NOVEMBER 2015 PBAC MEETING OUTCOMES – SUBSEQUENT DECISIONS NOT TO RECOMMEND

DRUG NAME, FORM(S), STRENGTH(S), SPONSOR, TYPE OF SUBMISSION	TGA INDICATION	CURRENT PBS LISTING	LISTING REQUESTED BY SPONSOR / PURPOSE OF SUBMISSION	PBAC OUTCOME
ADALIMUMAB 40 mg/0.8 mL injection, 2 x 0.8 mL cartridges 40 mg/0.8 mL injection, 2 x 0.8 mL syringes 40 mg/0.8 mL injection, 6 x 0.8 mL cartridges 40 mg/0.8 mL injection, 6 x 0.8 mL syringes Humira® AbbVie Pty Ltd Change to listing (Minor Submission)	Adalimumab is indicated for reducing signs and symptoms in moderate to severe rheumatoid arthritis, polyarticular juvenile idiopathic arthritis, psoriatic arthritis, Crohn's Disease, ulcerative colitis, chronic plaque psoriasis and active ankylosing spondylitis.	Adalimumab is currently listed for severe Crohn disease, severe active juvenile idiopathic arthritis, complex refractory fistulising Crohn disease, ankylosing spondylitis, severe chronic plaque psoriasis, severe active rheumatoid arthritis and severe psoriatic arthritis. For more details see the PBS Schedule.	Re-submission for Authority Required listing for the treatment of patients with moderate to severe ulcerative colitis.	The PBAC rejected the request to extend the PBS listing of adalimumab for the treatment of patients with moderate to severe ulcerative colitis on the basis that the evidence presented in the July 2015 PBAC meeting did not support the non-inferiority claim in the maintenance phase against infliximab.
			Comparator: infliximab	The PBAC recalled that it had previously accepted infliximab as the appropriate comparator.
			Clinical claim: The minor resubmission maintained that adalimumab was non-inferior to infliximab (in both induction and maintenance phase) and that this was supported by real world evidence presented in the July 2015 resubmission. However, the resubmission acknowledged the PBAC's conclusion in the July 2015 consideration where adalimumab was inferior to infliximab in the induction phase.	The PBAC did not accept the non-inferiority claim in the maintenance phase. The PBAC reiterated its previous conclusions from the July 2015 PBAC meeting that the risk of bias was high for the maintenance phase. The data for the maintenance phase were incomplete due to a large number of discontinuations and substantial loss to follow-up (adalimumab PSD, July 2015). The PBAC maintained its view that, in UC, based upon available data, adalimumab is likely to be inferior to infliximab overall, and a claim of non-inferiority cannot be justified.
			Economic claim: Cost-minimisation analysis to infliximab.	Not accepted. Given that inferiority (compared with infliximab) in the maintenance phase is also likely, there is no basis to accept the same price of infliximab.
			Sponsor's comments:	AbbVie is disappointed with the PBAC recommendation and remains committed to working to secure access for patients in need.
APREMILAST 10 mg tablet [4] & 20 mg tablet [4] & 30 mg tablet [19], 1 pack 30 mg tablet, 56 Otezla	Apremilast is indicated for the treatment of signs and symptoms of active psoriatic arthritis in adult patients, and the treatment of adult	Not currently PBS listed.	Re-submission to request an Authority Required listing for the treatment of severe active psoriatic arthritis.	The PBAC did not recommend the listing of apremilast for the treatment of severe active psoriatic arthritis on the basis that the place of apremilast in the clinical management algorithm and therefore the nominated comparators are inappropriate. The PBAC identified issues with the modelled economic evaluation, and considered that a reliable estimate of cost-effectiveness could not be determined at the place in therapy

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Celgene Pty Ltd New listing (Major Submission)	patients with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy.			proposed by the resubmission.
			Comparator: adalimumab	Not Accepted. The PBAC considered that adalimumab, or any bDMARD for the treatment of PsA, is not an appropriate comparator because the more appropriate place of apremilast is earlier in the clinical management algorithm than the bDMARDs. The PBAC reiterated that leflunomide, or another DMARD used for the treatment of PsA, is the appropriate comparator.
			Clinical claim: Clinical claim: Inferior in terms of comparative effectiveness and non-inferior in terms of safety (“equivalent” in terms of short-term safety but “superior” in terms of long-term safety), compared to adalimumab.	Accepted
			Economic claim: Cost-utility analysis to adalimumab.	Not Accepted. The PBAC considered that, given the unclear patient population likely to use apremilast, this model did not adequately assess the cost-effectiveness of apremilast in its proposed place in therapy. The PBAC therefore considered that a cost-minimisation analysis compared to leflunomide would be a more appropriate economic evaluation.
			Sponsor’s Comment:	Celgene is disappointed with the views expressed by the PBAC which are not consistent with the feedback from clinical Rheumatologists who firmly agree there is a genuine unmet need with respect to the proposed place in therapy.

