JULY 2017 PBAC OUTCOMES – DEFERRALS

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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 deferred making a decision on the listing of PKU Synergy® for the dietary management of Phenylketonuria (PKU) or hyperphenylalaninaemia in children from 10 years of age. The PBAC considered it would be appropriate to seek advice from the Nutritional Products Working Party, regarding matters raised in the sponsor's pre-PBAC advice, prior to making its decision.
		Sponsor comment	Nutricia will continue to work with the PBAC and the Nutritional Products Working Party regarding the matters raised in the pre-PBAC advice.
BALSALAZIDE Capsule containing balsalazide sodium 750 mg Colazide® Fresenius Kabi Australia Pty Ltd New Listing (Major Submission)	Ulcerative colitis	To request a new maximum quantity for the current Authority Required (Streamlined) listing.	The PBAC deferred making a decision on the request to increase the maximum quantity of the currently listed pharmaceutical item balsalazide (Colazide®) to 280 capsules, to allow further analysis of utilisation and consideration of the impact that an increase in maximum quantity may have on wastage, as well as allow for consideration of the impact of higher doses on the quality use of medicines and the cost-effectiveness of balsalazide treatment.
		Sponsor comment	The company looks forward to working with the PBAC on this application.

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BARICITINIB Tablet 2 mg Tablet 4 mg Olumiant® Eli Lilly Australia Pty Ltd (Major Submission)	Severe active rheumatoid arthritis	To request an Authority Required listing for the treatment of severe active rheumatoid arthritis under certain conditions.	The PBAC was of a mind to reject baricitinib for treatment of severe rheumatoid arthritis (RA) based on uncertain clinical need and efficacy and concerns about the safety profile, particularly in relation to serious adverse events. However, the PBAC deferred making a recommendation on the listing of baricitinib pending the provision of the relevant TGA delegate's overview. Although the PBAC considered an alternative cost-minimisation approach against the cheapest listed bDMARD might be appropriate, more detail would be required to establish the equi-effective doses. However, the PBAC did not finalise its view at this time, pending any further input from the sponsor in response to the committee's views about incorporating the safety differences into the economic evaluation.
		Sponsor Response	Lilly expects full registration of baricitinib soon and looks forward to working with the PBAC on listing baricitinib following its consideration at the earliest possible opportunity.
DAPAGLIFLOZIN Tablet 10 mg (as propanediol monohydrate) Forxiga® AstraZeneca Pty Ltd Change to listing (Major Submission)	Type 2 diabetes mellitus (T2DM)	To request an Authority Required (STREAMLINED) listing for dapagliflozin in combination with metformin and a dipeptidyl peptidase 4 inhibitor for the treatment of patients with T2DM.	The PBAC deferred making a decision regarding the Authority Required (STREAMLINED) listing for dapagliflozin for the treatment of type 2 diabetes, in combination with metformin and any dipeptidyl peptidase-4 (DPP4) inhibitor, to allow further work to establish a price for treatment with dapagliflozin + a DPP4 inhibitor + metformin that could be considered cost-effective. The PBAC acknowledged that it was reasonable that the addition of dapagliflozin to metformin and a DPP4 inhibitor may have some therapeutic benefit. However, the PBAC considered that the non-inferiority of dapagliflozin + a DPP4 inhibitor + metformin compared to the nominated comparators was uncertain. The PBAC considered that the approach to the cost-minimisation analysis was inappropriate and that although it was reasonable to assume that this triple therapy would have some therapeutic benefit, there was no evidence to suggest that the benefit of metformin + dapagliflozin + a DPP4 inhibitor would be of the same magnitude as the incremental benefit of adding either dapagliflozin or a DPP4 inhibitor to

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			metformin. Therefore, the PBAC was of the view that it would not be cost effective for dapagliflozin + a DPP4 + metformin treatment to be at the same price as the sum of the component parts. In addition, the financial impacts remained underestimated.
		Sponsor comment	The sponsor had no comment.
DAPAGLIFLOZIN with METFORMIN Tablet (modified release) containing 5 mg dapagliflozin (as propanediol monohydrate) with 1000 mg metformin hydrochloride Tablet (modified release) containing 10 mg dapagliflozin (as propanediol monohydrate) with 500 mg metformin hydrochloride Tablet (modified release) containing 10 mg dapagliflozin (as propanediol monohydrate) with 1000 mg metformin hydrochloride Xigduo® XR AstraZeneca Pty Ltd Change to listing (Minor Submission)	Type 2 diabetes mellitus (T2DM)	To request an Authority Required (STREAMLINED) listing of dapagliflozin with metformin for the treatment of T2DM in combination with a dipeptidyl peptidase 4 inhibitor.	The PBAC deferred making a decision regarding the Authority Required (STREAMLINED) listing for dapagliflozin and metformin fixed dose combination (FDC) in combination with a dipetidyl peptidase 4 (DPP4) inhibitor for the treatment of type 2 diabetes mellitus (T2DM) to allow further work to establish a price for treatment with dapagliflozin + a DPP4 inhibitor + metformin that could be considered cost-effective.
		Sponsor comment	The sponsor had no comment.

