

## **9.1 POST MARKET REVIEW OF PBS MEDICINES USED TO TREAT ASTHMA IN CHILDREN**

### **The Review**

In November 2012, following a request by the Minister, the Pharmaceutical Benefits Advisory Committee (PBAC) agreed on the Terms of Reference (ToR) for the Post-Market Review of PBS Medicines Used to Treat Asthma in Children (the Review), and to consider the Review's findings.

The objective of this Review was to systematically evaluate the body of clinical evidence about asthma medicine interventions to ensure the most appropriate management of children living with asthma.

### **Terms of Reference**

1. Review the evidence on the efficacy and safety of single ingredient and combination product use of inhaled long-acting beta<sub>2</sub>-agonist in children not previously considered by the PBAC in making recommendations to the Minister.
2. Review the DUSC report on utilisation of combination inhaled corticosteroid (ICS)/ long-acting beta<sub>2</sub>-agonists (LABA) considered by PBAC and supplement this analysis with any additional data and clinical information sources available in Australia.
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.
4. Identify and review recent (past five years) healthcare professional and consumer education in the area of medication management in children with asthma.
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.

### **Background**

The need for this Review was first identified by the Paediatric Medicines Advisory Group (PMAG, 2010), which found that 40% of the children supplied with a fixed dose combination (FDC) product (of LABA and ICS), had not first been prescribed a single ingredient product (an ICS). PMAG considered that the extent of FDC use in paediatric asthma was a serious quality use of medicines issue and subsequently referred the matter to the Drug Utilisation Sub-Committee (DUSC) of the PBAC.

In 2011, the DUSC review indicated that there was a very high rate of initiation to a FDC without prior use of a single ingredient inhaler. This was contrary to asthma management guidelines (Asthma Management Handbook 2006, National Asthma Council Australia) of that time. The DUSC noted the issues and advised sponsors that this is a complex area of treatment and further clarification of the issues surrounding asthma management in children was needed.

In April 2012, the National Medicines Policy (NMP) Committee recommended to the Minister for Health the initiation of the Review, to ensure that medicines for treating asthma in

children continue to be used safely and appropriately. The NMP Committee developed the draft ToR for this Review.

The Review was conducted during 2013 and included reviewing the published literature for: comparative trials and large observational studies on the safety and efficacy of ICS and ICS/LABA combinations; educational interventions conducted recently in Australia (past 5 years); and evidence on effective interventions to improve management and quality use of medicines in children with asthma. Open public consultation was conducted at several stages during the Review. A Reference Group was also formed to assist in reviewing the evidence and forming options for PBAC consideration. Members of the Reference Group included experts in clinical management of asthma and representatives of health professional and consumer organisations.

### **Main Findings of the Review**

*TOR 1. Review the evidence on the efficacy and safety of single ingredient and combination product use of inhaled long-acting beta<sub>2</sub>-agonist in children not previously considered by the PBAC in making recommendations to the Minister.*

#### Findings from a literature review of published trials and large observational studies (2000 to 2013)

A literature search was conducted by the Quality Use of Medicines Pharmacy Research Centre (QUMPRC), University of South Australia to identify comparative trials and studies on the efficacy and safety of combined treatment with LABA and ICS in children with asthma. The search was restricted to English language articles published between 2002 and November 2013 from four electronic databases and industry websites. Seven systematic reviews (including a total of 26 randomised control trials) and five separate randomised control trials (not included in the systematic reviews) were identified that addressed comparative safety and efficacy of LABA in combination with ICS versus same or higher doses of ICS monotherapy. Five large observational studies were identified, however not included as they did not report on children and/or relevant outcomes.

In children with poorly controlled asthma, the evidence showed that there was no additional improvement when LABA was added to ICS, compared to treatment with same dose ICS with respect to preventing asthma exacerbations requiring corticosteroids or hospitalisation. This differs from evidence in adults, which shows that commencing a LABA/ICS does significantly reduce the risk of exacerbations requiring oral corticosteroids compared to the same dose ICS. The addition of LABA to ICS was found to be more effective than same dose ICS alone for improving lung function (FEV<sub>1</sub>) but this was not found to translate into a reduction of symptoms in children. (See Table 1 below)

Table 1: Results for exacerbations and changes in FEV<sub>1</sub> in RCTs comparing addition of LABA to ICS versus same doses of ICS in children with persistent asthma and having received ICS

