

**PHARMACEUTICAL BENEFITS ADVISORY COMMITTEE (PBAC) MEETING OUTCOMES  
SEPTEMBER 2022 PBAC INTRACYCLE MEETING**

The PBAC outcomes and recommendations are presented in alphabetical order by drug name.

*Submission items*

<b>DRUG NAME, FORM(S), STRENGTH(S), SPONSOR, TYPE OF SUBMISSION</b>	<b>DRUG TYPE AND USE</b>	<b>LISTING REQUESTED BY SPONSOR / PURPOSE OF SUBMISSION</b>	<b>PBAC OUTCOME</b>	
<p>AZACITIDINE</p> <p>Tablet 200 mg Tablet 300 mg</p> <p>Onureg®</p> <p>Celgene Pty Limited</p> <p>(New PBS listing)</p>	<p>Acute myeloid leukaemia</p>	<p>To request a General Schedule Authority Required (STREAMLINED) listing for maintenance therapy in certain patients with acute myeloid leukaemia who are not candidates for (including those who choose not to proceed to) haematopoietic stem cell transplantation.</p>	<p>Recommended</p>	<p>The PBAC recommended oral azacitidine as maintenance therapy in patients with acute myeloid leukaemia (AML) who achieve complete remission or complete remission with incomplete blood count recovery following induction chemotherapy with or without consolidation treatment, and who are not candidates for (including those who choose not to proceed to) haematopoietic stem cell transplantation. The PBAC was satisfied that oral azacitidine provides, for some patients, a significant improvement in efficacy including improved overall survival and relapse free survival. The PBAC considered that the resubmission's changes to the economic model parameters adequately addressed its previous concerns and that oral azacitidine would be acceptably cost-effective at the price proposed in the resubmission. Further, the PBAC considered that the resubmission's changes to the financial estimates were reasonable.</p>
<p>CANNABIDIOL</p> <p>Oral liquid 100 mg per mL, 100 mL</p> <p>Epidyolex®</p> <p>Chiesi Australia Pty Ltd</p> <p>(Matters arising)</p>	<p>Lennox-Gastaut syndrome (LGS)</p>	<p>Resubmission to request a General Schedule Authority Required listing for the adjunctive treatment of seizures in patients with LGS aged 2 years and older.</p>	<p>Recommended</p>	<p>The PBAC recommended the listing of cannabidiol for the treatment of seizures associated with LGS in patients who have not achieved adequate seizure control with at least two other anti-epileptic drugs. The PBAC considered the revised proposal for listing provided by the sponsor addressed its outstanding concerns regarding the cost-effectiveness of cannabidiol.</p>

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<p>QUADRIVALENT INFLUENZA VACCINE (SURFACE ANTIGEN, INACTIVATED, CELL-BASED)</p> <p>Injection 15 microgram in 0.5 mL needle-free pre-filled syringe Injection 15 microgram in 0.5 mL pre-filled syringe with attached needle</p> <p>Flucelvax® Quad</p> <p>Seqirus (Australia) Pty Ltd</p> <p>(New listing)</p>	<p>Prevention of influenza</p>	<p>To request National Immunisation Program listing for the prevention of influenza.</p>	<p>Recommended</p>	<p>The PBAC recommended that quadrivalent influenza virus vaccine, surface antigen, inactivated, cell-based (QIVc), Flucelvax® Quad, be a designated vaccine for the purposes of the <i>National Health Act 1953</i>, for vaccination against influenza in Aboriginal and Torres Strait Islander peoples aged ≥5 to &lt;65 years, people at increased risk of influenza disease complications aged ≥5 to &lt;65 years and pregnant women. The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of QIVc would be acceptable with a small price premium compared to egg-based quadrivalent influenza virus vaccines and the acknowledgment of potential benefits associated with the diversification of vaccine manufacturing.</p>
<p>RUXOLITINIB</p> <p>Tablet 5 mg Tablet 10 mg</p> <p>Jakavi®</p> <p>Novartis Pharmaceuticals Australia Pty Limited</p> <p>(Change to PBS listing)</p>	<p>Graft versus host disease</p>	<p>To request a General Schedule Authority Required (STREAMLINED) listing for the treatment of patients with moderate to severe chronic graft versus host disease (GVHD) who are refractory to, dependent on or intolerant of corticosteroids.</p>	<p>Not recommended</p>	<p>The PBAC did not recommend ruxolitinib for the treatment of patients with chronic GVHD. The PBAC considered that the changes made in the resubmission did not sufficiently address the Committee's previous advice regarding the requirements of a simple resubmission. Overall, the PBAC considered that ruxolitinib was not acceptably cost-effective at the price proposed, noting that the economic model was not revised as requested; the financial implications were increased compared with the previous submission; and the proposed risk sharing arrangement (RSA) would not adequately manage the risk associated with the uncertain treatment duration.</p> <p><u>Sponsor Comment:</u></p> <p>Novartis is disappointed that the PBAC did not recommend ruxolitinib for the treatment of chronic graft vs host disease. We will continue to work with the PBAC to resolve the outstanding issues.</p>

