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

The PBAC noted utilisation reports with associated stakeholder responses from the September 2016 Drug Utilisation Sub-Committee (DUSC) meeting, which were provided in items 10.03 to 10.08 of the PBAC agenda. DUSC minutes relating to these items were provided to the PBAC. The September 2016 DUSC outcome statement is available here.

ANTIFUNGAL MEDICINES

This report reviewed the utilisation of systemic antifungal medicines, including a predicted versus actual analysis of voriconazole for prophylaxis against invasive fungal infections in certain high risk patients.

In the 2015-16 financial year, 91,874 people received systemic antifungal medicines on the PBS. There were 203,228 prescriptions supplied at cost of $35,564,069. Terbinafine and griseofulvin were the most widely used medicines with over 30,000 people supplied each of the medicines.

The number of fluconazole, itraconazole and posaconazole prescriptions has increased over time. The number of voriconazole prescriptions decreased after peaking in 2012 and its use has been lower than expected.

There was a sharp increase in the use of fluconazole from 1 April 2016 coinciding with the PBS listing changing from Authority Required (STREAMLINED) to a Restricted Benefit.

Outcome: The PBAC noted the sharp increase in fluconazole utilisation in the second quarter of 2016 and considered that this increase may be due to treatment of vaginal candidiasis. The PBAC noted that fluconazole for this indication is available over the counter and that the current PBS restrictions do not include vaginal candidiasis. The PBAC agreed with the DUSC that the use of fluconazole should be monitored closely to see if the increase continues.

ANTIPSYCHOTIC MEDICINES

This report reviewed the use of PBS listed antipsychotic medicines, with a focus on changes in use of 25 mg quetiapine in the 24 months after the restriction was altered to remove repeats from PBS prescriptions.

Previous reports1 from DUSC raised concern about the utilisation of PBS listed antipsychotics for non-subsidised and off-label indications such as sedation. Trends of inappropriate prescribing were most evident for quetiapine 25 mg tablets where there were high and growing numbers of prescriptions despite this strength not generally being considered to be a therapeutic dose to treat the PBS subsidised indications of schizophrenia and bipolar disorder.

[1] June 2013 DUSC Outcome Statement, available at the DUSC outcome statements page; February and June 2013 DUSC reports, available at the DUSC public release documents page.

In response to this concern the PBAC recommended that the number of repeats of 25mg quetiapine be reduced from five to zero. This listing was considered to be sufficient for dose titration in bipolar disease and schizophrenia, and would encourage regular prescriber review for patients treated for non-subsidised indications.

DUSC found that the intervention to change the listing of the 25 mg strength to allow no repeats from 1 January 2014 was effective in supporting its intended use as a titrating dose for PBS listed indications and reducing inappropriate use. There were 136,000 fewer prescriptions of quetiapine 25mg dispensed through the PBS in 2015 compared with 2013.

DUSC considered that while the use of quetiapine 25 mg had decreased, vigilance is still needed to encourage the appropriate use antipsychotics as off-label prescribing is still evident. Limited data are available to weigh up the benefits and harms of off-label prescribing of antipsychotics. Widespread use of antipsychotics in the elderly was considered to remain an issue.

Outcome: The PBAC noted the DUSC report and considered the lower use of quetiapine 25mg to be an encouraging sign that inappropriate prescribing of quetiapine is in decline. The PBAC requested that DUSC continue to monitor use of antipsychotics including monitoring for any shift from low dose quetiapine to other low dose antipsychotic preparations.

MIFEPRISTONE AND MISOPROSTOL

This report compared the compared the predicted and actual use of mifepristone and misoprostol supplied through the PBS for medical termination of pregnancy.
When recommending this listing, the PBAC considered that medical termination of pregnancy with mifepristone and misoprostol allows a choice for women who have decided to undergo a termination, and its availability through the PBS was considered unlikely to result in an increase in overall terminations of pregnancy.

DUSC found that the data available to date suggests the introduction of mifepristone and misoprostol on the PBS has not increased the number of terminations of pregnancy in Australia per year.

The proportion of terminations of pregnancy undertaken by the medical method has been lower than predicted. Factors contributing to this may include that the proportion of women choosing medical rather than surgical termination may have been overestimated, jurisdictional laws in some states and medical indemnity insurance requirements may pose a barrier, there are a low number of certified prescribers, and there is some private prescribing not captured in the PBS dataset.

Outcome: The PBAC noted the DUSC report and informative stakeholder responses. The PBAC agreed that multiple factors have contributed to the low proportion of terminations of pregnancy undertaken using the medical method. The PBAC considered that the proportion of terminations undertaken by the medical method with mifepristone and misoprostol may gradually increase as these barriers are overcome.

