

**JULY 2020 PBAC OUTCOMES – SUBSEQUENT DECISIONS NOT TO RECOMMEND**

<b>DRUG NAME, FORM(S), STRENGTH(S), SPONSOR, TYPE OF SUBMISSION</b>	<b>TGA INDICATION</b>	<b>CURRENT PBS LISTING</b>	<b>LISTING REQUESTED BY SPONSOR / PURPOSE OF SUBMISSION</b>	<b>PBAC OUTCOME</b>
<p>AMINO ACID FORMULA WITH CARBOHYDRATE, VITAMINS, MINERALS AND TRACE ELEMENTS WITHOUT PHENYLALANINE, SUPPLEMENTED WITH DOCOSAHEXAENOIC ACID</p> <p>Sachets containing oral powder 33 g, 30</p> <p>PKU Synergy®</p> <p>Nutricia Australia Pty Ltd</p> <p>New listing (Minor Submission)</p>	<p>N/A</p>	<p>PKU Synergy® is not currently PBS listed.</p>	<p>Resubmission to request a Restricted Benefit listing for the dietary management of phenylketonuria (PKU)</p>	<p>The PBAC did not recommend the listing of PKU Synergy® for the dietary management of PKU or hyperphenylalaninaemia in children from 10 years of age or adults. The PBAC maintained its previous view that there were other products with better nutritional profiles for this patient population and that there was no clinical need for this product.</p>
			<p>Comparator: PKU Express 20® and PKU Lophlex®</p>	<p>The PBAC previously accepted PKU Express 20® and PKU Lophlex® as appropriate comparators.</p>
			<p>Clinical claim: That PKU Synergy® will enable patients who are non-compliant in their dietary therapy and patients with a higher tolerance to phenylalanine, to meet micronutrient requirements in a smaller volume of product.</p>	<p>The PBAC noted the advice from the Nutritional Products Working Party (NPWP) that the resubmission did not adequately address previous concerns that the product would provide enough copper and phosphorus for patients on a relaxed diet; and if diets were sufficiently relaxed to meet requirements for these nutrients, that there was no clinical need for PKU Synergy®.</p>
			<p>Economic claim: Cost-minimisation versus PKU Express 20® and PKU Lophlex®</p>	<p>The PBAC noted the resubmission did not provide a rationale for requesting a higher approved ex-manufacturer price per gram of protein equivalent compared with the comparators.</p>
			<p>Sponsor's comment:</p>	<p>Nutricia would like to thank the PBAC and the NPWP for the opportunity to comment on the PBAC outcome. Nutricia are disappointed that the NPWP was not supportive of, and the PBAC did not recommend, the listing of PKU Synergy®.</p> <p>Nutricia does not share the concerns raised by PBAC and the NPWP, namely that PKU Synergy® does not provide sufficient copper and phosphorous, and a one sachet dose would be confusing to patients. However, in light of these concerns, Nutricia has undertaken a new clinical trial using</p>

**JULY 2020 PBAC OUTCOMES – SUBSEQUENT DECISIONS NOT TO RECOMMEND**

DRUG NAME, FORM(S), STRENGTH(S), SPONSOR, TYPE OF SUBMISSION	TGA INDICATION	CURRENT PBS LISTING	LISTING REQUESTED BY SPONSOR / PURPOSE OF SUBMISSION	PBAC OUTCOME
				<p>PKU Synergy® in patients taking Kuvan® (BH4) for at least one year, which should be sufficiently long term to address the PBACs concerns and prove the efficacy of the product. Nutricia will then consider a reapplication to the PBAC.</p>
<p><b>BELIMUMAB</b></p> <p>Injection 200 mg in 1 mL pre-filled pen</p> <p>Benlysta®</p> <p>GlaxoSmithKline Australia Pty Ltd</p> <p>New listing (Major Submission)</p>	<p>Belimumab is indicated as add-on therapy for reducing disease activity in adult patients with active, autoantibody-positive systemic lupus erythematosus (SLE) with a high degree of disease activity despite standard therapy.</p>	<p>Belimumab is not currently PBS listed.</p>	<p>Resubmission to request a Section 100 (Highly Specialised Drugs Program) Authority Required listing for the treatment of patients with active autoantibody-positive SLE with a high degree of disease activity, despite defined ongoing standard therapy.</p>	<p>The PBAC did not recommend belimumab for the treatment of patients with active autoantibody-positive SLE with a high degree of disease activity despite ongoing standard therapy.</p> <p>The PBAC considered there is a clinical need for effective and safe treatments for SLE, particularly for patients with severe active disease who have failed, or are intolerant to, other therapies.</p> <p>The PBAC maintained its view from November 2019 that the evidence demonstrated a modest clinical benefit in a subset of patients. The PBAC considered that the incremental cost effectiveness ratio (ICER) was likely to have been underestimated by the submission, and that belimumab was not suitably cost-effective at the price proposed in the resubmission.</p>
			<p>Comparator: Placebo/standard of care (SOC)</p>	<p>The PBAC accepted that SOC was an appropriate comparator, consistent with the November 2019 PBAC meeting.</p>
			<p>Clinical claim: Superior effectiveness and inferior safety compared with SOC</p>	<p>The PBAC noted that the BLISS-SC trial found that belimumab plus SOC resulted in a 13% increase in the proportion of Systemic Lupus Erythematosus Responder Index responders at Week 52 compared with placebo plus SOC (RD = 0.13; 95% CI: 0.06, 0.20). The PBAC considered that the claim of superior effectiveness compared to SOC was supported by a modest clinical</p>

