment of SBS in patients who are dependent on parenteral nutrition for survival.	The PBAC did not recommend the listing of teduglutide for the treatment of patients with Type III (chronic) intestinal failure associated with short bowel syndrome on the basis of an unclear clinical place in therapy and the very high and uncertain incremental cost-effectiveness ratio (ICER). The PBAC considered the use of teduglutide in clinical practice was unclear with regards to the appropriate time to commence and cease treatment, and the appropriate patient population, requiring treatment with the medicine. The PBAC considered the outcome of a 20% reduction in weekly parenteral support volume may not be a clinically important change for all patients, especially if volume reductions did not result in fewer days per week of parenteral support. Additionally, the PBAC noted that there was no statistically significant difference in patients' quality of life between the teduglutide and placebo arms in the clinical trial, although noted this may be due to the design and size of the trial and that some sub-group analyses were suggestive of quality of life benefit. The PBAC considered the economic model as presented in the submission to be overly optimistic and noted that the financial impact of listing teduglutide was uncertain due to issues with the proposed PBS restriction.
		Sponsor Comment:	Shire will work with the Department of Health and the PBAC so that patients with this rare disease are able to access teduglutide treatment in Australia.
TIOTROPIUM Solution for oral inhalation 2.5 micrograms (as bromide monohydrate) per actuation (60 actuations) Spiriva® Respimat® Boehringer Ingelheim Pty Ltd	Severe asthma	Resubmission to request the current Restricted Benefit listing for severe asthma be changed to Authority Required (STREAMLINED).	The PBAC did not recommend amending the Restricted Benefit listing of tiotropium for severe asthma to an Authority Required (STREAMLINED) listing. The PBAC confirmed that it did not consider that the use of different restriction levels to manage a Risk Sharing Arrangement was appropriate and that this may lead to confusion for consumers and prescribers. Further, the PBAC restated that it considered that this approach may not adequately address the sponsors concerns, which could be met by other approaches.

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Change to listing (Minor Submission)		Sponsor Comment:	The Sponsor had no comment.