Outcomes	Comparative risks		Relative effect (95% CI) p value	No participants (No. RCTs)	Quality of the evidence (GRADE)
	LABA with ICS	ICS			
Exacerbations (requiring systemic corticosteroids)	63 per 1000	68 per 1000	RR 0.92 (0.60,1.40) p = 0.69	1084 (8 studies)*	Low
Exacerbations (requiring hospital admissions)	31 per 1000	19 per 1000	RR 1.65 (0.83, 3.25), p = 0.15	1266 (6 studies)*	Low
FEV <sub>1</sub> Changes in L at endpoint			WMD 0.08 L (0.06, 0.11) p < 0.00001	Not able to be determined for all studies (9 studies)	Moderate
FEV <sub>1</sub> % predicted at endpoint			WMD 2.35% (0.07, 4.64) p = 0.044	476 (5 studies)	Moderate
FEV <sub>1</sub> % predicted			MD 1.6%	39 (Carroll W)	Not assessed

RR: risk ratio; WMD: weighted mean difference (Ni Chroinin, Lasserson et al 2009)

There was also no difference between LABA added to ICS compared to higher dose ICS in preventing exacerbations requiring corticosteroids or hospitalisation, or in changing measures of FEV<sub>1</sub> in children. LABA added to ICS was found to significantly improve morning and evening peak expiratory flow (PEF) compared to higher dose ICS, but this was not found to translate into a reduction in symptoms in children (see Table 2).

Table 2 . Results for exacerbations in trials comparing addition of LABA to ICS versus higher doses of ICS in children with persistent asthma

Outcomes	Comparative risks		Relative effect (95% CI, P value)	No of participants (RCTs)	Quality of the evidence (GRADE)
	LABA with ICS	ICS			
Exacerbations (requiring oral corticosteroids)	54 per 1000	36 per 1000	RR 1.5 (0.65 to 3.48) p = 0.34	441 (2 studies)	Low
Exacerbations (requiring hospital admissions)	17 per 1000	6 per 1000	RR 2.21 (0.74 to 6.64) p = 0.16	1026 (4 studies)	Low
Morning PEF			MD 7.55L/min (3.57, 11.53) p=0.0002	4 studies	Not assessed
Evening PEF			MD 5.5L/min (1.21, 9.79) P=0.012	3 studies	Not assessed
FEV <sub>1</sub> Changes in L at endpoint			WMD 0.01 L (-0.03 to 0.05) p < 0.47	544 (2 studies)	Moderate

RR: risk ratio; WMD: weighted mean difference. MD mean difference ( Ni Chroinin, Lasserson et al 2009)..

The main findings with regard to safety include:

- Higher doses of ICS were found to reduce short term rate of growth in children more than ICS/LABA combinations (Bisgaard, Le Roux et al 2006)

- A meta-analysis of trials reported a higher risk of hospitalisation for children taking LABA alone; however there was no significant difference in hospitalisations for the group taking the fixed dose combination of LABA/ICS (McMahon, Levenson et al 2011).
- No trials or studies were identified that assessed the efficacy and/or safety of combination LABA/ICS when used intermittently for asthma symptoms or for respiratory conditions other than asthma.

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

The QUMPRC undertook an analysis of utilisation to supplement the original findings of the DUSC analysis. The supplemental analysis, 'Utilisation of Medicines to Treat Asthma in Children Report', used pharmacy claim data collected by Medicare Australia from 1 July 2007 to 30 June 2013. This included under co-payment data from June 2012.

#### Main findings from the Utilisation of Medicines to Treat Asthma in Children Report

- There is minimal use of PBS subsidised LABA as a single agent in children.
- Fluticasone/salmeterol (Seretide®) was the most commonly dispensed fixed dose combination in the 0 to 18 age group, with peak utilisation in 6 to 7 years olds.
- Fluticasone was the most commonly dispensed ICS in the 0 to 18 age group, with peak utilisation around 5 years of age.
- Over 90% of PBS prescriptions for the prevention of asthma symptoms are prescribed by GPs.
- Similar results were reported from both the DUSC and QUMPRC analyses on the percentage of children (aged under 18yrs with concession status) who initiated a fixed dose combination of ICS/LABA without prior dispensing of an ICS in the previous two years; being 83% and 79% respectively.