**JULY 2020 PBAC OUTCOMES – SUBSEQUENT DECISIONS NOT TO RECOMMEND**

DRUG NAME, FORM(S), STRENGTH(S), SPONSOR, TYPE OF SUBMISSION	TGA INDICATION	CURRENT PBS LISTING	LISTING REQUESTED BY SPONSOR / PURPOSE OF SUBMISSION	PBAC OUTCOME
				benefit in a subset of patients, and the claim of inferior safety was reasonable.
			Economic claim: Cost-effectiveness and a cost-utility analysis compared with SOC	The PBAC considered that the ICER was likely to have been underestimated by the submission, as some of the assumptions applied in the economic model may not be reasonable and likely favoured belimumab.
			Sponsor's comment:	GSK is disappointed by the PBAC's decision not to recommend Benlysta® (belimumab) for the treatment of patients with SLE, which is the only new clinically effective therapy to be approved for this indication in 50 years. GSK welcomes the PBAC's acknowledgement of the clinical need for effective treatments for SLE, particularly for the group of patients who are not responding to current therapies, given the debilitating impact this condition can have on people's lives and specifically their individual quality of life. GSK will now review the feedback from the PBAC and consider our position.
<p><b>BROLUCIZUMAB</b></p> <p>Solution for intravitreal injection 19.8 mg in 0.165 mL pre-filled syringe</p> <p>Beovu®</p> <p>Novartis Pharmaceuticals Australia Pty Ltd</p> <p>New listing (Minor Submission)</p>	<p>Brolucizumab is indicated for the treatment of neovascular (wet) age-related macular degeneration (AMD).</p>	<p>Brolucizumab is not currently PBS listed.</p>	<p>Resubmission to request the Authority Required PBS listing for the treatment of patients with subfoveal choroidal neovascularisation (CNV) due to AMD.</p> <p>Comparator: Aflibercept (main), ranibizumab (secondary)</p> <p>Clinical claim: Non-inferior effectiveness and safety compared with aflibercept</p>	<p>The PBAC did not recommend brolucizumab for the treatment of patients with subfoveal CNV due to AMD. The PBAC considered brolucizumab is likely inferior to aflibercept in terms of comparative safety. The PBAC recalled it had previously considered brolucizumab was non-inferior in terms of comparative efficacy but did not accept that the evidence supported less frequent dosing.</p> <p>The PBAC accepted that aflibercept and ranibizumab were appropriate comparators, consistent with the November 2019 PBAC meeting.</p> <p>The PBAC considered that the claim of non-inferior effectiveness compared with aflibercept was reasonable, consistent with the November 2019 PBAC meeting, but did not accept that the evidence supported less frequent dosing. The PBAC considered brolucizumab is likely inferior to aflibercept in terms of comparative safety, based</p>

