| **Drug Name, form(s), strength(s) and Sponsor** | **Drug Type and Use** | **Listing requested by Sponsor / Purpose of Submission** | **PBAC Recommendation** |
| --- | --- | --- | --- |
| FEBUXOSTAT, 80 mg tablet, 28 and 120 mg tablet, 28  Adenuric®  A.Menarini Australia Pty Ltd | Gout | To request Authority Required (STREAMLINED) General Schedule listing for the treatment of chronic gouty arthritis associated with hyperuricaemia. | The PBAC did not recommend the listing of febuxostat. The PBAC considered the submission did not establish that febuxostat is superior in terms of comparative effectiveness over allopurinol. The PBAC considered that the trials presented in the submission overall did not demonstrate superior effectiveness to allopurinol for patient-relevant outcomes such as reduction in acute gout attacks or tophi, or improvement in quality of life (QoL).  The PBAC considered that the advantage of a faster reduction in serum uric acid (sUA) did not translate into benefits over allopurinol for more clinically meaningful outcomes such as flare reduction, tophi resolution or health-related quality of life (HRQoL). Therefore the PBAC did not support the submission’s assumption that attaining the biological sUA target would lead to clinically meaningful outcomes.  The PBAC recognised that there is a clinical need for an alternative treatment for patients, who are intolerant of allopurinol. The PBAC considered that an allopurinol-intolerant population consistent with the definition used in the NICE guidance for “Febuxostat for the management of hyperuricaemia in people with gout” may be an appropriate basis for defining a second-line treatment setting for febuxostat. However the PBAC noted that the submission did not present clinical evidence to support the use of febuxostat in a second-line setting. |
|  |  | Sponsor Comment: | Menarini is disappointed by the decision from the PBAC as there is a high clinical need and place in therapy for this treatment. However Menarini will work with PBAC to enable this treatment reaches the at-need patients. |
| FENTANYL, 100 microgram tablet: sublingual, 10 and 30, 200 microgram tablet: sublingual, 10 and 30 and 400 microgram tablet: sublingual, 10 and 30  Abstral®  A.Menarini Australia Pty Ltd | Palliative Care | To request Authority Required listing on the palliative care schedule for the management of breakthrough pain in patients with cancer who are already receiving maintenance opioid therapy for chronic pain and are unable to tolerate further escalation of morphine for breakthrough pain. | The PBAC acknowledged that a clinical need exists for alternative treatments for breakthrough pain in cancer patients.  However, the PBAC rejected the submission for fentanyl sublingual tablets for the treatment of breakthrough cancer pain. The PBAC considered the submission’s claims of non-inferior comparative efficacy and safety versus fentanyl lozenges were inadequately supported by the data presented in the submission. The PBAC was therefore unable to accept the submission’s cost-minimisation analysis.  The PBAC also considered that the appropriate clinical place of sublingual fentanyl was unclear, noting that it was possible that it would be used in a number of clinical settings in addition to that requested in the proposed restriction.  The PBAC considered that the evidence presented in the submission was inadequate to reliably inform an assessment of the comparative effectiveness and comparative safety of fentanyl sublingual (SL) tablets versus fentanyl lozenges. |
|  |  | Sponsor Comment: | Menarini is disappointed by the decision from the PBAC as there is a high clinical need and place in therapy for this treatment. However Menarini will work with PBAC to enable this treatment reaches the at-need patients. |
| FENTANYL, 100 micrograms/actuation nasal spray, 8 actuations and 400 micrograms/actuation nasal spray, 8 actuations  PecFent®  AstraZeneca Pty Ltd | Palliative Care | To request Authority Required listing on the palliative care schedule for the management of breakthrough pain in adults with cancer who are already receiving maintenance opioid therapy for chronic pain and are unable to tolerate further escalation of morphine for breakthrough pain. | The PBAC acknowledged that a clinical need exists for alternative treatments for breakthrough pain in cancer patients.  However, the PBAC rejected the submission for fentanyl nasal spray for the treatment of breakthrough cancer. The PBAC considered that the data presented did not adequately support the submission’s claims of non-inferior comparative efficacy and safety versus fentanyl lozenges. The PBAC was therefore unable to accept the submission’s cost-minimisation analysis.  The PBAC also considered that the appropriate clinical place of intranasal fentanyl was unclear, noting that it was possible that it would be used in a number of clinical settings in addition to that requested in the proposed restriction. |
|  |  | Sponsor Comment: | The Sponsor has no comment. |