*TOR 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.*

#### Further findings from the Utilisation of Medicines to Treat Asthma in Children Report

- Over 25% of prescriptions for fixed dose combination LABA/ICS inhalers were dispensed to children aged younger than the recommendations in the Australian asthma clinical guidelines in 2012/13.
- In children aged < 12 years initiating LABA/ICS with no prior dispensing for an ICS or oral corticosteroid in the previous two years, 59-71% (depending on the specific PBS item initiated) filled only one prescription in 12 months. In children who initiated LABA/ICS following a prescription for ICS or oral corticosteroids, their discontinuation rates following the initial LABA/ICS prescription were slightly lower; 49%-58% for children aged < 12 years.
- The high proportion of children receiving only one dispensing of a LABA/ICS fixed dose combination product is inconsistent with the indicated use of these medicines for preventative treatment of persistent asthma in children.

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

#### Main findings from the systematic literature review of Australian asthma educational activities (2008-2013)

A systematic review of active education interventions addressing use of asthma medicines in children within Australia was conducted by NPS MedicineWise. The search included four electronic databases and websites for Australian organisations that conduct health education for consumers and health professionals. There were 30 active educational activities that involve medication management in children identified. Of these, 19 are currently available and two will commence in 2014. The educational programs were divided into three categories: consumer focused education (12); consumer and health professional education (7); and health professional specific programs (11).

- The Asthma Child and Adolescent Program (ACAP) is well-established in schools and preschools. The program has provided emergency asthma management training to 72% of staff in schools and 48% of staff in preschools since 2010.
- There may be demand for broader education to parents and carers of children with asthma, as they accounted for over half (55%) of the 3487 callers in 2009–10, and around a third of the 2621 callers in 2010–11 to the national 1800 ASTHMA phone line.
- The Triple A (Adolescent Asthma Action) program trained over 2000 senior students as peer leaders, who then conducted educational sessions for more than 26,000 high school students from 35 schools across Australia.
- Limited details were available on the evaluation of the educational activities identified in this Review.

*TOR 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.*

A systematic literature review of interventions to improve prescribing and quality use of medicines in children with asthma was conducted by NPS MedicineWise. The search was restricted to English language articles published between 2002 and September 2013. They identified 98 studies and 15 systematic reviews investigating a diverse range of interventions. Studies were categorised according to target population (consumer, healthcare professional, or both) and then by predominant intervention type.

#### Findings from the systematic literature review of interventions to improve prescribing and QUM (2000 to 2013)

Overall, the review was unable to identify interventions that clearly and consistently demonstrated improvements in the key outcomes of interest. The majority of studies were conducted overseas and focussed on consumers. Low numbers of studies for some intervention types, and generally low to very low quality of evidence makes it difficult to draw conclusions regarding the effectiveness of interventions.

- Consumer education and behaviour interventions may have small benefits on healthcare utilisation, specifically emergency department and hospital visits.
- Healthcare professional reminders may slightly improve preventer use, but the evidence for this was of low strength.
- Overall, the literature review was unable to isolate intervention types that clearly and consistently improved prescribing, preventer use or healthcare utilisation.
- One randomised control trial found that children with infrequent intermittent asthma were less likely use ICSs and LABAs if they were treated by a GP who had received asthma education by the Practitioner Asthma Communication Education (PACE) Australia programme.

**The following opinions were provided by stakeholders during the stakeholder forum and submissions on the Review Terms of Reference for the Review:**