OSTEOPOROSIS MEDICINES

This report reviewed the utilisation of medicines for the treatment of osteoporosis, including an assessment of the predicted and actual use of denosumab.

In 2015, close to 500,000 patients were treated with osteoporosis medicines through the PBS. Prior to 2015, the rate of treatment with osteoporosis medicines was in decline despite reports of increasing prevalence. DUSC noted that this may be attributed to safety concerns with the use of some of the medicines but also considered the clinical practice of taking drug "holidays" from the bisphosphonates may be a factor in the lower treatment rates.

Approximately half of all people starting osteoporosis therapy for the first time in 2015 were prescribed denosumab and a large number of people already on treatment with other medicines switched to denosumab. The higher than expected uptake of denosumab may relate to patient and clinician preference for a medicine given as a six-monthly subcutaneous injection. Although denosumab appears to be well tolerated and is viewed by clinicians to be comparatively safe, DUSC considered that ongoing vigilance and education is required to minimise the risk of coadministration of oral osteoporosis medicines with the injectable medicines, to recognise and manage adverse events of denosumab, and to understand the risk of vertebral fractures occurring after denosumab discontinuation.

Outcome: The PBAC considered that most of the use of osteoporosis medicines is for secondary prevention with uptake in the primary prevention population comparatively low.

The PBAC noted the very high uptake of denosumab and declining use of bisphosphonates. The PBAC recalled that the recommendation to list denosumab for osteoporosis was based on short-term efficacy and safety data in the context of the evidence and treatments available at that time. The PBAC noted that additional data has become available since then.

The PBAC noted that bone mineral density returns to approximately pre-treatment levels when denosumab is discontinued and that there have been reports of fractures following cessation. This differs from the bisphosphonates where the beneficial effects on bone may continue after discontinuing or when having a break from treatment.

The PBAC requested that the Department provide additional information to assist in determining whether a more comprehensive review of denosumab should be recommended. The PBAC made this request in the context of the quality use and ongoing cost-effectiveness of treatment for a highly prevalent condition where patients may be treated for long periods of time.

RIFAXIMIN FOR PREVENTION OF HEPATIC ENCEPHALOPATHY

This report was a predicted versus actual use comparison of rifaximin for hepatic encephalopathy.

In the period from 1 December 2013 to 31 March 2016, 2,892 people were supplied at least one PBS/RPBS prescription for rifaximin. The number of patients supplied rifaximin was higher than predicted in both the first and second years of listing.

The number of prescriptions per patient per year was lower than estimated. This may indicate poor adherence or intermittent use.

Outcome: The PBAC noted the report on the use of rifaximin and agreed that another utilisation review should be considered in 24 months' time.

TESTOSTERONE

This report that assessed the impact of the PBS restriction changes to testosterone that occurred on 1 April 2015.

In the year after the restriction change, there was a 20% reduction in the number of people supplied PBS-subsidised testosterone and a 60% reduction in the number of people starting subsidised testosterone for the first time compared to the year before.

The most extensive restriction changes were for people aged 40 years or older who had androgen deficiency not caused by a pituitary or testicular disorder. In this group, there was an 86% reduction in patients starting subsidised testosterone for the first time.

The PBAC noted the DUSC report on the use of testosterone and the comprehensive responses from a broad range of stakeholders.

The PBAC considered the overall reduction in testosterone utilisation to be consistent with the intended impact of the revised restrictions to reduce PBS subsidised use in patients without established androgen deficiency where clinical evidence and safety data are varied and where cost-effectiveness is not known. The findings of the DUSC analysis confirm that the greatest change has been a reduction in the number of people aged 40 or older commencing treatment for androgen deficiency not caused by a pituitary or testicular disorder. There was little change in the number of people initiating treatment for classical androgen deficiencies.

The PBAC considered that changes in the restrictions were made to ensure that that therapy was guided by appropriate testing and consultation. The PBAC noted concerns raised by stakeholders regarding potential issues with accessing specialist prescribers. The PBAC considered that the restriction wording requiring prescribing 'in consultation with' one of the listed specialties offers flexibility with how the consultation can be conducted.

The PBAC recommended extending the list of specialist prescribers for patients under 18 years of age with androgen deficiency due to established pituitary or testicular disorders to include general paediatricians. The PBAC noted that use of testosterone in the younger age groups had been stable over the past few years. The PBAC considered the addition of general paediatricians to the list of prescribers may improve access for younger people in rural and remote areas.

The PBAC requested that DUSC undertake a further utilisation review in 2 years.