| FLUTICASONE FUROATE AND VILANTEROL TRIFENATATE, fluticasone furoate 100 microgram/actuation + vilanterol trifenatate 25 microgram/actuation, inhalation: powder for, 30 actuations  Dry powder inhaler (DPI)  Breo® Ellipta®  GlaxoSmithKline Australia Pty Ltd | Chronic Obstructive Pulmonary Disease (COPD) | To request a Restricted Benefit General Schedule listing for the symptomatic treatment of chronic obstructive pulmonary disease (COPD), where FEV1 is less than 50% of predicted normal and there is a history of repeated exacerbations despite regular beta-2 agonist bronchodilator therapy. | The PBAC rejected the submission requesting PBS-listing for fluticasone furoate and vilanterol (FF/VI) 100/25 for the treatment of COPD. The PBAC did not accept the submission’s claim that FF/VI 100/25 is non-inferior in terms of safety compared to fluticasone proprionate and salmeterol (FP/SAL) 500/50. Further, the PBAC considered that there was no clear unmet clinical need for FF/VI in COPD particularly in light of the changing clinical place of ICS in COPD.  The PBAC was unable to assess the comparative efficacy of FF/VI FDC and the component therapies given concurrently. The PBAC advised that it would have been preferable to assess the components fluticasone furoate and vilanterol individually before undertaking an assessment of the FDC.  The PBAC considered that the submission’s claim with regard to comparative safety was not supported. Overall, the PBAC considered that the short duration of the trial precluded the possibility of concluding that FF/VI 100/25 and FP/SAL 500/50 are non-inferior in terms of comparative safety.  The PBAC raised a number of safety concerns regarding the FF/Vl FDC: the different dosing in patients with asthma and COPD may be problematic in patients with both asthma and COPD; that neither component of the FDC is available as a single product; there is limited long term safety data for vilanterol; and concerns have been raised about the risk of pneumonia in regard to the use of ICS in COPD. The PBAC considered this in the context of the evolving clinical place of ICS/LABA FDCs in the management of COPD. |
|  |  | Sponsor Comment: | This is a disappointing outcome for COPD patients. GSK is committed to ensuring patients with COPD have access to the once daily ICS/LABA combination FF/VI. GSK will engage with PBAC to understand and address the issues raised.  The totality of the safety evidence presented in the submission supports a conclusion of non-inferior safety associated with use of FF/VI in COPD. This evidence is not outlined in the PBAC statement above. Regulatory bodies such as the FDA, European Regulatory agency and TGA have reviewed the comparative efficacy and safety data for FF/VI and FP/SAL and have concluded there is no increase in safety risk with FF/VI. |
| INDACATEROL AND GLYCOPYRRONIUM (FDC), indacaterol 110 microgram + glycopyrronium 50 microgram inhalation: powder for, 30 capsules  Ultibro Breezhaler 110/50®  Novartis Pharmaceuticals Australia Pty Ltd | Chronic Obstructive Pulmonary Disease (COPD) | To request Restricted Benefit General Schedule listing for once daily maintenance bronchodilation in patients with chronic obstructive pulmonary disease (COPD) currently on LABA or LAMA monotherapy and requiring further relief from symptoms. | The PBAC rejected the submission requesting PBS-listing for indacaterol/glycopyrronium fixed does combination (FDC) for the treatment of COPD. The PBAC considered that the cost-minimisation approach used, where the price of the FDC was cost-minimised to the sum of the prices of the component products (dose adjusted) was not justified by the evidence presented in the submission.  The PBAC considered the submission’s claim that the FDC is superior in terms of comparative effectiveness and equivalent in terms of safety over either of the components given as monotherapy was reasonable. The PBAC noted that the incremental gain in FEV1 for this comparison was below the minimum clinically important difference (MCID) of 100 mL specified in the submission. However, the Committee considered that it was reasonable to accept that the incremental gain associated with add-on therapy would not be as great as the incremental gain associated with monotherapy compared with placebo.  The PBAC considered that while the results of the BEACON study showed no significant difference in FEV1 between indacaterol/glycopyrronium FDC compared to the component products given concurrently, at four weeks, the duration of the trial was too short to reliably demonstrate long-term non-inferiority, particularly in terms of other patient relevant endpoints such as effect on frequency of exacerbations and quality of life measures. As COPD is a chronic disease, the PBAC considered that longer-term data, demonstrating incremental clinical and patient relevant benefits of the FDC compared to the component products given concomitantly would be required to justify the price requested in the submission.  As the incremental gain in FEV1 of indacaterol/glycopyrronium FDC was not able to be translated into more clinically relevant measures of effect (e.g., frequency of exacerbations, hospitalisations), the PBAC considered it was unable to determine and value the incremental benefit associated with use the FDC compared with use of components given concurrently. Therefore, the Committee was unable to determine an appropriate price for the FDC. |
|  |  | Sponsor Comment: | The Sponsor believes that the submission covers the best possible summary of evidence in accordance with the PBAC’s fixed dose combination guidelines providing a cost saving alternative for concurrent LABA plus LAMA bronchodilator therapy. Novartis is committed to working with the PBAC to ensure the timely availability of Ultibro Breezhaler 110/50 to COPD patients. |