- FDCs should not be used to treat children under the age of five years as there is a lack of evidence on effectiveness and safety in this age group.
- Leukotriene receptor agonists have shown promise in the treatment of exercise induced bronchoconstriction. Based on the current evidence, the PBS restriction that prevents use in combination with an ICS should be reviewed.
- The impact of ICS on growth and other side effects are of concern to both parents and prescribers. However stakeholders noted that any concerns about using FDCs in children were not widely discussed.
- Users perceive greater risks from older established treatments such as ICS, compared to the potentially incomplete side effect profile of fixed dose combination products.
- Use of fixed dose combinations of LABA/ICS have been associated with non-responsiveness to treatment, based on development of tolerance to the LABA component. Tolerance to short acting beta-agonists (SABA) can make treating asthma flare-ups difficult.
- The patient-relevant outcomes identified by stakeholders are not routinely measured in clinical trials.
- Cost is a significant factor for families, especially as one or more family members may have asthma.
- PBS restrictions require stabilisation on each component medicine which is not practical, more expensive for patients, and not safe as it increases the chance of LABA being taken as monotherapy.
- The diagnosis of asthma is difficult at first presentation to the GP. Children may not return for follow-up visits for a variety of reasons and there may not be the opportunity to review and change medications.
- There appears to be less awareness of paediatric management approaches for asthma and adult management techniques are being applied in some cases when treating children.
- Some GPs may consider that prescribing medicines to stop symptoms is acceptable and therefore may prescribe fixed dose combinations of LABA/ICS in conditions other than asthma.
- Some patients are confused about different asthma medications, despite the education work that has been done in this area.
- Education programs should be offered to patients and their families at a time when they are most receptive to hearing and taking in the advice and information e.g. during the follow-up phase and not during the acute phase of an asthma exacerbation.
- There is a lack of recent, paediatric specific education for GP's on the treatment of asthma, although general education on asthma with paediatric components is currently available. Specific paediatric courses should be developed for both health professionals and consumers.
- Home visiting programs conducted by pharmacists and nurses have shown some promise but the evidence on these programs has not yet been published.
- The specific requirements of people from non-English speaking backgrounds need to be taken into account when communicating asthma management.
- A multifaceted approach to paediatric specific asthma education is needed, involving a range of settings and stakeholders, including healthcare professionals and consumers. Schools and childcare settings were considered particularly important for childhood asthma education.
- Some pharmacists considered that they could be more actively involved as part of the asthma primary care team for newly-diagnosed children potentially under a modified Pharmacy Asthma Management Service.

- Asthma care plans provide a useful form of communication between health care professionals, carers, school staff and others involved in a child's life. The way these are used currently may not promote maximum benefit.

### **PBAC Consideration and Advice to the Minister for Health**

Overall the PBAC accepted the findings of the Review that showed there is minimal evidence to support the use of combined LABA/ICS over ICS alone in children with persistent asthma. The PBAC noted that no evidence was found to support the use of combined LABA/ICS for intermittent asthma or other respiratory conditions.

The PBAC acknowledged the stakeholder comments and recognised the challenges in accurately diagnosing and treating asthma in the general practice setting. The diagnostic challenges, combined with the marketing and availability of samples of fixed dose combination LABA/ICS in general practice are likely reasons for the high use of these inhalers in first line treatment of childhood asthma.

The PBAC noted that the utilisation review of PBS data conducted by the QUMPRC produced very similar results to the utilisation review considered by DUSC.

The PBAC considered the following eighteen options presented in the Review. These options were compiled over the course of the Review and arose from stakeholder feedback, the research conducted and from discussions with the Review Reference Group.

#### PBS Restriction Changes

1. *Change the PBS restriction to "Authority Required Streamlined" for prescribing fixed dose combination LABA/ICS.*

The PBAC noted this change would be difficult to implement for children alone. Specifying restrictions for specific age groups may be problematic as there is inconsistency between the age specified in the product information and recommendations in clinical guidelines for some of these medicines (see table 3 below). However, the PBAC noted that an Authority Required restriction for children could be reconsidered in the future if other recommendations associated from this Review are not effective in changing current prescribing patterns.

**PBAC Advice: The PBAC did not recommend that the current PBS restriction be changed to an Authority Required (streamlined) restriction for fixed dose combination LABA/ICS listings at this time.**

2. *Remove the current PBS restriction for fluticasone propionate/salmeterol xinafoate (Seretide®) that requires children aged less than 12 years to be stabilised on concomitant ICS and LABA inhalers prior to commencing the fixed dose combination.*

The PBAC agreed that this option is consistent with the guidelines in the National Asthma Council (NAC) Asthma Handbook, which no longer recommend stabilising children on single product inhalers before adding LABA to ICS. The current guidance to transition from ICS to fixed dose combination ICS/LABA is based on evidence which indicates there is increased risk associated with LABA if it is taken alone. The original PBS requirement for concomitant therapy was included following consideration of fixed dose combinations by PBAC in March 2000 and was based upon the clinical approach and evidence presented at that time.

**PBAC Advice: The PBAC recommended the current PBS restriction for fluticasone propionate/salmeterol xinafoate (Seretide®) be amended to be consistent with the NAC guidelines, by removing the requirement to stabilise patients on separate ICS and LABA inhalers prior to initiating Seretide®.**

3. *Include a minimum age limit for children in the PBS restriction in line with the relevant product information and/or the 2014 NAC Guidelines.*

Table 3. provides a comparison of the age recommendations provided in the respective product information documents with the Asthma Handbook, and notes where there is differences in the recommendations.

