

MARCH 2016 PBAC OUTCOMES – DEFERRALS

DRUG NAME, FORM(S), STRENGTH(S), SPONSOR, TYPE OF SUBMISSION	DRUG TYPE AND USE	LISTING REQUESTED BY SPONSOR / PURPOSE OF SUBMISSION	PBAC OUTCOME
<p>IBRUTINIB 140 mg capsules, 90</p> <p>Imbruvica®</p> <p>Janssen-Cilag Australia Pty Ltd</p> <p>New listing</p> <p>(Minor Submission)</p>	<p>Chronic lymphocytic leukaemia and small lymphocytic lymphoma</p>	<p>Re-submission to request Authority Required (STREAMLINED) listing for the treatment of relapsed or refractory chronic lymphocytic leukaemia and relapsed or refractory small lymphocytic lymphoma.</p>	<p>The clinical evidence provided to the PBAC in the original submission included a Phase 3 randomised controlled trial. The PBAC also relied upon a publication of a three-year follow up of a Phase 1b/2 trial, which preceded the Phase 3 trial, given its more mature follow up data.</p> <p>The PBAC considered that there was a high clinical need for a second-line treatment for patients with relapsed or refractory chronic lymphocytic leukaemia (CLL) or small lymphocytic lymphoma (SLL) with certain genetic abnormalities including a 17p deletion, 11q deletion or TP53 mutation. The PBAC noted that these patient subgroups had the poorest outcomes with conventional treatment.</p> <p>The PBAC considered that ibrutinib was not cost-effective at the price proposed by the sponsor for the broader restriction for the relapsed or refractory CLL or SLL population requested by the sponsor. However, the PBAC considered that using its revised eligibility criteria for this high need patient population, ibrutinib could be cost-effective at the price proposed by the sponsor.</p> <p>The PBAC deferred the submission for ibrutinib pending further discussion with the sponsor regarding the eligible patient population, price and risk-sharing arrangements.</p>
		<p>Sponsor Comment:</p>	<p>Janssen are concerned by the PBAC's recommendation to restrict access to a narrow population. Ibrutinib has demonstrated superior and consistent efficacy in relapsed/refractory CLL or SLL in patients who are unsuitable for treatment or retreatment with fludarabine, regardless of whether they have genetic abnormalities such as 17p deletion, 11q deletion or TP53 mutation. The PBAC's proposed PBS restriction would create inequity by denying access to patients without genetic abnormalities who have not received prior treatment</p>

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			with, or who cannot tolerate a fludarabine based regimen. Janssen will seek to work with the PBAC and Department of Health to address these issues as soon as possible in the interests of providing timely access for patients with relapsed or refractory CLL who are not suitable for treatment or retreatment with a fludarabine based regimen.
<p>IDELALISIB 100 mg tablet, 60 150 mg tablet, 60</p> <p>Zydelig®</p> <p>Gilead Sciences Pty Ltd</p> <p>New listing</p> <p>(Minor Submission)</p>	<p>Follicular lymphoma</p>	<p>Re-submission for Authority Required (STREAMLINED) listing for the treatment of relapsed/refractory follicular lymphoma that has progressed despite prior treatment with rituximab and an alkylating agent.</p> <p>Sponsor Comment:</p>	<p>The PBAC deferred the resubmission for idelalisib for the treatment of follicular lymphoma that is refractory to both rituximab and an alkylating agent. The PBAC noted the modifications to the economic model and the price proposed by the sponsor, which were in line with the PBAC's request at the November 2015 meeting.</p> <p>The PBAC noted recent global concerns about an increased rate of serious adverse events, including deaths, mostly due to infections in current on-going clinical trials studying idelalisib in combination with other medicines. The PBAC noted that, while these on-going trials are being carried out in different diseases or in different patients populations compared to the patient population for which listing is being sought, these serious adverse events represent harms in addition to those raised in clinical data provided in the submission.</p> <p>The PBAC requested the sponsor to update the PBAC on adverse events in the clinical areas in which listing is being sought, and if, or how, the recent emergence of additional serious adverse events in the current trials may impact patients if idelalisib becomes available in the broader PBS population.</p> <p>Gilead welcomes the opportunity to provide the update requested and to work with the PBAC to make idelalisib available for patients with relapsed/refractory follicular lymphoma.</p>

