

**NOVEMBER 2016 PBAC MEETING – DEFERRALS**

DRUG, SPONSOR, TYPE OF SUBMISSION	DRUG TYPE OR USE	LISTING REQUESTED BY SPONSOR / PURPOSE OF SUBMISSION	PBAC OUTCOME
<p>ADALIMUMAB</p> <p>Injection 40 mg in 0.8 mL pre-filled pen Injection 40 mg in 0.8 mL pre-filled syringe</p> <p>Humira®</p> <p>AbbVie Pty Ltd</p> <p>Change to listing</p> <p>(Major submission)</p>	<p>Hidradenitis suppurativa (HS)</p>	<p>Resubmission to request an Authority Required listing for the treatment of moderate to severe HS.</p>	<p>The PBAC deferred making a recommendation on whether adalimumab should be listed for the treatment of moderate-to-severe HS pending further discussion with the sponsor regarding an acceptable price and risk-sharing arrangements.</p> <p>The PBAC reaffirmed that there is a high clinical need for an effective treatment for moderate-to-severe HS, and that the chronic nature of the inflammatory skin disease causes significant morbidity and poor quality of life.</p> <p>The PBAC considered that the claim of superior comparative effectiveness was adequately supported by the data for the first 12 weeks of treatment. The PBAC considered that while the claim of superior comparative effectiveness was likely to be reasonable beyond week 12, the magnitude of the incremental benefit, as measured by the proportion of continuing patients who maintain a response to treatment, remained the key uncertainty.</p> <p>The PBAC considered that the incremental cost per quality adjusted life year gained, of \$45,000-\$75,000, was uncertain and unacceptably high at the requested price.</p>
		<p>Sponsor Comment:</p>	<p>AbbVie welcomes the PBAC's reconfirmation of the high clinical need in this disease area and is committed to working with the Department to ensure that PBS funded Humira is made available for patients with HS.</p>

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<p>GOSERELIN</p> <p>Implant, 3.6 mg Implant 10.8 mg</p> <p>Zoladex® Implant</p> <p>Medical Oncology Group of Australia</p> <p>Change to listing</p> <p>(Minor submission)</p>	<p>Chemotherapy-induced menopause</p>	<p>To request a Restricted Benefit listing for the prevention of chemotherapy-induced menopause in breast cancer.</p> <p>Sponsor Comment:</p>	<p>The PBAC deferred making a decision regarding amending the current listing of goserelin 3.6 mg implant to allow for PBS-subsidised access for the preservation of fertility in premenopausal women with breast cancer undergoing chemotherapy. The PBAC considered that there is a clinical need for preserving fertility in all premenopausal women undergoing chemotherapy and that the submission's proposal to restrict use to only patients with breast cancer was inequitable.</p> <p>The sponsor had no comment.</p>
<p>IVACAFTOR</p> <p>Sachet containing granules 50 mg</p> <p>Sachet containing granules 75 mg</p> <p>Kalydeco®</p> <p>Vertex Pharmaceuticals (Australia) Pty Ltd</p> <p>Change to listing</p> <p>(Major submission)</p>	<p>Cystic fibrosis</p>	<p>To request a Section 100 (Highly Specialised Drugs Program) listing of a new form of ivacaftor; and an extension to the current ivacaftor listing for patients aged 6 and above who have a G551D or other gating (class III) mutation in the cystic fibrosis transmembrane regulator (CFTR) gene to include patients aged 2-5 years.</p> <p>Sponsor Comment:</p>	<p>The PBAC deferred making a recommendation regarding listing ivacaftor granules for the treatment of cystic fibrosis in patients aged 2 to 5 years with a G551D mutation or other class III gating mutation in the CFTR gene to allow further negotiation with the sponsor. The PBAC noted the difficulty in demonstrating the incremental benefit (and therefore the cost-effectiveness) of earlier initiation of treatment with ivacaftor and requested that the Department work with the sponsor to navigate this challenge.</p> <p>Note: The PBAC subsequently considered additional information relating to the issues identified in their deferral. For more information see November 2016 – positive recommendations.</p> <p>The sponsor had no comment.</p>
<p>NIVOLUMAB</p> <p>Injection concentrate for I.V.</p>	<p>Squamous non-small cell lung cancer (NSCLC)</p>	<p>Resubmission to request a Section 100 (Efficient Funding of Chemotherapy)</p>	<p>The PBAC deferred making a recommendation regarding the listing of nivolumab for the treatment of squamous NSCLC on the basis of concerns regarding the variation in the extent of effectiveness in</p>

