MARCH 2019 PBAC OUTCOMES – 1ST TIME DECISIONS NOT TO RECOMMEND

DRUG NAME, FORM(S), STRENGTH(S), SPONSOR, TYPE OF SUBMISSION	DRUG TYPE AND USE	LISTING REQUESTED BY SPONSOR / PURPOSE OF SUBMISSION	PBAC OUTCOME
ALECTINIB Capsule 150 mg Alecensa® Roche Products Pty Ltd Change to listing (Minor Submission)	Non-small cell lung cancer (NSCLC)	To request a change in the authority level of the current listing from Authority Required (Telephone) to Authority Required (STREAMLINED) and an increase in the maximum number of repeats from 1 to 5.	The PBAC did not recommend the requested changes to the PBS-listing of alectinib to lower the authority level from Authority Required (Telephone) to Authority Required (STREAMLINED) and to allow for an increased number of repeats from one to five. The PBAC considered that increasing the repeats from one to five could inappropriately extend the treatment duration in some patients, with the risk of continuing an ineffective treatment and/or unmanaged toxicity, and that the impact on the cost-effectiveness of such extended treatment is unclear. The PBAC further considered that because the use of ALK-inhibitors is continuing to increase, an Authority Required (STREAMLINED) listing would be inappropriate at this time until the ALK-inhibitor market had stabilised. The PBAC would be willing to reconsider a future request for lowering the authority level and increasing repeats for continuing treatment when longer-term PBS utilisation data (at least 24 months) is available for alectinib, and advised that this should be considered in the context of all PBS-listed ALK-inhibitors for this indication.
		Sponsor Comment:	Roche is disappointed with the decision and is committed to ensuring optimal outcomes for patients with ALK-positive NSCLC. Roche put forward this application based on patient and clinical community feedback on the current PBS listing. Roche will work with the relevant stakeholders to progress a future change to the PBS listing.

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CABOZANTINIB Tablet 20 mg Tablet 40 mg Tablet 60 mg Cabometyx® Ipsen Pty Ltd Change to listing (Major Submission)	Renal cell carcinoma (RCC)	To request an extension to the current listing for the treatment of Stage IV clear cell variant RCC to include previously untreated patients.	The PBAC did not recommend the listing of cabozantinib for the first line treatment of stage IV clear cell variant renal cell carcinoma. The PBAC considered that, for the comparison of cabozantinib versus sunitinib, the magnitude of the clinical benefit in terms of progression free survival was uncertain due to the small sample size and high risk of bias in the clinical trial, and the PBAC noted there was no demonstrated benefit in overall survival or safety. The PBAC considered that the revised incremental cost-effectiveness ratio for cabozantinib versus sunitinib, based on the PBAC's preferred assumptions, was high. For the comparison versus nivolumab + ipilimumab, the PBAC considered that cabozantinib may be inferior to nivolumab + ipilimumab, based on the clinical evidence presented.
		Sponsor Comment:	The sponsor had no comment.
EXENATIDE Injection 2 mg in 0.85 mL single dose autoinjector Bydureon® BCise® AstraZeneca Pty Ltd New listing (Major Submission)	Type 2 diabetes mellitus (T2DM)	To request an Authority Required (STREAMLINED) listing for use in combination with metformin or sulfonylurea for the treatment of patients with T2DM.	The PBAC did not recommend exenatide 2 mg once weekly autoinjector for the treatment of T2DM on the basis that the indirect treatment comparison presented in the submission did not support the claim that exenatide autoinjector was non-inferior in effectiveness to the currently PBS-listed exenatide dual chamber pen. While there may be patient-related benefits of using the autoinjector formulation due to ease of administration, the PBAC noted there was a low clinical need to list a new formulation of exenatide due to the availability of other weekly antidiabetic agents on the PBS for the same patient population.
		Sponsor comment:	AstraZeneca was disappointed to learn that the PBAC did not recommend Bydureon BCise. This device is equivalent to the current presentation and its ease of administration enables patients to better manage their T2DM. AstraZeneca will work with the PBAC to ensure that patients can access Bydureon BCise.

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LENALIDOMIDE Capsule 5 mg Capsule 10 mg Capsule 15 mg Capsule 25 mg Revlimid® Celgene Pty Ltd Change to listing (Minor Submission)	Multiple Myeloma	To request the current Authority Required (written) listings of lenalidomide for multiple myeloma be amended to Authority Required (STREAMLINED).	The PBAC decided not to recommend a change to the restriction level of the existing PBS listings for lenalidomide for multiple myeloma from Authority Required (Written) to Authority Required (STREAMLINED). Lenalidomide is currently PBS listed for the treatment of patients with newly diagnosed multiple myeloma who are ineligible for a stem cell transplant and relapsed or refractory multiple myeloma. The PBAC did not consider the proposed increase in the rebate for the newly diagnosed multiple myelomaND MM population was sufficient to mitigate the risk of use outside the intended PBS population due to the change in authority level.
		Sponsor Comment:	Celgene is committed to working with the PBAC to secure equitable access to Multiple Myeloma treatments for patients and physicians.
NERATINIB Tablet 40 mg Nerlynx® Specialised Therapeutics Pty Ltd New listing (Major Submission)	Early breast cancer	To request an Authority Required listing for extended adjuvant treatment of patients with early-stage Human epidermal growth factor receptor-2 positive (HER2+) overexpressed/amplified breast cancer who have received prior adjuvant trastuzumab based therapy.	The PBAC did not recommend an Authority Required listing of neratinib for extended adjuvant treatment of patients with early-stage HER2+ overexpressed/amplified breast cancer who have received prior adjuvant trastuzumab based therapy. The PBAC considered that the clinical place for neratinib is unclear given the changing treatment landscape of early stage HER2+ breast cancer, emerging therapies, and the small and uncertain benefit of neratinib balanced against the substantial risk of adverse events, in particular severe diarrhoea. The PBAC considered the economic analysis presented to be highly uncertain, and the uptake and financial estimates to be overestimated.
		Sponsor Comment:	The sponsor had no comment.

