The Thoracic Society
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LEADERS IN LUNG HEALTH

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Monday 4 March 2013

PBS Post-Market
Department of Health and Ageing
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Dear Committee Members,

Re: Submission for the Review of Pharmaceutical Benefits Scheme Medicines Used to Treat Asthma in Children

Thank you for addressing this important issue. The Thoracic Society of Australia and New Zealand are pleased to make the attached submission in which we provide information relevant to the defined terms of reference of the review.

This submission has been prepared by 2 of our members who were also authors of the TSANZ Position Paper on *"The role of corticosteroids in the management of childhood asthma"* which was most recently revised in 2010 and which we believe is relevant to your review. Prof. Peter van Asperen is currently a Senior Staff Respiratory Physician at The Children's Hospital at Westmead and Macintosh Professor of Paediatric Respiratory Medicine in the Sydney Medical School, University of Sydney. Prof Craig Mellis is also a Paediatric Respiratory Physician who is currently Associate Dean and Head of Central Clinical School at the Sydney Medical School, University of Sydney. Their conflict of interest declarations are included in the TSANZ Position Paper, a copy of which is attached to this submission, although they have informed us that neither the MSD (Aust) Paediatric Respiratory Physician Advisory Board or the GSK Paediatric Respiratory Taskforce have met in the last 2 years. Both have also recently published articles for health care professionals highlighting the current evidence based guidelines for management of children with asthma and raising concerns about the inappropriate prescribing of combination ICS/LABA in children as highlighted in their response to TOR 4.

We have attached for your information a copy of the TSANZ Position Paper *"The role of corticosteroids in the management of childhood asthma"*, (2010) and would be happy to supply any of the other articles referenced in the submission if this would be assist the Committee. We hope that our submission is helpful to the Committee and look forward to hearing of the outcome of the review in due course.

Yours Sincerely,

Prof Paul Reynolds
President

Prof Matthew Peters
President Elect

Prof Peter Wark
Chair, Clinical Care
& Resources Sub-Committee

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TSANZ Submission for the Review of PBS Medicines Used to Treat Asthma in Children

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We offer the following information which we hope will be useful to the Committee in addressing the Terms of Reference for its review of "Pharmaceutical Benefits Scheme Medicines Used to Treat Asthma in Children".

1. Review the evidence on the efficacy and safety of single ingredient and combination product use of inhaled long acting beta2 agonist in children not previously considered by the PBAC in making recommendations to the Minister.

The evidence for the efficacy and safety of medicines used to treat asthma in children have been recently extensively reviewed (1,2) and we have provided copies of these publications as we believe they may be useful for the Committee's deliberations.

In brief these reviews highlight:

- That there is established evidence for the relative efficacy and safety of leukotriene receptor antagonists (LTRAs) and inhaled corticosteroids (ICS) and their appropriate roles in the management of children with asthma.
- That the majority of children with asthma who require preventer therapy will be well controlled on either an LTRA or low dose ICS.
- That there is limited evidence for the benefits of adding long acting beta2 agonists (LABAs) to ICS in children with asthma and no studies have been performed in children under 4 years of age.
- That there is evidence of an increased risk of severe asthma episodes and hospitalisation, loss of effectiveness of short acting beta2 agonists and loss of protection against exercise-induced bronchoconstriction with LABA use in children with asthma.
- That the addition of an LTRA is an alternative to the addition of a LABA in children not adequately controlled on ICS.

Two studies published since these reviews add further relevant information in regard to the last 2 dot points (3,4). An FDA meta-analysis of controlled trials comparing LABA use versus non-LABA use in different age groups concluded that children aged 4-11years appeared to be at highest risk of severe asthma outcomes although further studies were required in children to assess the risk in children using simultaneous ICS (3). A study targeting asthmatic children with the Arg^{16} polymorphism in the beta2 receptor gene (which predisposes to down-

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regulation of the beta2 receptor and increased susceptibility of exacerbations with LABA use) demonstrated significantly better clinical outcome with the addition of Montelukast compared to the addition of Salmeterol in children not adequately controlled on ICS alone (4).