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<p>TIXAGEVIMAB AND CILGAVIMAB</p> <p>Pack containing 1 vial of tixagevimab 150 mg in 1.5 mL and 1 vial of cilgavimab 150 mg in 1.5 mL</p> <p>Evusheld®</p> <p>AstraZeneca Pty Ltd</p> <p>(New PBS listing)</p>	<p>Pre-exposure prevention of COVID-19</p>	<p>To request a General Schedule Authority Required listing for pre-exposure prevention of COVID-19 in individuals 12 years or older who are severely immunocompromised due to a specific medical condition or because of treatment with immunosuppressive therapies that render them unlikely to mount an adequate immune response to immunisation.</p>	<p>Not recommended</p>	<p>The PBAC did not recommend the PBS listing of tixagevimab and cilgavimab (Evusheld) for pre exposure prophylaxis (PrEP) against COVID-19 because, in the view of the PBAC, there was uncertainty about the clinical place in treatment; uncertainty about the dose and duration of protection against the Omicron or future variants of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus; a lack of information on the safety and effectiveness of the proposed repeat dosing regimen; a high and highly uncertain incremental cost-effectiveness ratio; and a very high overall cost as requested by the sponsor.</p> <p>In considering the application, the PBAC noted the Department of Health and Aged Care's advice that when the Commonwealth purchase contract for 36,000 courses of tixagevimab 150 mg and cilgavimab 150 mg (Evusheld 150-150 mg) for the National Medical Stockpile was agreed early in 2022, it was expected by the Department that a single dose of Evusheld 150-150 mg would provide PrEP against symptomatic COVID for at least 6 months and potentially for 12 months or even longer. This expectation was founded on the available results from the PROVENT clinical trial conducted when the predominant SARS-CoV-2 variants circulating were Alpha, Beta, Gamma, Delta, and Epsilon.</p> <p>The PBAC noted more recent publicly available information on Omicron indicates Evusheld 150-150 mg does not protect to the same extent as past variants and AstraZeneca has proposed a doubling of the dose to tixagevimab 300 mg and cilgavimab 300 mg (Evusheld 300-300mg), together with 6-monthly repeat dosing at 300-300 mg, to address this diminution in effectiveness (Astra Zeneca, 14 July 2022). In the PBAC's view, the outcomes of two observational studies conducted early during the Omicron variant outbreak provide some evidence of effectiveness for the Evusheld 300-300 mg dose in a vaccinated, immunocompromised population (Young-Xu, 2022; Al Jurdi, 2022). In relation to effectiveness and safety of 6-monthly repeat dosing, the evidence was limited to pharmacokinetic modelling and no in-human evidence was presented.</p> <p>The PBAC noted the Therapeutic Goods Administration (TGA) is evaluating an application from AstraZeneca to vary the currently recommended dose from Evusheld 150-150 mg once, to Evusheld 300-300 mg 6-monthly. However, the TGA had not finalised its considerations on the effectiveness or safety of this approach at the time of PBAC consideration.</p> <p>The PBAC was concerned that:</p> <ul style="list-style-type: none"> <li>The population most likely to benefit from PrEP in the context of an evolving and cyclic disease was not well defined by the sponsor's application, creating the potential that the sponsor proposed PBS eligible population would include many individuals who would gain little benefit and exclude other individuals who would benefit.</li> </ul>