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ENZALUTAMIDE Capsule 40 mg Xtandi® Astellas Pharma Australia Pty Ltd Change to listing (Minor Submission)	Prostate cancer	Resubmission to request an Authority Required listing for the treatment of asymptomatic metastatic castration resistant prostate cancer in chemotherapy-naïve patients	The PBAC deferred recommending an extended PBS listing for enzalutamide for the treatment of metastatic castrate-resistant prostate cancer (mCRPC) prior to docetaxel, on the basis that the proposal to achieve a cost-effective listing was unacceptable. The PBAC advised that further negotiations between the sponsor and the Department regarding the proposed price of enzalutamide, the proposed financial caps and the size of the patient population are required, to ensure that an acceptable incremental cost effectiveness ration (ICER) is achieved. In its consideration of the major resubmission in March 2017, the PBAC requested that the sponsor adjust the assumption of the duration of post-docetaxel treatment with enzalutamide in the active surveillance arm of the economic model, and stated that the ICER should remain at $45,000 - $75,000/QALY. In the minor resubmission, the sponsor made requested adjustments to the model but also proposed various other strategies to deliver an acceptable ICER. The probability that these strategies actually delivered the requested ICER could not be accurately determined. The PBAC was concerned that the size of the proposed patient population is uncertain, and that the proposed subsidisation caps may not be reached, resulting in a higher average DPMQ and a higher ICER than those proposed in the minor resubmission.
		Sponsor comment	Astellas will consider the issues raised by the PBAC and continue to investigate options to improve access to enzalutamide for metastatic castration resistant prostate cancer, chemotherapy-naïve patients.
GLECAPREVIR with PIBRENTASVIR Tablet containing 100 mg glecaprevir with 40 mg pibrentasvir Maviret® Abbvie Pty Ltd	Chronic hepatitis C virus (HCV) infection	To request General Schedule and Section 100 (Highly Specialised Drugs Program) Authority Required (STREAMLINED) listings for the treatment of chronic HCV infection, regardless of genotype.	The PBAC was of a mind to recommend the Authority Required General Schedule and Section 100 listing of glecaprevir with pibrentasvir on a cost-minimisation basis with the relevant lowest priced alternative regimen in the General Statement for Drugs for the Treatment of Hepatitis C, for the treatment of chronic hepatitis C infection for patients with genotypes 1-6, with or without cirrhosis. However, the PBAC deferred making a final recommendation pending the provision of the relevant TGA delegate's overview.

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New listing (Major Submission)		Sponsor comment	The sponsor had no comment.
NICOTINE Gum 2 mg Gum 4 mg Lozenge 2 mg Lozenge 4 mg Nicotinell Chewing gum® Nicotinell lozenge® Orion Laboratories Pty Ltd T/A Perrigo Australia New Listing (Major Submission)	Nicotine dependence	To request a Restricted Benefit listing for nicotine chewing gum and lozenges to aid smoking cessation in patients with nicotine dependence.	The PBAC deferred making a recommendation on whether nicotine gum and lozenges should be listed on the PBS as monotherapies for smoking cessation, pending further clarity on the appropriate use of nicotine gum and lozenges, and its implications for the economic analysis and financial estimates. The PBAC recalled that while considering the PBS retention criteria for medicines that were available over the counter at its April 2015 Special meeting, the Committee had considered that retaining nicotine replacement therapies (NRTs) on the PBS was important, recognising that smoking cessation was a public health priority area. The PBAC considered that the proposed maximum quantity was substantially underestimated, given that the requested restrictions require the gum or lozenges to be the sole form of PBS-subsidised smoking cessation medicine permitted in a twelve-month period. The PBAC consider that this could result in under-treatment for some patients and trigger discontinuation in others. The disparity in the requested maximum quantities also flowed on to the estimation of equi-effective doses, resulting in substantial uncertainty in the cost-minimisation analysis. The PBAC considered that the appropriate place in clinical therapy for nicotine gum and lozenges would be as combination therapy with long acting forms of currently listed smoking cessation therapies (nicotine patches, varenicline or bupropion). However, no evidence was provided in the submission about the cost-effectiveness of combination treatment. The PBAC considered that further clinical evidence and revised utilisation estimates for combination use of NRTs were warranted before the comparative efficacy and cost-effectiveness of combination treatment could be appropriately determined by the