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<p>infusion 40 mg in 4 mL Injection concentrate for I.V. infusion 100 mg in 10 mL</p> <p>Opdivo®</p> <p>Bristol-Myers Squibb Australia Pty Ltd</p> <p>Change to listing</p> <p>(Major submission)</p>		<p>Authority Required (STREAMLINED) listing for the treatment of locally advanced or metastatic squamous NSCLC with progression on or after prior chemotherapy.</p>	<p>patients over 75 years, especially given the high incremental cost-effectiveness ratio (ICER) presented in the resubmission and doubts about the ability of the proposed risk share arrangement to achieve the sponsor's intended effect on this ICER. The PBAC requested that the Department hold discussions with the sponsor in order to develop a proposal for a Managed Entry Scheme (MES) to address these concerns.</p> <p>On the basis of the direct evidence presented by the submission, for every 100 squamous NSCLC patients treated with nivolumab in comparison to docetaxel:</p> <ul style="list-style-type: none"> <li>• Approximately 15 additional patients would be expected to be alive at 18 months. There was a 3.2 month difference in median overall survival time favouring patients treated with nivolumab over those treated with docetaxel;</li> <li>• Approximately 17 fewer patients would experience a drug-related Grade 3 or 4 serious adverse event and 29 fewer patients would experience drug-related Grade ≥3 neutropenia, but 5 more patients would experience endocrine-related adverse events.</li> </ul>
<p>NIVOLUMAB</p> <p>Injection concentrate for I.V. infusion 40 mg in 4 mL Injection concentrate for I.V. infusion 100 mg in 10 mL</p>	<p>Non-squamous non-small cell lung cancer (NSCLC)</p>	<p>Resubmission to request a Section 100 (Efficient Funding of Chemotherapy) Authority Required (STREAMLINED) listing for the treatment of locally advanced or metastatic non-</p>	<p>The PBAC deferred making a recommendation regarding the listing of nivolumab for the treatment of non-squamous NSCLC on the basis of concerns regarding the variation in the extent of effectiveness in patients over 75 years, especially given the high incremental cost-effectiveness ratios (ICERs) presented in the resubmission and doubts about the ability of the proposed risk share arrangement to achieve the sponsor's intended effect on these</p>

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<p>Opdivo®</p> <p>Bristol-Myers Squibb Australia Pty Ltd</p> <p>Change to listing</p> <p>(Major submission)</p>		<p>squamous NSCLC with progression on or after prior chemotherapy.</p>	<p>ICERs. The PBAC requested that the Department hold discussions with the sponsor in order to develop a proposal for a Managed Entry Scheme (MES) to address these concerns.</p> <p>On the basis of the direct evidence presented by the submission, for every 100 non-squamous NSCLC patients treated with nivolumab in comparison to docetaxel:</p> <ul style="list-style-type: none"> <li>• Approximately 16 additional patients would be expected to be alive at 18 months. However, whilst nivolumab doubled median overall survival compared to docetaxel in PD-L1 positive patients, there was no meaningful median overall survival difference between nivolumab and docetaxel in PD-L1 negative patients;</li> <li>• Approximately 43 fewer patients would experience a drug-related Grade 3 or 4 adverse event, 27 fewer patients would experience drug-related neutropenia, but an additional 9 patients would experience a Grade 3 or 4 endocrine adverse event. These differences would be expected to be fairly similar for both PD-L1 positive and negative patients.</li> </ul> <p>The comparative benefits for nivolumab versus pemetrexed, via an indirect comparison, were unable to be determined with confidence.</p>
		<p>Sponsor Comment:</p>	<p>The sponsor is committed to working with the PBAC to ensure the earliest possible PBS listing of nivolumab for all eligible NSCLC patients, who have progressed on or after platinum based chemotherapy.</p>
<p>PIRFENIDONE</p> <p>Capsule 267 mg</p> <p>Esbriet®</p>	<p>Idiopathic pulmonary fibrosis (IPF)</p>	<p>Resubmission to request a Section 100 (Highly Specialised Drugs Program) Authority Required listing for the treatment of IPF.</p>	<p>The PBAC deferred making a recommendation on whether pifrenidone should be listed for the treatment of idiopathic pulmonary fibrosis to allow for further discussions regarding an acceptable price and risk sharing arrangement.</p>