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			<ul style="list-style-type: none"> <li>• AstraZeneca acknowledged the duration of protection against COVID-19 given by Evusheld 150-150 mg is shorter for the Omicron variants than it was for earlier variants of the SARS-CoV-2 virus. The PBAC opined that, based on the information provided by AstraZeneca, the TGA approved single dose of 150-150 mg could provide as little as three months protection from symptomatic disease caused by the Omicron variants. Protection against severe and critical illness appears to be maintained although the size of the effect was uncertain.</li> <li>• While the observational studies provide some support, there was no evidence from controlled clinical studies to support the AstraZeneca proposition that doubling the Evusheld dose (from 150-150 mg to 300-300mg) will address the limited duration of protection. There was no clinical evidence for 6-monthly repeat dosing.</li> <li>• The safety of the higher and more frequent dosing regimen has not been established.</li> <li>• Although the economic modelling used assumptions that were favourable to Evusheld 300-300 mg, the incremental cost-effectiveness ratio (ICER) for the proposed dosing regimen at the proposed price was unacceptably high at \$115,000 to &lt;\$135,000 per Quality Adjusted Life Year (QALY) gained.</li> <li>• The changing nature of the pandemic adds additional uncertainty about the future value of treatment with Evusheld 300-300 mg (i.e., the value proposition could be worse than estimated now).</li> <li>• Uptake of Evusheld 300-300 mg was likely to be significantly overestimated by the application.</li> <li>• At an estimated cost that could exceed \$1 billion per year, the opportunity cost of subsidy is potentially very high.</li> </ul> <p>The PBAC made extensive suggestions for consideration by AstraZeneca which included limiting its subsidy request to a once-off dose per patient in line with the available evidence; refining the target population to those with the greatest clinical need; reducing the price; and time-limiting the subsidy period given the uncertainty over the future role of this medicine in view of the evolving nature of the SARS-CoV-2 virus.</p> <p>The PBAC noted that AstraZeneca is welcome to make a further application to the PBAC for PBS listing at any time. The PBAC noted that the Department would work with AstraZeneca and the PBAC to expedite any future application, considering the evolution of the pandemic.</p> <p><u>Sponsor Comment:</u></p> <p>AstraZeneca are committed to addressing the concerns raised by the PBAC and we welcome the opportunity to work with the Department of Health and</p>
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				Aged Care to ensure a timely reassessment of Evusheld. AstraZeneca acknowledges the PBAC assessment process requires a high degree of certainty for therapies to be listed on the PBS. We note the status of the updated dosing regimen which is currently under evaluation by the TGA. AstraZeneca will continue to collect data as new variants evolve and work with the PBAC to further define the appropriate patient population.
<p>VOSORITIDE</p> <p>Powder for injection 0.4 mg with diluent Powder for injection 0.56 mg with diluent Powder for injection 1.2 mg with diluent</p> <p>Voxzogo®</p> <p>BioMarin Pharmaceutical Australia Pty Ltd</p> <p>(New PBS listing)</p>	<p>Achondroplasia</p>	<p>To request a General Schedule Authority Required listing for the treatment of patients with achondroplasia whose epiphyses are not closed.</p>	<p>Deferred</p>	<p>The PBAC deferred making a recommendation for vosoritide for the treatment of patients with achondroplasia whose epiphyses are not closed to allow for further consultation with the sponsor regarding a cost-effective price. In deciding to defer making a recommendation, the PBAC affirmed its view that there was a high clinical need for effective treatments for achondroplasia, however, the Committee considered that a further price reduction was required to achieve an incremental cost-effectiveness ratio within a cost-effective range.</p> <p><u>Sponsor Comment:</u></p> <p>BioMarin is extremely disappointed that the substantial price reduction offered in the early resolution resubmission was not accepted. We acknowledge the PBAC's recognition of the high clinical need for effective treatments for achondroplasia, such as vosoritide, and will continue to seek to gain PBAC recommendation and PBS listing.</p>