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<p>IDELALISIB 100 mg tablet, 60 150 mg tablet, 60</p> <p>Zydelig®</p> <p>Gilead Sciences Pty Ltd</p> <p>New listing</p> <p>(Minor Submission)</p>	<p>Chronic lymphocytic leukaemia (CLL) and small lymphocytic lymphoma (SLL).</p>	<p>Re-submission for Authority Required (STREAMLINED) listing for the treatment CLL in patients with progressive disease despite previous treatment.</p>	<p>The PBAC deferred the resubmission for idelalisib for the second-line treatment of CLL and SLL. The PBAC noted the modifications to the economic model and the price proposed by the sponsor, which were in line with the PBAC's request at the November 2015 meeting.</p> <p>The PBAC noted recent global concerns about an increased rate of serious adverse events, including deaths, mostly due to infections in current on-going clinical trials studying idelalisib in combination with other medicines. The PBAC noted that, while these on-going trials are being carried out in different diseases or in different patients populations compared to the patient population for which listing is being sought, these serious adverse events represent harms in addition to those raised in clinical data provided in the submission.</p> <p>The PBAC requested the sponsor to update the PBAC on adverse events in the clinical areas in which listing is being sought, and if, or how, the recent emergence of additional serious adverse events in the current trials may impact patients if idelalisib becomes available in the broader PBS population.</p>
		<p>Sponsor Comment:</p>	<p>Gilead welcomes the opportunity to provide the update requested and to work with the PBAC to make idelalisib available for patients with progressive CLL despite previous treatment.</p>
<p>OLAPARIB 50 mg capsule, 4 x 112</p> <p>Lynparza®</p> <p>AstraZeneca Pty Ltd</p> <p>New listing</p> <p>(Major Submission)</p>	<p>Ovarian, fallopian tube or primary peritoneal cancer</p>	<p>Authority Required (STREAMLINED) listing for the treatment of platinum-sensitive relapsed ovarian, fallopian tube or primary peritoneal cancer with high-grade serous features or a high grade serous component.</p>	<p>The PBAC deferred its decision on whether olaparib should be listed in the Pharmaceutical Benefits Schedule for the maintenance treatment of women with a <i>BRCA1</i> or <i>BRCA2</i> gene mutation (<i>BRCAM</i>) and high grade serous ovarian, fallopian tube or primary peritoneal cancer.</p> <p>The PBAC considered that there was a strong clinical need for an oral maintenance treatment with tolerable side effects like olaparib, which was reinforced by the consumer input, and that the data demonstrated an improvement in overall survival in the requested</p>

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			<p>subgroup with a <i>BRCA1</i> or <i>BRCA2</i> gene mutation. However, the incremental cost-effectiveness ratio (ICER) presented in the submission was substantially underestimated and unacceptably high at the price proposed by the sponsor because of concerns with key aspects of the modelled economic evaluation which would need to be addressed before the PBAC could complete its decision.</p> <p>The PBAC noted that, on the basis of the overall intention to treat (ITT) population (i.e. including (BRCA wildtype, mutant and unknown) from the head-to-head trial comparing olaparib with placebo, the median progression-free survival for women on olaparib were approximately 8.4 months; whereas median progression-free survival for women on placebo were 4.8 months. The PBAC further noted that, for every 100 patients treated with olaparib in comparison with placebo over a 37.3 months median duration of follow-up, there were:</p> <ul style="list-style-type: none"> <li>• approximately four additional Grade 3 or higher cases of fatigue;</li> <li>• approximately four additional Grade 3 or higher cases of anaemia; and</li> <li>• approximately three additional Grade 3 or higher cases of neutropenia.</li> </ul> <p>The PBAC noted that in the BRCA mutant subgroup of the head-to-head trial comparing olaparib with placebo, the median progression-free survival for women on olaparib was approximately 11.2 months compared to 4.3 months for women on placebo. The PBAC further noted that, for every 100 patients treated with olaparib in comparison with placebo over a 37.3 months median duration of follow-up, there were:</p> <ul style="list-style-type: none"> <li>• approximately five additional Grade 3 or higher cases of fatigue;</li> <li>• approximately three additional Grade 3 or higher cases of anaemia; and</li> <li>• approximately two additional Grade 3 or higher cases of</li> </ul>

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			<p>neutropenia.</p> <p>The PBAC considered that, on balance, the data from clinical trial demonstrated that olaparib results in a significant improvement in progression-free survival and improvement in overall survival in women with a <i>BRCA</i> mutation. The PBAC also considered that access should be restricted to patients with germline class 4 or 5 <i>BRCA</i> mutations only. Further issues around the testing would be addressed by the Medical Services Advisory Committee (MSAC).</p>
		Sponsor Comment:	The sponsor has no comment