Drug Utilisation Sub-Committee
Outcome Statement 1 June 2017

The Drug Utilisation Sub-Committee (DUSC) of the Pharmaceutical Benefits Advisory Committee (PBAC) held its 90th meeting on 1 June 2017.

DUSC has a national focus of excellence in collecting, analysing and interpreting data on the utilisation of medicines in Australia for use by the PBAC. Review of the utilisation of medicines is an essential management tool in facilitating the objectives of the National Medicines Policy.

Submissions to the PBAC

DUSC noted that 27 major submissions had been received for the July 2017 meeting of PBAC. DUSC provided detailed advice to the PBAC on projected usage and financial cost for the major submissions where there is high cost, uncertain utilisation, first medicine in class or quality use of medicines concerns. The agenda for the July 2017 PBAC meeting can be found on the PBS website.

Utilisation of PBS Listed Medicines

DUSC regularly examines utilisation of PBS items when there is at least 24 months of prescription data available and where DUSC or the PBAC has highlighted items of interest. When an analysis of utilisation is to be undertaken sponsors are notified, provided with a copy of the report and an opportunity to comment prior to the DUSC meeting. Reviews to be considered by the PBAC are also published in the PBAC meeting agenda.

All reports, Sponsor comments and DUSC assessment of the reports are subsequently provided to the PBAC.

The PBAC is committed to understanding consumer perspectives and integrating them into its consideration of medicines and vaccines. Consumers are able to provide their views about medicine utilisation reviews to the PBAC via a web interface.

Full restrictions for PBS listed medicines are available in the PBS Schedule.

DUSC reviewed the utilisation of the following PBS medicines in June 2017:

Ulcerative colitis

A range of medicines is listed on the PBS for the management of ulcerative colitis, including corticosteroids, 5-aminosalicylates (in oral and rectal forms), immunomodulators and biologics. Mesalazine is the most commonly prescribed medicine and use of all forms of mesalazine is increasing. Biologics have only been listed relatively recently and their use is low in the context of the entire market, although use is increasing.

The PBS restriction for oral mesalazine, balsalazide and olsalazine require the patient to have had a documented hypersensitivity reaction to a sulphonamide or be intolerant to sulfasalazine. PBS data indicate that at least half of all patients who initiated treatment for UC in 2015 initiated on mesalazine. DUSC noted advice from clinicians that mesalazine may be used in preference to sulfasalazine because it is better tolerated, requires less intensive

monitoring, has a lower pill burden, and when patients report prior adverse reactions to antibiotics. In addition, sulfasalazine reduces sperm count and the peak age for onset of inflammatory bowel disease coincides with peak reproductive years. DUSC also considered that the increasing number of prescriptions for mesalazine may be due to dose escalation and requested further analysis to examine this. DUSC considered that the extensive use of mesalazine in place of sulfasalazine, and the possible use of higher doses, may not reflect cost-effective use.

The DUSC requested that the report be provided to the PBAC.

Crohn disease

The number of patients treated with biologics for severe refractory adult Crohn disease, fistulising Crohn disease and moderate to severe refractory Crohn disease in children and adolescents had increased steadily from 2007 to 2016. In 2016, 7,505 patients received a biologic for severe adult refractory Crohn disease, 2,135 for fistulising Crohn disease and 824 patients received treatment for paediatric Crohn disease. The proportion of patients continuing on biologic therapy for each of its listed Crohn indications was substantially higher than anticipated.

DUSC noted that of the adult patients with severe refractory Crohn disease initiating on biologic therapy in 2011, around 60% remained on treatment after five years. DUSC noted this is much higher than the continuation rates in the clinical trials, which may partly be due to some patients switching to a second (or third) biologic agent. DUSC commented that the continuation rates in fistulising Crohn disease seem high and considered patients may not be ceasing treatment after fistula closure. However, DUSC acknowledged that the restrictions do not include rules or advice of when patients should stop or restart treatment and therefore patients may be receiving continuous treatment.

DUSC noted biologics are being initiated as per their restrictions for prior therapies in the majority of cases.

The DUSC requested that the report be provided to the PBAC.

Botulinum toxin type A for chronic migraine

There were 3,517 and 5,444 patients treated with botulinum toxin for chronic migraine in the first and second year of PBS listing, respectively. The number of patients treated was substantially higher than predicted. This could be due to an underestimate of the eligible population, an underestimate of the uptake rate, or use earlier in the treatment pathway.

