March 2015 PBAC OUTCOMES - DEFERRALS

DRUG NAME, FORM(S), STRENGTH(S), SPONSOR, TYPE OF SUBMISSION	DRUG TYPE OR USE	LISTING REQUESTED BY SPONSOR / PURPOSE OF SUBMISSION	PBAC OUTCOME
BENDAMUSTINE powder for injection, 100mg and 25mg (DPMA 200mg) Ribomustin® Janssen-Cilag Pty Ltd (Major submission)	Non-Hodgkin's Lymphoma and Mantle Cell Lymphoma	The submission sought section 100 Authority Required listing for bendamustine in combination with rituximab for the treatment of indolent Non-Hodgkin's Lymphoma and Mantle Cell Lymphoma in previously untreated patients. The submission also sought listing of bendamustine monotherapy for patients with rituximab-refractory Non-Hodgkin's Lymphoma.	The PBAC deferred its decision on bendamustine in previously untreated indolent Non-Hodgkin's Lymphoma and Mantle Cell Lymphoma to enable either: the submission of a more reliable economic evaluation to substantiate the requested price; or the Department to negotiate a price that helps mitigate the risks associated with the true cost-effectiveness of bendamustine remaining unknown. The PBAC considered that the submitted model did not provide a reliable basis for estimating the cost-effectiveness of bendamustine because it did not reflect the course of the disease, including the different levels of progression. The PBAC also noted the pending trial data (the BRIGHT trial), and also the high price compared with other brands of bendamustine imported under the TGA Special Access Scheme. <u>For previously untreated indolent Non-Hodgkin's Lymphoma and Mantle Cell Lymphoma:</u> On the basis of head-to-head StiL trial, the comparison of bendamustine plus rituximab and R-CHOP resulted in: • An improvement in median progression-free survival of approximately 38 months (StiL trial). • No overall survival benefit was demonstrated in the StiL trial, however median overall survival was not reached at the time of analysis. On the basis of head-to-head trial presented in the submission, for every 100 patients treated with bendamustine plus rituximab in comparison with R-CHOP there would be: • Approximately 39 to 48 fewer cases of grade 3-4 neutropenia based on the StiL and BRIGHT trials respectively • Approximately 22 to 35 fewer cases of neuropathy based on the StiL and BRIGHT trials respectively • Approximately 2 to 13 fewer cases of infectious episodes based on the BRIGHT and StiL trials respectively <u>For patients with rituximab-refractory indolent Non-Hodgkin's Lymphoma:</u> The PBAC did not recommend bendamustine in the rituximab-refractory patient population. The PBAC considered that, given the lack of comparative information presented in the submission, it was not possible to draw any conclusions regarding the comparative effectiveness, safety and cost-effectiveness of bendamustine in this setting.

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		Sponsor Comment:	The sponsor is disappointed with the outcome and does not agree with the rationale for the deferral and rejection of its requested PBS listings. The sponsor is, however, working to resolve the issues raised by the PBAC, so that patients can access this important medicine sooner.
BUPRENORPHINE 15 microgram/hour patch, 2 25 microgram/hour patch, 2 30 microgram/hour patch, 2 40 microgram/hour patch, 2 Norspan® Mundipharma Pty Ltd (Minor submission)	Pain	The submission sought to list additional strengths for the same indications currently applying to the existing patches.	The PBAC deferred its recommendation until further advice could be sought regarding the clinical place and appropriateness for additional strengths of buprenorphine patches, and recommended that the Department consult with organisations representing physicians experienced in pain management.
		Sponsor Comment:	The sponsor had no comment.
OXYCODONE HYDROCHLORIDE + NALOXONE HYDROCHLORIDE, modified release tablet, 2.5 mg/1.25 mg, 15 mg/7.5 mg , and 30 mg/15 mg Targin® Mundipharma Pty Ltd (Minor submission)	Chronic pain	The submission sought listing of three additional strengths of oxycodone + naloxone.	The PBAC deferred its recommendation until further advice could be sought regarding the clinical place of additional strengths of oxycodone with naloxone, and recommended that the Department consult with organisations representing physicians experienced in pain management.
		Sponsor Comment:	The sponsor had no comment.

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RITUXIMAB injection for infusion 500mg/50mL Mabthera® Roche Products Pty Ltd. (Major submission)	Severe active granulomatosis with polyangiitis and microscopic polyangiitis	The submission sought Section 100 Authority Required listing for rituximab for remission induction in patients with severe active granulomatosis with polyangiitis and microscopic polyangiitis.	The PBAC deferred its decision on whether the listing of rituximab should be extended to include remission induction of patients with granulomatosis polyangiitis and microscopic polyangiitis because it could not determine whether rituximab was cost-effective at the price proposed. Given that no further data is likely to become available to inform this consideration, in the context of high clinical need, the PBAC deferred the submission to enable the Department to negotiate an appropriate price. Further to its consideration of the submission, the PBAC also noted that rituximab is being used in a broad range of other non-cancer indications, for which there may also be a high clinical need and requested that the Department work with the sponsor to find a way forward to facilitate a broader listing for this medicine.
		Sponsor Comment:	Roche is pleased that the PBAC has recognised the high clinical need for rituximab in patients with severe active granulomatosis with polyangiitis and microscopic polyangiitis but is concerned by the delay in access for these patients. Given that the other non-cancer indications are off-label, Roche seeks the advice of the PBAC and the DOH on how a broader listing can be appropriately implemented.
SORAFENIB 200 mg tablet Nexavar® Bayer Australia Ltd (Major submission)	Radioactive iodine refractory differentiated thyroid cancer	The resubmission sought section 85 Authority required listing for sorafenib for the treatment of locally advanced or metastatic, radioactive iodine refractory differentiated thyroid cancer. The first submission was considered at the July 2014 PBAC meeting.	The PBAC deferred its decision on sorafenib for the treatment of locally advanced or metastatic radioactive iodine refractory differentiated thyroid cancer because the submission had not provided a reliable estimate of the cost-effectiveness of sorafenib in this setting. The PBAC wished to see the results of its request for a price reduction to an otherwise accepted sensitivity analysis of the submitted modelled economic evaluation. The PBAC considered that the clinical data did not adequately demonstrate a statistically significant gain in overall survival and therefore the life-years gained of 9.9 months in the economic evaluation was implausible. On the basis of direct randomised evidence presented by the submission, for patients treated with sorafenib in comparison with placebo plus best supportive care, there would be: • Approximately 5 months difference in median progression-free survival. • An unknown possible difference in median overall survival.

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			For every 100 patients treated with sorafenib in comparison with placebo plus best supportive care: • Approximately 38 additional patients would experience at least one treatment-emergent adverse event of Grade 3 or greater severity over a period of 10 – 12 months of treatment with sorafenib (compared to 8 – 9 months of observation in the placebo plus best supportive care arm). • Approximately 20 additional patients would experience a hand-foot skin reaction of at least Grade 3 severity over a period of 10 – 12 months of treatment with sorafenib (compared to 8 – 9 months of observation in the placebo plus best supportive care arm). • Approximately 7 additional patients would experience hypertension of at least Grade 3 severity over a period of 10 – 12 months of treatment with sorafenib (compared to 8 – 9 months of observation in the placebo plus best supportive care arm).
		Sponsor Comment:	The Sponsor intends to continue working with the PBAC to make sorafenib available to those Australian patients with RAI-DTC that could benefit from the product.