PBAC CONSIDERATION OF THE REPORT OF THE DRUG UTILISATION SUB-COMMITTEE

The PBAC noted reports with associated stakeholder responses from the September 2022 Drug Utilisation Sub-Committee (DUSC) meeting, which were provided in Items 10.02, 10.03, 10.04, 10.07 and 10.08 of the PBAC Agenda. DUSC minutes relating to these items were provided to the PBAC. The outcomes of the DUSC consideration of these items are available in the November 2022 DUSC outcome statement.

UTILISATION OF MEDICINES FOR NON-SMALL CELL LUNG CANCER (NSCLC), INCLUDING AN ASSESSMENT OF THE PREDICTED VERSUS ACTUAL USE OF DURVALUMAB

Outcome

The PBAC considered the overall NSCLC market to be stable and noted that over time, utilisation of immunotherapies has been declining, whilst utilisation of targeted therapies has been increasing.

The PBAC noted pembrolizumab was the most common NSCLC immunotherapy. The PBAC considered its high level of utilisation compared to other immunotherapies may have been due to clinician preference and clinical inertia. The PBAC noted the differences in treatment regimen between immunotherapies and commented that patients may be less likely to be treated with combination therapies due to their toxicity. Additionally, the PBAC commented on the lack of data demonstrating a greater level of clinical effectiveness associated with pembrolizumab compared to other NSCLC immunotherapies. The PBAC noted epidermal growth factor receptor (EGFR) inhibitors were the most commonly used targeted therapy. The PBAC noted osimertinib was the most common EGFR inhibitor used and noted the growth in utilisation following its extension to listing from second-line to the first-line setting.

The PBAC noted the utilisation of durvalumab for the treatment of Stage III NSCLC was different from what was estimated. The PBAC commented that this may be due to recent evidence of the benefits of targeted therapy in Stage III NSCLC patients. Additionally, the PBAC considered the added risk of toxicity following chemotherapy and patients being restricted to only ever being treated with one immunotherapy as other reasons why utilisation may have differed.

The PBAC noted that durvalumab patients were adhering to the two-weekly dosing regimen and noted the average treatment duration and average prescriptions per patient were different from what was estimated. The PBAC commented that these findings did not correspond with the predicted versus actual analysis of the number of durvalumab prescriptions supplied and noted that the final estimates did not apply a half-cycle correction to adjust for the date of PBS listing.

MEDICINES FOR MELANOMA INCLUDING A UTILISATION REVIEW OF NIVOLUMAB FOR ADJUVANT TREATMENT

Outcome

The PBAC noted that the total number of patients utilising medications with listings for adjuvant use (following complete surgical resection) was similar to the number of patients estimated by the submission for nivolumab as adjuvant therapy in melanoma. The PBAC noted the actual number of patients using nivolumab in the first year of listing was different from predicted, suggesting that the listing of the BRAF and MEK inhibitors in late 2019 as well as pembrolizumab in 2020Q3 have contributed to the difference.

The PBAC noted that in the CheckMate-238 trial for adjuvant nivolumab the majority of patients were aged less than 65 years old which differed from the interquartile range seen in this analysis of 65-75 years. This difference in age may also explain the difference in time on treatment. The trial reported patients had a median of 24 doses at two weekly intervals which is approximately equivalent to 336 days. The results from the DUSC analysis indicated that the median time on treatment was 231 days with treatment breaks and 211 days without. The PBAC noted the difference in treatment length was likely due to an older and frailer PBS population.

The PBAC noted the final net effective cost of adjuvant nivolumab was calculated based on the advice from the July 2019 PBAC meeting which suggested 9% of patients would receive 240 mg at two weekly intervals, 88% at 480 mg four weekly and 3% as weight-based dosing (paragraph 5.7, November 2019 PBAC Public Summary Document). The PBAC noted the data from this analysis suggested that 75% of patients were dosing at 480 mg per supply, approximately 20% were dosing at 240 mg per supply and the remaining 5% were either dose reductions or dosing according to weight.

The PBAC noted nivolumab entered the unresectable melanoma market in 2016Q2 and did not substantially affect the market. Following a change in the restriction in 2018Q3 which allowed for combined use with ipilimumab as first-line immunotherapy with a BRAF V600 negative variant and subsequent extension in 2019Q4 to include BRAF V600 positive variants, the utilisation of nivolumab in the unresectable setting grew substantially. The PBAC considered that the growth of nivolumab use could be attributed to the combined listings with nivolumab and also an increasing prevalent pool due to no cessation criteria. The PBAC considered emerging evidence for the superiority of combined ipilimumab and nivolumab in BRAF variant positive patients as first-line treatment may have also contributed to the increased use.