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*Non-submission items*

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<p>RESTRICTION CHANGES TO COVID-19 ANTIVIRALS</p> <p>MOLNUPIRAVIR</p> <p>Capsule 200 mg</p> <p>Lagevrio®</p> <p>Merck Sharp &amp; Dohme (Australia) Pty Ltd</p> <p>NIRMATRELVIR AND RITONAVIR</p> <p>Pack containing 4 tablets nirmatrelvir 150 mg and 2 tablets ritonavir 100 mg, 5</p> <p>Paxlovid®</p> <p>Department of Health (Commonwealth)</p> <p>(Change to PBS listing)</p>	<p>Antivirals - treatment of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection</p>	<p>To seek PBAC advice on changing the restriction to support use in “unvaccinated” or “suboptimally vaccinated” patients. Options include reducing from two conditions to one condition (defining high risk) for people identifying as Aboriginal or Torres Strait Islander, or including “unvaccinated” or “suboptimally vaccinated” as a condition helping to define high risk (across the whole population).</p> <p>To seek PBAC advice for listing these medicines in the Doctor’s Bag Schedule.</p>	<p>Recommended</p>	<p>The PBAC recommended amending the PBS listings for molnupiravir and nirmatrelvir + ritonavir, so that people identifying as Aboriginal or Torres Strait Islander, and 30 years of age or more, require only one condition (from the current list of conditions) to meet the definition of high risk for the purpose of PBS eligibility.</p> <p>The PBAC recommended that molnupiravir and nirmatrelvir + ritonavir both be added to Prescriber’s Bag supplies (Medical Practitioner and Nurse Practitioner), with the quantity being two bottles of molnupiravir (40 capsules per bottle) and two cartons of nirmatrelvir + ritonavir (30 tablets divided in 5 daily-dose blister cards, per carton).</p>

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<p>RESTRICTION CHANGES TO LEFLUNOMIDE</p> <p>LEFLUNOMIDE</p> <p>Tablet 10 mg Tablet 20 mg</p> <p>Various brands</p> <p>Various sponsors</p> <p>(Change to PBS listing)</p>	<p>Immunosuppressant</p> <p>Severe active psoriatic arthritis</p> <p>Severe active rheumatoid arthritis</p>	<p>To consider whether leflunomide should be changed to a Restricted Benefit listing on the PBS.</p>	<p>Recommended</p>	<p>The PBAC recommended that the authority level of leflunomide on the PBS be amended from Authority Required (STREAMLINED) to Restricted Benefit for the same indications and clinical criteria as the existing listings. The PBAC noted this would reduce the administrative burden of prescribing these medicines to patients but was not expected to increase the cost to Government.</p>

Version 2

Items amended

RUXOLITINIB (Jakavi®) – Purpose of submission for item amended

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**Resubmission pathways**

<p>*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:</p>	
<b>Standard re-entry</b>	<p>The Standard Re-entry Pathway is the default pathway for resubmissions and also applies where:</p> <ul style="list-style-type: none"> <li>● an applicant chooses not to accept the PBAC nominated resubmission pathway; or</li> <li>● 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</li> <li>● an applicant decides to lodge later than the allowable timelines for the other pathways.</li> </ul>
<b>Early re-entry pathway</b>	<p>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 High Added Therapeutic Value (HATV) for the proposed population. Applicants who accept this pathway are eligible for PBAC consideration at the immediate next meeting.</p>
<b>Early resolution pathway</b>	<p>For medicines or vaccines deemed by the PBAC to represent HATV AND where the PBAC considers that the remaining issues could be easily resolved, including when:</p> <ul style="list-style-type: none"> <li>● 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</li> <li>● 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.</li> </ul> <p>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.</p>
<b>Facilitated resolution pathway</b>	<p>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.</p>