**JULY 2020 PBAC OUTCOMES – SUBSEQUENT DECISIONS NOT TO RECOMMEND**

DRUG NAME, FORM(S), STRENGTH(S), SPONSOR, TYPE OF SUBMISSION	TGA INDICATION	CURRENT PBS LISTING	LISTING REQUESTED BY SPONSOR / PURPOSE OF SUBMISSION	PBAC OUTCOME
				<p>on the clinical trial evidence of a significant difference in serious adverse events between brolocizumab and aflibercept, and changes made to the approved Product Information to reflect an emerging safety signal of retinal vasculitis and/or retinal vascular occlusion.</p> <p>Economic claim: Cost-minimisation versus ranibizumab</p> <p>The PBAC considered the cost-minimisation analysis was not adequately supported as the claim of non-inferior safety of brolocizumab was uncertain.</p> <p>Sponsor's comment: Novartis disagrees with the decision of the PBAC not to recommend the listing of Beovu® on the PBS for the treatment of wet AMD. Beovu® has now been approved in more than 30 countries, including all major markets, and Novartis and Australian clinicians believe that Beovu® represents an important treatment option for patients with wet AMD, with an overall favourable benefit-risk profile. Novartis will continue to work collaboratively with the PBAC, the Department of Health and the Federal Government to help ensure that Australians with wet AMD receive access to Beovu® through the PBS at the earliest opportunity.</p>
<p>OCRELIZUMAB</p> <p>Solution concentrate for I.V. infusion 300 mg in 10 mL</p> <p>Ocrevus®</p> <p>Roche Products Pty Ltd</p> <p>New listing</p>	<p>Ocrelizumab is indicated for the treatment of patients with primary progressive multiple sclerosis (PPMS) to delay the progression of physical disability.</p> <p>Ocrelizumab is also indicated for the treatment of patients</p>	<p>Ocrelizumab is currently PBS listed for relapsing-remitting multiple sclerosis (RRMS).</p>	<p>Resubmission to request a Section 100 (Highly Specialised Drugs Program – Public and Private Hospitals) Authority Required listing for the treatment of adult patients with PPMS in certain circumstances.</p>	<p>The PBAC did not recommend extending the listing of ocrelizumab to include patients with early, MRI-active PPMS. The PBAC considered that the key subgroup analysis that was relied on in the submission was inconsistent with the requested PBS population, which led to difficulties in assessing the cost-effectiveness of ocrelizumab. The PBAC considered that the economic model had likely underestimated the incremental cost-effectiveness ratio (ICER) as the likely treatment effect and residential care costs had been overestimated.</p> <p>The PBAC noted the high clinical need for effective treatments to delay the progression of disability in PPMS.</p>

**JULY 2020 PBAC OUTCOMES – SUBSEQUENT DECISIONS NOT TO RECOMMEND**

<b>DRUG NAME, FORM(S), STRENGTH(S), SPONSOR, TYPE OF SUBMISSION</b>	<b>TGA INDICATION</b>	<b>CURRENT PBS LISTING</b>	<b>LISTING REQUESTED BY SPONSOR / PURPOSE OF SUBMISSION</b>	<b>PBAC OUTCOME</b>
(Major Submission)	with relapsing forms of multiple sclerosis (RMS) to the delay the progression of physical disability and to reduce the frequency of relapse.		Comparator: Best supportive care (BSC)	The PBAC reaffirmed its view expressed in its November 2017 consideration that BSC was the appropriate comparator.
			Clinical claim: Superior comparative effectiveness and inferior comparative safety compared with placebo	<p>The PBAC considered that the claim of superior comparative effectiveness in the early and MRI-active population was adequately supported, but that subgroup results applied in the economic model likely overestimated the magnitude of the benefit in the requested PBS population (due to limitations of the subgroup data and the potential lack of applicability of the subgroup results to the requested listing).</p> <p>The PBAC reaffirmed its view expressed at its November 2017 meeting that ocrelizumab is of inferior comparative safety to placebo.</p>
			Economic claim: Cost-effectiveness basis compared with BSC	<p>The PBAC considered that the economic model had likely underestimated the ICER as the likely treatment effect and the residential care costs had been overestimated.</p> <p>The PBAC also considered that it would also be informative to include the impact of appropriate discontinuation criteria in the economic model.</p>
			Sponsor's comment:	Roche is disappointed with the outcome given the genuine unmet need for an effective treatment option for patients with PPMS. Roche will continue to support the MS community in Australia whilst we evaluate the options available within the parameters of the existing data to find a suitable path forward. Roche would like to take this opportunity to thank the many healthcare professionals, and broader members of the MS community, who supported the resubmission.