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			Committee.
		Sponsor comment	The sponsor thanks the committee for its thorough review and its clear interest in our products as both mono therapy and as part of combination use. We look forward to working with the PBAC to address the few remaining issues in this submission so that these important medicines can be made more accessible and help more people quit smoking.
PEGFILGRASTIM Injection 6 mg in 0.6 mL single use pre-filled syringe Neulasta® Ristempa® Amgen Australia Pty Ltd Change to listing (Minor Submission)	Prophylaxis of chemotherapy induced neutropenia	To request a Section 100 (Highly Specialised Drug) Authority Required listing for the treatment of patients for primary prophylaxis of chemotherapy induced neutropenia in patients with early stage breast cancer in patients receiving docetaxel and cyclophosphamide based chemotherapy.	The PBAC deferred making a decision regarding the listing of pegfilgrastim for primary prophylaxis of febrile neutropenia in certain patients being treated for breast cancer to allow further negotiation between the sponsor and the Department on the proposed restriction and impact on the PBS. The PBAC was of the view that the need for, and effectiveness of primary prophylaxis was more dependent on the type of chemotherapy than the tumour type. The PBAC considered that in this context the current restrictions which are based on tumour type may be inequitable and that a restriction based on the risk of febrile neutropenia may be more appropriate if a cost-effective price for pegfilgrastim can be achieved with the sponsor.
		Sponsor comment	The sponsor had no comment.
PEMBROLIZUMAB Powder for injection 50 mg Solution for I.V. infusion 100 mg in 4 mL Keytruda® Merck, Sharp and Dohme (Australia) Pty Ltd Change to listing	Classical Hodgkin's lymphoma	To request a Section 100 (Efficient Funding of Chemotherapy) listing for the treatment of patients with refractory classical Hodgkin's lymphoma, or those who have relapsed after 3 or more prior lines of therapy.	The PBAC deferred making a recommendation on whether pembrolizumab should be listed on the PBS for the treatment of relapsed or refractory classical Hodgkin's Lymphoma (rrcHL) for further discussion with the sponsor on determining the basis of cost-minimisation against brentuximab vedotin (BV). The PBAC also noted that the TGA Delegate's Overview was not available prior to the PBAC meeting. The PBAC agreed with the sponsor that pembrolizumab treatment showed promising overall response rates in a heavily pre-treated, refractory patient population, and that the clinical claim of non-inferiority compared with BV was supported by the evidence provided.

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(Major Submission)			The PBAC noted that the Phase III KN204 trial evidence comparing pembrolizumab with BV would not be available until 2020, and that the clinical data presented in this submission were based on a comparison across single-arm studies with no common reference arm, with the key pembrolizumab study (KN087) having immature data. The PBAC also noted that the due to the populations included in these studies the results were not comparable.
		Sponsor comment	MSD looks forward to working with the PBAC and Department, so that patients with relapsed or refractory classical Hodgkin's lymphoma will be able to access Keytruda on the PBS as soon as possible.
RALTEGRAVIR Tablet 600 mg (as potassium) Isentress HD® Merck, Sharp and Dohme (Australia) Pty Ltd New Listing (Major Submission)	Human immunodeficiency virus (HIV) infection	To request a Section 100 (Highly Specialised Drugs Program - Community Access) Authority Required (STREAMLINED) listing for the treatment of patients with HIV infection in combination with other antiretroviral agents.	The PBAC was of a mind to recommend raltegravir 600 mg tablets be listed on the PBS for the treatment of HIV infection on a cost-minimisation basis compared with raltegravir 400 mg tablets, noting that raltegravir 600 mg tablets should be available only under special arrangements under Section 100 – Highly Specialised Drugs Program (Community Access). However, the PBAC deferred making a recommendation pending the TGA Delegate's Proposed Regulatory Action.
		Sponsor comment	MSD is disappointed with the outcome but is looking forward to working with the PBAC to ensure HIV-infected patients have access to the new formulation of Isentress as soon as possible.
SAXAGLIPTIN with DAPAGLIFLOZIN Tablet containing saxagliptin 5 mg with dapaglifozin 10 mg Qtern® AstraZeneca Pty Ltd	Type 2 diabetes mellitus (T2DM)	To request an Authority Required (STREAMLINED) listing for dapagliflozin with saxagliptin in combination with metformin for the treatment of T2DM.	The PBAC deferred making a decision regarding the Authority Required (STREAMLINED) listing for dapagliflozin/saxagliptin fixed dose combination (FDC) for treatment of type 2 diabetes in combination with metformin to allow further work to establish a cost effective price offer for dapagliflozin in triple therapy with a DPP4 inhibitor and metformin. The PBAC noted that they deferred the submission requesting this listing (refer to dapagliflozin July 2017 major submission) and therefore the cost effectiveness of treatment in this setting had not yet been established. The PBAC also noted that the extent of use was likely to be underestimated.