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PEMBROLIZUMAB Solution concentrate for I.V. infusion 100 mg in 4 mL Keytruda® Merck Sharp and Dohme (Australia) Pty Ltd Change to listing (Major Submission)	Metastatic colorectal carcinoma (CRC)	To request a Section 100 (Efficient Funding of Chemotherapy) Authority Required (STREAMLINED) listing for the treatment of locally advanced or metastatic CRC in patients with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) tumours, who have progressed following prior treatment.	The PBAC decided not to recommend the Section 100 (Efficient Funding of Chemotherapy) listing of pembrolizumab as a second-line treatment option for locally advanced (unresectable) or Stage IV (metastatic) colorectal cancer (CRC) with deficient mismatch repair (dMMR). The PBAC noted that the sponsor amended the submission to exclude patients with microsatellite instability-high (MSI-H) as MSI-H testing is not available in Australia. The PBAC considered that the limited evidence provided suggested that the benefit of pembrolizumab was modest in dMMR mCRC. The PBAC considered that insufficient evidence was provided in the submission to evaluate the efficacy and safety of pembrolizumab in the second-line setting. In addition, the PBAC considered that the economic evaluation was unreliable and therefore, the cost-effectiveness estimates were highly uncertain. The PBAC considered that the nominated place in therapy, as a second-line treatment, was incorrect as the majority of patients in the key study had failed at least two prior lines of treatment. The PBAC considered that it would have been more appropriate to position pembrolizumab as a last-line treatment option. The PBAC therefore also considered that the nominated comparators were incorrect.
		Sponsor Comment:	MSD is disappointed by this outcome, but is collecting more data through ongoing clinical trials in the dMMR/MSI-H CRC population, and intends to lodge submissions for this cancer subtype in the near future.
RIVAROXABAN Tablet 2.5 mg Xarelto® Bayer Australia Ltd New listing (Major Submission)	Coronary Artery Disease (CAD) and Peripheral Artery Disease (PAD)	To request an Authority Required (STREAMLINED) listing in combination with aspirin for the treatment of patients at high risk of recurrent cardiovascular events in the stable phase of CAD and/or PAD.	The PBAC did not recommend the listing of rivaroxaban in combination with aspirin for the prevention of recurrent cardiovascular events in patients in the stable phase of CAD or PAD. The PBAC considered that the patient population should be more highly targeted to those patients who are likely to achieve the most favourable risk-benefit profile given the differing levels of absolute incremental benefit between patients groups that needs to be balanced against the high bleeding risk in some patients. The PBAC considered that the incremental cost-effectiveness was uncertain as the economic model submitted did not provide a reliable basis for decision-making.
		Sponsor Comment:	Bayer Australia is disappointed with regards to the PBAC decision. However, Bayer Australia hopes to continue to work with the PBAC and the

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			Department of Health in pursuing publicly subsidised access for patients suffering from chronic coronary arterial and peripheral arterial disease.
TIOTROPIUM Capsule containing powder for oral inhalation 18 micrograms (for use in HandiHaler) Spiriva® Boehringer-Ingelheim Pty Ltd Other business (Minor Submission)	Chronic obstructive pulmonary disease (COPD)	To request that Spiriva and Braltus brands of tiotropium not be 'a' flagged.	Contrary to what was requested in the minor submission, the PBAC advised that the Minister should determine that tiotropium (as bromide) 13 microgram powder for inhalation capsule (Braltus®) and tiotropium (as bromide monohydrate) 18 microgram powder for inhalation capsule (Spiriva®) are to be treated as equivalent, and accordingly 'a'-flagged in the Schedule of Pharmaceutical Benefits. The PBAC noted the two main differences between the Braltus® and Spiriva® products: both Braltus® and Spiriva® deliver the same dose of active substance to the patient (10 microgram per capsule) but have a different labelled metered dose (13 and 18 microgram per capsule respectively); Braltus® is delivered via a Zonda® device whereas Spiriva® is delivered via a HandiHaler device®. The PBAC noted that the Therapeutic Goods Administration has accepted that bioequivalence has been established between the Braltus® and Spiriva® products, and considered that the differences in the labelled metered dose and devices could be managed in the course of the regular patient education and counselling on the use of the devices that is provided to patients by prescribers and pharmacists.
		Sponsor Comment:	The sponsor had no comment.