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<p>Roche Products Pty Ltd</p> <p>New listing</p> <p>(Major submission)</p>			<p>The PBAC reaffirmed that best supportive care was an appropriate comparator for pirfenidone for IPF. Another novel agent for the treatment of IPF, nintedanib, was also considered at the November 2016 PBAC meeting and was a relevant secondary comparator.</p> <p>The PBAC noted the resubmission presented the same three head-to-head randomised clinical trials comparing pirfenidone with placebo as in the March 2016 and November 2015 submissions. A pooled meta-analysis of these trials was conducted, as was an indirect comparison comparing pirfenidone and nintedanib. On the basis of direct evidence in comparison to placebo presented by the submission, the PBAC reaffirmed that the claim of superior effectiveness and inferior safety, compared with placebo, was reasonable.</p> <p>A resubmission for nintedanib for the treatment of IPF was also considered by the PBAC at the November 2016 meeting. The PBAC noted the challenges of making comparisons across the nintedanib and pirfenidone submissions for IPF given that the two submissions adopted distinct economic modelling approaches. The PBAC noted that the available comparative evidence suggested that the two drugs are likely to be similarly clinically effective. Accordingly, the PBAC considered that any difference in incremental life years gained between the pirfenidone and nintedanib models contradicted the clinical evidence and was an artefact of the different modelling approaches. The PBAC considered that the only inputs that should result in a difference in the cost effectiveness of pirfenidone and nintedanib are the proposed drug costs and, potentially, any differences in costs or quality of life associated with differences in comparative safety.</p>

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			<p>In its comparative assessment of the outcomes of the pirfenidone and nintedanib models, the PBAC considered that the pirfenidone model may have resulted in an overestimate of the incremental benefit associated with pirfenidone (in terms of life years gained). Accordingly, the PBAC considered that the estimated cost effectiveness of pirfenidone was uncertain and likely to be unacceptable at the requested price.</p>
		Sponsor Comment:	Roche will continue to work with the PBAC to seek access at the earliest opportunity to pirfenidone for patients with IPF.
<p>SOMATROPIN</p> <p>All forms and strengths</p> <p>All brands</p> <p>Endocrine Society of Australia; Australian Paediatric Endocrine Group</p> <p>Change to listing</p> <p>(Major submission)</p>	Severe growth hormone deficiency	<p>Resubmission to request a Section 100 (Growth Hormone) Authority Required listing for the treatment of adults with severe growth hormone deficiency (GHD) and substantially impaired quality of life (QoL) at baseline.</p>	<p>The PBAC decided to defer making its decision on whether to list somatropin on the PBS for the treatment of adults with severe GHD and substantially impaired QoL at baseline. In making this decision, the PBAC considered that although there was a place for this drug in treatment of adults with severe GHD, the clinical benefit in terms of QoL was uncertain and the magnitude was likely overestimated. The PBAC therefore considered that the cost-effectiveness of the somatropin for this indication was uncertain. The PBAC deferred its decision to seek further comparative analysis on the range of clinical benefits provided by somatropin, to clarify the proposed PBS restriction, and discuss pricing in this setting with sponsors of somatropin products registered for use in adults.</p>
		Sponsor Comment:	The ESA and APEG will continue to work with the PBAC and the Department to ensure somatropin is available to adults with severe growth hormone deficiency.
<p>TIOTROPIUM with OLODATEROL</p> <p>Solution for oral inhalation containing tiotropium 2.5 micrograms (as bromide</p>	Chronic obstructive pulmonary disease (COPD)	To request a change to the current Authority Required (STREAMLINED) listing for tiotropium with olodaterol to include patients who have persistent COPD symptoms	The PBAC decided to defer the proposed change to the Authority Required (STREAMLINED) listing for tiotropium with olodaterol fixed dose combination (FDC) to allow patients taking either a LAMA or LABA to move straight to the FDC. The PBAC noted, the current Post-Market Review of COPD medicines includes matters that will be relevant to this request. Therefore, the PBAC considered that it