The proportion of neurologists that administered botulinum toxin for chronic migraine was close to that predicted and so was not a factor in the higher than expected use. Treatment rates in most states were similar (23-32 patients per 100,000) however treatment rates were substantially higher in the ACT (105 per 100,000) and substantially lower in the NT (5 per 100,000). The mean number of vials per treatment suggests that the dose used is consistent with recommendations.

The continuation rate on treatment at 24 weeks was more than double that predicted from trial data and is the main driver of high use. DUSC considered that there may be continued use in partial responders and that differences between trial and real world continuation rates may

include the subjective nature of the assessment (headache days) and the lack of alternative treatments.

The DUSC requested that the report be provided to the PBAC.

Inhaled tobramycin for *P. aeruginosa* infection in cystic fibrosis
The total number of patients using any form of inhaled tobramycin was higher than expected, but the proportion of these that used tobramycin inhalation powder (TIP) was lower than expected.

There was little difference in the pattern of use between TIP and tobramycin solution for inhalation (TSI). DUSC noted there are a number of factors that contribute to patient preference for TSI or TIP, including tolerance, nebuliser versus inhaler device, and climate, as the powder is less suitable in humid climates.

Analysis of PBS data consistently showed that patients received substantially fewer inhaled tobramycin prescriptions than would be expected for chronic *P. aeruginosa* infection. DUSC noted it is unclear from available data whether the patterns of use indicate poor adherence, use of other PBS or non-PBS antibiotics, treatment in non-PBS settings (e.g. hospitals) or a greater than expected proportion of use in accord with eradication or exacerbation protocols compared with chronic management.

The DUSC requested that the report be provided to the PBAC.

Upcoming Utilisation Analysis of PBS Listed Medicines

Utilisation of the following medicines and therapeutic areas have been selected for consideration at future DUSC meetings.

Predicted versus Actual Utilisation Analysis

- Lenalidomide for myelodysplastic syndrome
- Paclitaxel, nanoparticle albumin-bound, for metastatic adenocarcinoma of the pancreas
- Eculizumab for atypical haemolytic uraemic syndrome (aHUS)
- Sunitinib and everolimus for metastatic or unresectable, well-differentiated malignant pancreatic neuroendocrine tumour (pNET)
- Ivacaftor for cystic fibrosis

Analysis of multiple medicines in a treatment area

- Thalidomide, bortezomib, lenalidomide and pomalidomide for multiple myeloma
- Bevacizumab, cetuximab and panitumumab for metastatic colorectal cancer.

Other matters

At its September 2016 meeting, DUSC reviewed the utilisation of antifungal medicines for systemic use. DUSC noted that relative to other systemic antifungal medicines, the utilisation of fluconazole had risen sharply in the second quarter of 2016 after it became a Restricted Benefit. The PBAC (November 2016) agreed with the DUSC that the use of fluconazole should be monitored closely to see if the increase continues.

In a follow-up analysis, DUSC noted that the use of fluconazole and itraconazole has continued to rise. DUSC considered that this increase is mainly due to use for vulvovaginal candidiasis and dermatophyte infections, with increased prescribing by gynaecologists and dermatologists and a greater increase in the use of oral fluconazole in women compared to men. DUSC reiterated its previous view that this use may be outside the intended PBS listing, has not been assessed as cost-effective, and may be associated with substantial wastage given the pack size.

DUSC noted that 'serious or life threatening candida infections' could be open to broad interpretation. Until April 2010, fluconazole was listed for use in serious and life threatening candida infections where patients are unable to tolerate amphotericin B. The requirement for a patient to be unable to tolerate amphotericin B was removed from the restriction when amphotericin was discontinued and subsequently deleted from the PBS.

DUSC considered that measures may need to be taken to address any further increases in utilisation and requested that a range of options be prepared for stakeholder consultation and PBAC consideration. These could include reintroducing an authority required listing, strengthening the clinical criteria of 'serious or life threatening candida infections', assessing the cost-effectiveness of use in additional indications, or education initiatives.

An outcome statement will be available following each meeting of DUSC. For further information, please contact the DUSC Secretariat at DUSC@health.gov.au.

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Chair
Drug Utilisation Sub-Committee