

OTHER MATTERS

IPILIMUMAB: INCIDENCE AND COSTS OF TREATING ADVERSE EVENTS (Agenda item 12.01)

Correspondence from the South Australian Medicines Evaluation Panel (SAMEP) (dated 15 April 2015)

1 Purpose of Item

- 1.1 In a letter to the PBAC Chair dated 15 April 2015, SAMEP provided South Australian data on the incidence and the costs of treating adverse events associated with ipilimumab treatment since it was listed on the PBS, specifically with regard to the treatment of steroid-refractory ipilimumab-induced colitis.

2 Background

- 2.1 The PBAC recommended the listing of ipilimumab for the treatment of unresectable stage III or stage IV malignant melanoma in November 2012. In making its recommendation, the PBAC was concerned about the cost-effectiveness of ipilimumab and recommended listing subject to risk-share arrangements, including a pay for performance component.
- 2.2 In July 2011, the PBAC considered: “that the costs associated with the treatment [of] adverse drug effects were considerably underestimated as there may be more inpatient hospital cost as well as greater costs associated with the PBS subsidised treatment of adverse events.”
- 2.3 SAMEP initiated a review of infliximab for the treatment of ipilimumab-induced steroid refractory colitis. The review was undertaken due to an observed increase in the reported number of cases of colitis in metastatic melanoma patients being treated with ipilimumab.

3 Consideration of the evidence

- 3.1 Over a 16 month period of observation (1 August 2013 to 8 December 2014), 56 patients were dispensed PBS-subsidised ipilimumab from South Australian public hospitals. Over this period, eight patients were admitted to hospital and received infliximab for severe, steroid-refractory colitis secondary to ipilimumab. One other patient was admitted for surgical intervention but did not receive infliximab. Of the eight patients admitted to hospital and received infliximab, two received a colectomy as infliximab failed to resolve the colitis. The average length of stay was 21 days per patient (range 6-39 days), and the eight patients spent a total of 168 overnight bed days (OBD) in hospital for the treatment of colitis, with most patients having multiple acute admissions. The average cost to SA Health for an OBD was approximately \$2,357-\$2,880 per night. The estimated cost to SA Health for these eight patients

was between \$395,976 and \$483,840 for hospitalisation (including the cost of infliximab and surgery).

- 3.2 The following table outlines the differences between the ipilimumab submission to the PBAC, a published early access scheme in Australia (Peter MacCallum Cancer Centre, Victoria), and the SAMEP experience.

Table 1: Comparison of SAMEP review with ipilimumab submission values

Factor Considered	Values in the submission	Early access scheme in Australia ¹	Implied Values in SAMEP review	Relative Increase from submission to SAMEP
Percentage of patients with colitis	7.6%	7.7%	Unknown	Unknown
Percentage of patients with severe colitis (grade 3 or above)	5.3%	5.8%	16%	3 times more in South Australia
Cost associated with each severe adverse event	\$██████	N/A	\$50,000	██████ times more in South Australia

¹ Alexander M, Mellor J, McArthur G, and Kee D (2014) Ipilimumab in pretreated patients with unresectable or metastatic cutaneous, uveal and mucosal melanoma *MJA* 201(1) 49-53

² ABS Consumer Price Index, March 2015, Health CPI series A2331111C used to inflate the original costs from Dec 2010 to Dec 2013 to improve comparability (109.2/93.7)

- 3.3 The correspondence from SAMEP also stated that the panel are aware of a number of ipilimumab-treated patients admitted to hospital with immune-related hypophysitis. At the time of the correspondence, the number of patients with immune-related hypophysitis had not been quantified.

4 PBAC outcome

- 4.1 The PBAC noted that the incidence of serious adverse events occurring in South Australia is higher than the incidence seen in CT-020, the pivotal trial in the ipilimumab submission to the PBAC. The data from SAMEP also suggested that the rate of steroid-refractory ipilimumab-induced colitis requiring hospitalisation and the associated resources and costs were significantly underestimated in the ipilimumab submission from November 2012.
- 4.2 The PBAC considered that the underestimation of both the incidence of adverse events (such as severe colitis), and the costs associated with treating such adverse events, would mean that the base case ICER for ipilimumab considered in November 2012 was underestimated. The PBAC also noted that the disutility associated with the incidence of severe colitis may have been underestimated in the ipilimumab submission.
- 4.3 The PBAC noted that emerging evidence, such as the data provided by SAMEP, indicated that the extent of colitis following any of the recent cancer immunotherapies in regular clinical practice is not yet known with confidence. The PBAC considered that the incidence of adverse events in broader clinical practice may not reflect the data from clinical trials, which is an area of uncertainty when providing early access to new therapies.

- 4.4 The PBAC welcomed the correspondence from SAMEP. The PBAC considered that it would be useful if such data were collected in a systematic way.