On the basis of the current evidence of the efficacy and safety of LABAs in children the recently revised TSANZ Position Paper on "The role of corticosteroids in the management of asthma in children" (2) makes the following recommendations in regard to the role of LABAs:

- In situations where effective control of asthma cannot be achieved with doses of 400 mcg/day BUD, or 200 mcg/day FP or HFA-BDP or 160mcg/day CIC, the main step up options include increasing the inhaled steroid dose or the addition of a long-acting beta-agonist (LABA) or a leukotriene antagonist. In the absence of evidence of safety and efficacy, the use of LABAs is not recommended in children aged 5 years or younger. (STRONG Recommendation, MODERATE QUALITY Evidence)
- In children with ongoing problems with exercise induced symptoms, despite inhaled corticosteroids, the addition of leukotriene antagonists have been shown to be effective and superior to long-acting beta-agonists, and do not have the problem of the development of tolerance.(STRONG Recommendation, MODERATE QUALITY Evidence)

The TSANZ recommendation that LABAs not be used in children 5 years or younger is consistent with the GINA guidelines for the diagnosis and management of asthma in children 5 years and younger (5).

2. Review the DUSC report on utilisation of combination inhaled ICS/LABA considered by PBAC and supplement this analysis with any additional data and clinical information sources available in Australia.

The findings of inappropriate prescribing of combination inhaled ICS/LABA as first line preventer treatment without prior trials of ICS alone as outlined in the DUSC report is consistent with previous analysis as highlighted in a recent review on "Cost considerations of therapeutic options for children with asthma" (6) and also seen in clinical practice when patients are referred to respiratory paediatricians for assessment of their asthma. What is also clear from clinical practice experience is that combination inhaled ICS/LABA is also being inappropriately prescribed as intermittent treatment and for conditions other than asthma such as persistent nonspecific cough. Despite the lack of evidence of the efficacy and safety of LABAs in young children, combination inhaled ICS/LABA was also found to be increasingly used in preschool children having increased from 0% in 2000 to 20% in 2005 of all asthma medication used in the previous 12 months in annual school entry surveys in the ACT (7).

3. Identify areas of prescribing for childhood asthma in Australia where clinical practice is inconsistent with clinical guidelines; and if there is evidence that supports this practice.

As highlighted above the main areas where clinical practice is currently inconsistent with clinical guidelines for childhood asthma is the inappropriate prescribing and over-prescription of combination inhaled ICS/LABA. Another area of concern is the prescription of asthma

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medicines for conditions other than asthma mainly because of a failure to recognise that there is another cause for persistent respiratory symptoms such as persistent cough as highlighted in the CICADA Position Statement (8).

4. Identify and review recent (past five years) healthcare professional and consumer education in the area of medication management in children with asthma.

There have been a number of healthcare professional publications over the last few years highlighting appropriate evidenced based management of childhood asthma (9-11) and more specifically the role of combination inhaled ICS/LABA (12). The revision of the Paediatric sections of the NAC Asthma Management Handbook, which is currently occurring, will also be evidence based with recommendations consistent with the TSANZ Position Paper. In addition the CICADA Position Statement has highlighted issues of managing children (and adults) presenting with persistent cough, particularly the importance of not attributing the cause of persistent cough in the absence of wheeze or breathlessness to asthma as asthma is rarely the cause of persistent isolated cough particularly in children (8). Consumer organisations such as the Asthma Foundations have also attempted to make consumers aware of these issues.

5. Identify effective interventions that have resulted in improvement of prescribing and quality use of medicines in the context of childhood asthma using overseas or Australian literature.

We would like to particularly highlight to the Committee the results of a recently published Australian study which evaluated the effectiveness of the Practitioner Asthma Communication and Education (PACE) Australia program, an innovative communication and paediatric asthma management program for general practitioners (13). The study found that GPs in the intervention group had more patients with infrequent intermittent asthma who had lower use of ICS & LABAs than patients of GPs in the non-intervention group, consistent with the current paediatric asthma guidelines (13).

In conclusion we would like to submit for the Committee's consideration the following suggestions to try to address the current discrepancy between evidence based management and clinical practice particularly in regard to the inappropriate prescription of combination inhaled ICS/LABA:

- Ongoing education on appropriate prescribing of asthma medicines in children – an opportunity for this will occur with the launch of the revised NAC Asthma Management Handbook due at the end of this year.
- Consideration of reintroducing PBS authority prescription requirements for combination inhaled ICS/LABA for children under 12 years of age.
- Consideration of extending the current PBS streamlined authority (3217) for the addition of Montelukast as an add on medication in children not controlled on ICS alone, as an alternative to LABA add on. This would be particularly useful in young children where current guidelines are not recommending the use of LABA add on in children 5 years and younger because lack of clinical trials in this age group.

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