Table 3. Comparison table for age recommendations

Medicine	Product Information (PI) recommend ages	NAC 7th ed. Handbook recommend ages	Comments
Seretide MDI 50/25mcg	>=4 years	>=6 years	NAC more restrictive
Seretide MDI 125/25mcg	>=12 years	>=6 years	PI more restrictive
Seretide MDI 250/25mcg	>=12 years	>=6 years	PI more restrictive
Seretide DPI 100/50mcg	>=4 years	>=6 years	NAC more restrictive
Seretide DPI 250/50mcg	>=12 years	>=6 years	PI more restrictive
Seretide DPI 500/50mcg	>=12 years	>=6 years	PI more restrictive
Symbicort DPI 100/6mcg	>=12 years	>=12 years	Equal
Symbicort DPI 200/6mcg	>=12 years	>=12 years	Equal
Symbicort DPI 400/12mcg	>=18 years	>=12 years	PI more restrictive
Symbicort MDI 50/3mcg	>=12 years	>=12 years	Equal
Symbicort MDI 100/3mcg	>=12 years	>=12 years	Equal
Symbicort MDI 200/6mcg	>=12 years	>=12 years	Equal
Flutiform MDI 50/5mcg	>=12 years	>=12 years	Equal
Flutiform MDI 125/5mcg	>=12 years	>=12 years	Equal
Flutiform MDI 250/10 mcg	>=18 years	>=12 years	PI more restrictive

Sources: Product Information documents available on drug sponsor websites and the Australian Asthma Handbook

The PBAC were particularly concerned about the small number of very young children under the age of four years prescribed fixed dose combination ICS/LABA products, where there is currently no evidence available regarding their efficacy or safety. The PBAC also noted the inconsistencies in the age recommendations provided in the Australian Asthma Guidelines and the product information (PI) documents for these medicines. In some doses of Seretide® and Symbicort® the age restriction according to the PI is older than the age recommendation in the NAC Australian Asthma Handbook. The current PBS restrictions for Symbicort® and Flutiform® include a population criteria stating patients must be aged 12 years or over.

**PBAC Advice:** The PBAC recommended the restriction for fluticasone propionate/salmeterol xinafoate (Seretide®) include a population criteria stating patients must be aged 4 years or over.

Educational activities

4. *Prescriber education on any PBS restriction changes to Asthma medicines.*
5. *Request NPS MedicineWise conduct a major educational programme on diagnosis and management of childhood asthma.*

The PBAC noted the recent NPS MedicineWise continuing education programme for health professionals on “Asthma: optimising control in children” and acknowledged their value.

**PBAC Advice:** The PBAC endorsed further NPS MedicineWise educational programs targeting quality use of medicines in children with asthma.

6. *Request that prescribing software packages are changed to include alerts that appear when asthma medicines are prescribed outside of Product Information age groups.*

It was noted that one brand of prescribing software already includes an alert signal for fluticasone propionate/salmeterol xinafoate (Seretide®) which informs prescribers that this product is indicated for children 4 years or older. Such alerts were considered to be worthwhile.

**PBAC Advice:** The PBAC recommended the Pharmaceutical Benefits Division write to all the prescribing software vendors to request the inclusion of a signal to alert prescribers to the minimum age for which these medicines are registered and indicated. (4 years for Seretide® and 12 years for Symbicort® and Flutiform®).

Regulation

7. *Request the TGA work with sponsors to update both product and consumer medicine information on asthma medicines by including or updating indicated age groups.*

The PBAC has previously noted that the PI documents for older drugs may not have been updated for many years. The PBAC is aware the TGA is currently attempting to address this issue with sponsors for a number of products.

**PBAC Advice:** No further action required at this stage

8. *Request the Department of Human Services (DHS) Compliance Section conduct a targeted feedback and audit program focusing on the PBS use of LABA/ICS in children.*

The PBAC agreed with the views provided by stakeholders that some prescribers may not be aware they are prescribing outside the guidelines and PBS restrictions. PBAC considered that audit processes that alerted these prescribers to current asthma management guidelines and PBS restrictions could be an effective means of raising awareness and changing prescriber behaviour where it is most needed.