ANALYSIS OF MEDICINES FOR THE TREATMENT OF TYPE 2 DIABETES

Outcome

The PBAC considered the DUSC analysis of medicines for the treatment of type 2 diabetes mellitus (T2DM) and noted the high use of glucagon-like peptide 1 (GLP-1) receptor antagonists (RAs) outside of the PBS restrictions. The PBAC considered that it would be appropriate to change the restriction type for GLP-1 RAs from Authority Required (STREAMLINED) to Authority Required (telephone/online). The PBAC considered that sulfonylureas were increasingly viewed by clinicians as contraindicated for most patients due to their association with weight gain and increased risk of hypoglycaemia. Noting the high cost of GLP-1 RAs compared to other available treatments, the PBAC further considered it would be appropriate to alter the dual therapy restrictions for GLP- 1 RAs, for use with metformin or a sulfonylurea, to remove the requirement for contraindication/intolerance to a combination of metformin and a sulfonylurea and replace this with a requirement for contraindication/intolerance to a sodium-glucose cotransporter-2 (SGLT2) inhibitor. The PBAC considered that changes to the restrictions for GLP-1 RAs, dipeptidyl peptidase 4 (DPP4) inhibitors and SGLT2 inhibitors to explicitly exclude their use in combination with some classes of medicines may be useful. The PBAC requested the draft restriction changes be presented at a future meeting. Noting the proportion of use of DPP4 inhibitors and SGLT2 inhibitors outside of the PBS restrictions, the PBAC considered that a price reduction of at least 15% in the cost of these medicines would be appropriate. The PBAC considered that it would be useful to review the utilisation of T2DM medicines again in 12-24 months.

TEDUGLUTIDE FOR SHORT BOWEL SYNDROME PROPOSED RESTRICTION CHANGES

Outcome

The PBAC reviewed the implications of altering the restriction for teduglutide for short bowel syndrome following the Department's further investigation of the implications of changing the definition of treatment failure as proposed by the sponsor (Item 10.05, paragraph 3.4, Ratified minutes of the July 2022 PBAC meeting).

The PBAC noted that the change in definition of treatment failure to 'baseline' instead of 'last assessment' would cause the treatment stability definition to become redundant. This was due to treatment stability referring to the previous application, but the previous application would always be referring to baseline.

The PBAC noted that the trial treatment break would also no longer be a requirement as patients would either be continuing treatment due to response compared to baseline or failing treatment due to a failure in response compared to baseline. The original intent of the treatment break was to gauge whether improvements were a result of natural adaptive changes in the gut as opposed to any effect of the drug. Prescribers would still be permitted to trial a voluntary treatment break and resume teduglutide treatment if considered appropriate.

The PBAC noted this change would also cause changes in the three current continuing restrictions as the subsequent and recommencement restrictions would no longer be required.

With respect to concerns raised in July 2022 concerning rigidity in the timing of parenteral support observations (i.e. in the 4 weeks immediately preceding the authority application), the PBAC acknowledged that the 4 weeks immediately preceding an authority application may not be accurately representative of the entire preceding treatment period. The PBAC therefore recommended flexibility in when the observations of parenteral support are conducted.

The PBAC noted that utilisation was much lower than expected and only a small proportion of patients had ceased treatment after a trial cessation period. The PBAC recommended the change in restriction from 'previous application' to 'baseline' to lower the burden on health practitioners and consumers to access teduglutide. The PBAC considered that the change in restriction would have nil financial implications noting from the July 2022 DUSC review that the number of treated patients was small.

ATEZOLIZUMAB FOR EXTENSIVE-STAGE (ES) SMALL CELL LUNG CANCER (SCLC)

Outcome

The PBAC noted the number of patients and prescriptions dispensed for atezolizumab was different from predicted. The PBAC noted that the estimated number of patients progressing from limited stage to ES, or proportion of ES-SCLC patients who have an Eastern Cooperative Oncology Group (ECOG) 0-1 could have resulted in the difference between predicted versus actual utilisation.

The PBAC noted the estimated number of grandfathered patients was uncertain as the patient access program had not commenced at the time of the submission. The PBAC noted that this may also have contributed to more patients being supplied treatment in Year 2.

The PBAC noted the mean time on treatment without breaks was 188 days.

The PBAC noted in the March 2020 submission that there was uncertainty around the estimated 100% uptake of the 1680 mg four weekly (Q4W) dosing regimen for continuing treatment. However, it was considered likely that most patients would be prescribed this new dosing regimen once it became available. The PBAC noted that this review demonstrated that most patients were still being prescribed the three-weekly regimen.

The PBAC considered that a further review of utilisation should be conducted in 12 - 24 months once more data is available to examine utilisation relative to the expenditure caps under the risk sharing arrangement.