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SITAGLIPTIN sitagliptin 100 mg tablet, 28 sitagliptin 50 mg tablet, 28 sitagliptin 25 mg tablet, 28 Januvia® SITAGLIPTIN and METFORMIN sitagliptin 50 mg + metformin hydrochloride 1000 mg tablet, 56 sitagliptin 50 mg + metformin hydrochloride 850 mg tablet, 56 sitagliptin 50 mg + metformin hydrochloride 500 mg tablet, 56 Janumet® SITAGLIPTIN and	Initial therapy in patients with type 2 diabetes mellitus to improve glycaemic control when diet and exercise do not provide adequate glycaemic control	Sitagliptin, sitagliptin and metformin, and sitagliptin metformin XR currently listed treatment for Diabetes mellitus type 2 under certain circumstances. For more details see the PBS Schedule.	An extension of the current Authority Required (STREAMLINED) listings of the Januvia®, Janumet® and Janumet® XR for use in combination with insulin in patients with type 2 diabetes, with or without metformin.	The PBAC rejected the minor resubmission to extend the PBS listing for sitagliptin for use in combination with insulin in patients with type 2 diabetes, with or without metformin. The PBAC recalled its July 2015 conclusion that the clinical data presented were not adequate to support a claim of non-inferior comparative effectiveness (as measured by reduction in HbA1c) and similar reduction in mean daily insulin dose for sitagliptin compared to dapagliflozin. With regard to the effect of sitagliptin on HbA1c, the PBAC considered that sitagliptin is effective in reducing HbA1c in combination with insulin. The PBAC noted the limitations on the available data, however concluded that sitagliptin is likely to be non-inferior to dapagliflozin in this regard. The PBAC reiterated its view that the increased daily insulin dose accompanying sitagliptin treatment should be taken into account in the cost-minimisation analysis of any future resubmission.
			Comparator: dapagliflozin	Accepted. This was unchanged in the minor re-submission as the PBAC had considered it appropriate. The PBAC had also noted that exenatide and insulin up-titration would have been appropriate secondary comparators but were not considered in the submission.

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METFORMIN XR sitagliptin 100 mg + metformin hydrochloride 1000 mg tablet: modified release, 28 sitagliptin 50 mg + metformin hydrochloride 1000 mg tablet: modified release, 56 Janumet XR® Merck Sharp & Dohme (Australia) Pty Limited Change to listing (Minor Submission)			Clinical claim: Non-inferior comparative effectiveness and similar comparative safety of sitagliptin compared with dapagliflozin	Accepted. The PBAC recalled its July 2015 conclusion that the clinical data presented were not adequate to support a claim of non-inferior comparative effectiveness (as measured by reduction in HbA1c) and similar reduction in mean daily insulin dose for sitagliptin compared to dapagliflozin. The PBAC noted the limitations on the available data, however concluded that sitagliptin is likely to be non-inferior to dapagliflozin in this regard.
			Economic claim: Cost-minimisation analysis to dapagliflozin.	Not accepted. The PBAC reiterated its view that the increased daily insulin dose accompanying sitagliptin treatment should be taken into account in the cost-minimisation analysis of any future resubmission.
			Sponsor comment:	The sponsor is disappointed with the PBAC's decision but will work with the PBAC to resolve the outstanding matters.
VINFLUNINE DITARTRATE 50 mg/2 mL injection, 2 mL vial 250 mg/10 mL injection, 10 mL vial Javlor	Vinflunine is registered for the treatment of adult patients with advanced or metastatic transitional cell carcinoma of the urothelial tract	Vinflunine is currently not listed on the PBS.	The re-submission requested listing under the Efficient Funding of Chemotherapy program for vinflunine for treatment of adult patients with advanced or metastatic transitional cell carcinoma of the urothelial tract (TCCU) after failure of a prior platinum-containing regimen	The PBAC did not recommend the Section 100 (Efficient Funding of Chemotherapy) listing of vinflunine (as ditartrate) for treatment of adult patients with advanced or metastatic transitional cell carcinoma of the urothelial tract (TCCU) after failure of a prior platinum-containing regimen, on the basis of insufficient evidence of comparative clinical benefit compared to alternative treatments and a high and highly uncertain incremental cost-effectiveness ratio.

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Pierre Fabre Australia Pty Ltd New listing (Major Submission)	(TCCU) after failure of a prior platinum-containing regimen		Comparator: Best supportive care and active therapy.	In regards to the comparator, the PBAC noted that the ESC considered that comparisons against both active chemotherapy and BSC were relevant. The PBAC reiterated their view from November 2011 that whilst BSC is an appropriate comparator in determining the efficacy of vinflunine, it is not relevant in Australian clinical practice as vinflunine will likely replace or defer other drugs. The PBAC considered that current standard of care is preferable for the determination of relative effectiveness and therefore the translatability of the trial data to the proposed use in Australia is an area of significant uncertainty.
			Clinical claim: Vinflunine is superior in terms of comparative effectiveness and inferior in terms of comparative safety over BSC. Vinflunine is superior in terms of comparative effectiveness and similar in terms of comparative safety over active chemotherapy.	Not accepted. The PBAC recalled at the November 2011 consideration that the Committee accepted that vinflunine is superior in terms of comparative efficacy over BSC but noted that the increment in overall survival is uncertain and, at best, is between 2.3 (ITT) and 2.6 months (eligible ITT) and was at a cost of significant treatment-related toxicity. On the basis of the head to head trial presented, vinflunine + BSC is more likely to cause serious adverse events; per 100 patients treated, 15 are more likely to have a serious adverse event than patients receiving BSC. The PBAC considered that the resubmission had not supported a claim that efficacy of vinflunine would provide a significant health benefit compared to active chemotherapy in patients with advanced or metastatic TCCU.
			Economic claim: Listing was sought on the basis that vinflunine is cost-effective compared with best supportive care.	Not accepted. The PBAC reiterated their view from November 2011 that the intention to treat (ITT) population in the clinical trial should be used in considering the effectiveness of vinflunine as the ITT population more closely approximates the likely PBS population. The PBAC noted that the use of the ITT

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				population in economic model resulted in an ICER/QALY of $75,000 – $105,000, which the Committee considered was not cost-effective.
			Sponsor's comment:	Pierre Fabre is disappointed by the PBAC decision, however will continue to work with the Department towards reimbursement of vinflunine for metastatic bladder cancer patients.