**PBAC Advice:** The PBAC requested the Pharmaceutical Benefits Division write to the Department of Human Services to request the PBS compliance area consider implementing compliance activities that raise prescriber awareness of the current National Asthma Council Guidelines and PBS restricted indications regarding use of fixed dose combination LABA/ICS in children.

9. *Include the date of birth of the patient on the prescription.*

The PBAC recalled that the inclusion of date of birth on all prescriptions had previously been a recommendation made by the Paediatric Medicines Advisory Group.

**PBAC Advice: The PBAC requested the Pharmaceutical Benefits Division follow up on the Paediatric Medicines Advisory Group recommendation to implement this previously, and provide advice to PBAC about the current status of this change.**

#### Process

10. *Submissions to the PBAC should provide a reasonable level of information on the use of medicines in children as a matter of routine.*

11. *The PBAC may also wish to write to the TGA to request that pharmaceutical companies provide paediatric evidence if listing a medicine for an illness which has a substantial proportion of paediatric patients.*

The PBAC considered that the current PBAC Submission Guidelines already request evidence which includes trial or study participants whose characteristics (age, gender, race etc) overlap with the population for whom subsidy is requested.

**PBAC Advice: No further action required at this stage**

#### Value

12. *The PBAC to reconsider the value of FDC use in childhood asthma.*

The PBAC discussed the difficulty in reviewing the cost effectiveness in children of different age groups where there is a paucity of data and suggested the preferred approach initially is to target improved prescribing as a means of achieving cost effective use of these medicines.

**PBAC Advice: No further action required at this stage**

13. *The PBAC is requested to consider the utilisation evidence on the use of FDCs in asthma of all ages.*

It is possible that there are similar issues in adult prescribing as observed in paediatric prescribing. The PBAC considered that the current value of the inhaled ICS/LABA products to be of some concern in all age groups. This may require re-evaluation in the future.

**PBAC Advice: The PBAC did not consider a post market review of asthma medications in all age groups was a priority at this stage.**

#### Research

14. *Write to NHMRC and/or Australian Centre for Asthma Monitoring to facilitate further Australian research to address current evidence gaps in asthma literature. The evidence gaps identified through the course of the review are:*

- a. The patient relevant outcomes and safety of ICS/LABA step up compared with other step up options including ICS/montelukast and higher dose ICS in children with asthma not adequately controlled on low dose ICS.
- b. Which patients are more at risk of down regulation of the beta receptors when on LABAs? Is there potential for genetic targeting to help direct the most appropriate step up option in children with asthma not adequately controlled on low dose ICS?

- c. The relative value of intermittent ICS, intermittent ICS/LABA and intermittent oral corticosteroids in the management of acute asthma exacerbations for all degrees of asthma severity, not just those uncontrolled while taking regular ICS for more than 28 days.
- d. The effectiveness and cost effectiveness of educational interventions on both prescribing practice and patient outcomes.
- e. Assessment of compliance with evidence based guideline recommendations.
- f. Evidence on the degree to which issues of patient compliance with any pharmacotherapy actually affect patient outcomes and treatment pathways.
- g. Interventions which promote shared decision making and the effectiveness of shared decision making on patient relevant outcomes.
- h. Healthcare provider interventions that effectively promote behavioural change.

**PBAC Advice: The PBAC requested the Pharmaceutical Benefits Division write to NH&MRC and the Australian Centre for Asthma Monitoring to inform them of the Review outcomes and raise the need for further research in the areas listed above**

Additional Options

- 15. *There are formulations of montelukast which are available in other countries for children six months to two years; the PBAC may wish to invite a submission from the sponsor for listing of this product.*
- 16. *Change the current montelukast listing from streamlined authority to a restricted benefit restriction on the PBS.*
- 17. *The PBAC to review current PBS restrictions for montelukast.*
- 18. *The PBAC could reconsider the listing of montelukast for use in people over 14 years.*

The PBAC discussed the potential merits of reconsidering and broadening current PBS restrictions for montelukast and noted the already increasing use of these medicines in Australian children. The PBAC noted the stakeholder comments on the options regarding the alternate use of montelukast in the report but also noted the lack of evidence available on this medicine. Should the sponsor of montelukast wish to submit new data and revised age groups, the PBAC will consider any such submission.

**PBAC Advice: No further action required.**