| LURASIDONE HYDROCHLORIDE, 40 mg tablet, 30 and 80 mg tablet, 30  Latuda®  Dainippon Sumitomo Pharma Ltd | Schizophrenia | To request Authority Required (STREAMLINED) General Schedule listing for the treatment of schizophrenia. | The PBAC rejected the submission on the basis that non-inferiority with the comparators was not established because of the fundamental limitations of the trials presented. The PBAC considered that therefore the cost-minimisation approach used was not justified by the evidence presented in the submission.  The PBAC considered that the clinical data presented did not adequately support a claim of non-inferior comparative effectiveness and safety. The PBAC noted that trial 254 was designed as a safety and tolerability trial, and did not provide sufficient basis to assess the clinical effectiveness of lurasidone compared with ziprasidone. Other trial data provided in the submission included anomalous results such as a higher numerical result for the 40mg strength compared with the 120mg strength.  Overall, the PBAC did not consider that the clinical data provided in the submission, or identified during the evaluation (Luecht et al) established non-inferiority of lurasidone with the comparators.  The PBAC noted that based on these trials, for every 100 patients treated with lurasidone compared to the alternatives:   * 11 fewer patients on 40 mg lurasidone, and 17 fewer patients on lurasidone 120mg, would achieve 30% or greater reduction from baseline in Positive and Negative Symptom Scale (PANSS) score at six weeks compared to patients taking olanzapine 15 mg. * 21 fewer patients on 80 mg lurasidone, and 8 fewer patients on lurasidone 160mg, would achieve 30% or greater reduction from baseline in PANSS score at six weeks compared to patients taking quetiapine 600 mg. * Up to five more patients would experience insomnia. * Up to 10 more patients would experience akasthisia compared to olanzapine and quetiapine, while three fewer patients would experience akasthisia compared to ziprasidone. * Up to four more patients would experience vomiting. |
|  |  | Sponsor Comment: | The sponsor has no comment. |
| TRAMETINIB, 500 microgram tablet, 30 and 2 mg tablet, 30  Mekinist®  GlaxoSmithKline Australia Pty Ltd | Melanoma | To request Authority Required General Schedule listing of trametinib for use, in combination with dabrafenib for the treatment of patients with BRAF V600 mutation positive unresectable stage III or metastatic (stage IV) melanoma. | The PBAC rejected the submission on the basis that the superior comparative effectiveness of trametinib with dabrafenib over dabrafenib monotherapy had not been established. The PBAC also noted the higher rate of adverse events with combination therapy compared with dabrafenib monotherapy.    The PBAC considered that the BRF113220 trial did not provide a robust basis for making a subsidisation recommendation. The PBAC considered that the COMBI-D trial may inform future determinations of the treatment effect of trametinib, but noted that the current data are not mature. |
|  |  | Sponsor Comment: | GSK acknowledges that the submission was based on early phase II data which has some inherent uncertainty but believes this could be considered under a Managed Entry framework. During the evaluation process trametinib was TGA approved for use in combination with dabrafenib. GSK will continue to work with the PBAC to ensure the earliest possible access to the combination of dabrafenib and trametinib. |
| UMECLIDINIUM BROMIDE AND VILANTEROL TRIFENATATE, umeclidinium bromide 62.5 microgram/actuation + vilanterol trifenatate 25 microgram/actuation inhalation: powder for, 30 actuations  AnoroTM Ellipta®  GlaxoSmithKline Australia Pty Ltd | Chronic Obstructive Pulmonary Disease (COPD) | To request a Restricted Benefit listing for the treatment of adult patients with chronic obstructive pulmonary disease (COPD) where symptoms persist despite regular bronchodilator treatment with a long acting muscarinic agonist (LAMA) and/or long acting beta2-agonist (LABA); or for the treatment of adult patients who have been stabilised on a combination of a LAMA and a LABA in separate devices. | The PBAC rejected the submission requesting PBS-listing for umeclidinium/vilanterol (UMEC/VI) FDC for the treatment of COPD. The PBAC considered that the cost-minimisation approach used, where the price of the fixed dose combination (FDC) was cost-minimised to the sum of the prices of indacaterol plus tiotropium was not justified by the evidence presented in the submission.  The PBAC also considered that having a combination product available without having the individual components available was problematic. Patients with COPD cannot be treated in the stepwise manner recommended without changing the LABA and LAMA medications. The PBAC considered there were also risks that patients may transition to combination therapy earlier than clinically necessary due to the individual components being unavailable, or that patients will be prescribed triple therapy with UMEC/VI plus a LABA or LAMA single agent.  The PBAC was unable to assess the comparative efficacy of UMEC/VI FDC and the component therapies given concurrently. The PBAC advised that it would have been preferable to assess the components umeclidinium and vilanterol individually before undertaking an assessment of the FDC.  The PBAC considered that the submission’s claims with regard to comparative safety may not be reasonable. The PBAC noted that there was a slight increase in adverse event rates for UMEC/VI in the presented trial data. |
|  |  | Sponsor Comment: | GSK is disappointed with this outcome for COPD patients, and considers that there is an important place for UMEC/VI in the treatment of COPD. GSK welcomes the Committee’s acceptance of tiotropium + indacaterol as the appropriate comparator and looks forward to engaging further with the Committee to address their remaining concerns. |