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monohydrate) with olodaterol 2.5 micrograms (as hydrochloride) per dose, 60 doses  Spiolto® Respimat®  Boehringer Ingelheim Pty Ltd  Change to listing  (Minor submission)		despite regular monotherapy with a long-acting muscarinic antagonist (LAMA) or a long-acting beta-2 agonist (LABA).  Sponsor Comment:	would be more appropriate to defer making a decision on this request until it has considered the Post-market Review of COPD medicines.  The sponsor had no comment.
TOLVAPTAN  Tablet 15 mg Tablet 30 mg Pack containing 28 tablets 15 mg and 28 tablets 45 mg Pack containing 28 tablets 30 mg and 28 tablets 60 mg Pack containing 28 tablets 30 mg and 28 tablets 90 mg  Jinarc®  Otsuka Australia Pharmaceutical Pty Ltd  New listing  (Major submission)	Autosomal dominant polycystic kidney disease (ADPKD)	To request an Authority Required listing for the treatment of ADPKD.  Sponsor Comment:	The PBAC deferred consideration of this item until the TGA evaluation has further progressed.  Whilst disappointed by the deferral, Otsuka Australia Pharmaceutical look forward to the PBAC consideration of tolvaptan for ADPKD at its March 2017 meeting.

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<p>VORINOSTAT</p> <p>Capsule 100 mg</p> <p>Zolinza®</p> <p>Merck Sharp &amp; Dohme (Australia) Pty Ltd (submitted by Rare Cancers Australia)</p> <p>New listing</p> <p>(Major submission)</p>	<p>Relapsed or refractory cutaneous T-cell lymphoma</p>	<p>Resubmission to request an Authority Required listing for the treatment of relapsed or chemotherapy refractory cutaneous T-cell lymphoma.</p>	<p>The PBAC deferred its decision on whether to recommend the Authority Required listing of vorinostat for the treatment of cutaneous T-cell lymphoma. The PBAC considered that the uncertainty of the cost-effectiveness analysis presented in the previous submission was diminished in the context of a substantial price reduction offered in the resubmission. The PBAC then considered that given the high and unmet clinical need in a small group of patients, the reasonable evidence of some clinical benefit, and the modest overall financial impact, it would be appropriate to seek further clarification from the sponsor regarding the financial impact of listing on the PBS, specifically, the patient numbers and an agreement for a Risk Sharing Arrangement.</p>
		<p>Sponsor Comment:</p>	<p>Rare Cancers Australia (RCA) is greatly encouraged by the PBAC's decision to defer its recommendation regarding vorinostat in the treatment of cutaneous T-cell lymphoma. RCA is confident the manufacturer of vorinostat will provide the additional clarifications requested by the PBAC and that an appropriate Risk Sharing Arrangement can be agreed upon.</p>