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New Listing (Major Submission)		Sponsor comment	The sponsor had no comment.
TENOFOVIR with EMTRICITABINE Tablet containing tenofovir disoproxil maleate 300 mg with emtricitabine 200 mg Tenofovir Disoproxil Emtricitabine Mylan 300/200® Alphapharm Pty Ltd (trading as Mylan Australia) Change to listing (Minor Submission)	Human immunodeficiency virus (HIV) pre-exposure prophylaxis (PrEP)	To request an Authority Required (STREAMLINED) listing for PrEP in adults at high risk of HIV infection.	The PBAC deferred making a recommendation on tenofovir with emtricitabine for HIV Pre-exposure Prophylaxis (PrEP) to seek further information regarding its cost-effectiveness based on the model developed by the Kirby Institute. Specifically the Committee requested additional analyses considering alternative uptake scenarios where the extent of uptake is reduced and use is limited to medium and high risk individuals, and varying the tenofovir with emtricitabine price. The PBAC noted the results for the Kirby model were presented for a number of scenarios based on different uptake in individuals at high, medium or low risk of infection. Only two of the scenarios presented considered use in individuals at high and medium risk of infection, the population which the PBAC agreed to be appropriate. Further, both of the scenarios assumed 90% uptake in high risk individuals and the PBAC considered that this level of uptake was unlikely to be achieved in clinical practice. The PBAC considered alternative scenarios assuming lower uptake in medium and high risk individuals would be informative. The PBAC considered that the acceptable incremental cost effectiveness ratio (ICER) for PrEP would be at the low end of the range previously accepted for other population preventative interventions with large opportunity costs. The PBAC considered the utilisation estimates were highly uncertain and difficult to predict, however utilisation was likely overestimated.
		Sponsor comment	Mylan Australia is committed to working with the PBAC and other key stakeholders to address the points raised, to provide appropriate and timely access to PrEP for the community.

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TENOFOVIR with EMTRICITABINE Tablet containing tenofovir disoproxil fumarate 300 mg with emtricitabine 200 mg Truvada® Gilead Sciences Pty Ltd Change to listing (Major Submission)	Human immunodeficiency virus (HIV) pre-exposure prophylaxis (PrEP)	Resubmission to request an Authority Required (STREAMLINED) listing for PrEP in adults at medium to high risk of HIV infection.	The PBAC deferred making a recommendation on tenofovir with emtricitabine (TDF/FTC) for HIV Pre-exposure Prophylaxis (PrEP) to seek additional results from the cost-effectiveness model developed by the Kirby Institute to inform its decision-making. Specifically the Committee requested results for alternative uptake scenarios where the extent of uptake is reduced and use is limited to medium and high risk individuals, and for sensitivity analyses varying the tenofovir with emtricitabine price to be undertaken for these additional scenarios. The PBAC considered the proposed general schedule PBS listing for use in individuals at high and medium risk of infection according the Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine (ASHM) Guidelines, to be appropriate. The PBAC accepted, based on the evidence presented, that TDF/FTC as PrEP appeared to be effective in reducing the transmission of HIV. The PBAC reaffirmed its previous advice that it considered the claim of non-inferior comparative safety was not strongly supported by the available data, however given the duration of experience with TDF/FTC for the treatment of HIV, the claim of non-inferior comparative safety was probably reasonable. The PBAC noted that the price of TDF/FTC was a key driver of the cost-effectiveness of TDF/FDC for PrEP in the economic model developed by the sponsor, and despite noting a number of issues with this economic model, that TDF/FTC was not cost-effective at the requested price. The PBAC noted the submission included an economic model assessing the cost-effectiveness of PrEP developed by the Kirby Institute and considered that the Kirby model was likely to be more robust and reliable than the model developed by the sponsor. The PBAC noted the results for the Kirby model were presented for a number of scenarios based on different uptake in individuals at high, medium or low risk of infection. The PBAC noted that only two of the

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			scenarios presented considered use in individuals at high and medium risk of infection, the population proposed in the resubmission which the PBAC agreed to be appropriate. Further, both of the scenarios assumed 90% uptake in high risk individuals and the PBAC considered that this level of uptake was unlikely to be achieved in clinical practice. The PBAC considered alternative scenarios assuming lower uptake in medium and high risk individuals would be informative. The PBAC considered that the acceptable incremental cost effectiveness ratio (ICER) for PrEP would be at the low end of the range previously accepted for other population preventative interventions with large opportunity costs. The PBAC considered the utilisation estimates for PrEP were highly uncertain and difficult to predict, however agreed that the submission likely underestimated utilisation in year 1 and overestimated it in years 2-5. The PBAC noted that the submission estimated annual expenditure exceeding $200 million per year in five of the six years of the estimates and considered the opportunity cost was unacceptably high at the proposed price.
		Sponsor comment	Gilead are assessing the PBAC comments and working with the community to determine the next steps. Gilead is aware that there are now generic companies providing multiple brands of tenofovir with emtricitabine.