NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Technology Appraisals and Guidance Information Services

Static List Review (SLR) report

Title and TA publication number of static topic:	**TA10; Inhaler systems (devices) in children under the age of 5 years with chronic asthma, and TA38; Inhaler devices for routine treatment of chronic asthma in older children (5-15 years)**
Final decision:	The guidance will remain on the 'static guidance list'.

Publication date:	TA10 – August 2000 TA38 – March 2002
1. Date added to static list:	June 2005
2. Current guidance:	**TA10** 1.1 For children under the age of 5 years with chronic stable asthma both corticosteroids and bronchodilator therapy should be routinely delivered by pressurised metered dose inhaler (pMDI) and spacer system, with a facemask where necessary. 1.2 Where this combination is not clinically effective for the child and depending on the child's condition, nebulised therapy may be considered and in the case of children

	aged 3 to 5 years, a dry powder inhaler (DPI) may also be considered. 1.3 Choice of device to be made within the pMDI and spacer range should be primarily governed by specific individual need and the likelihood of good compliance. Once these factors have been taken into account, choice should be made on the basis of cost minimisation. **TA38** 1.1 It is recommended that in addition to therapeutic need (including chosen drug and dose), the following factors be taken into account when choosing inhaler devices for individual children with chronic asthma: • the ability of the child to develop and maintain an effective technique with the specific device • the suitability of a device for the child's and carer's lifestyles, considering factors such as portability and convenience • the child's preference for and willingness to use a particular device. 1.2 The general recommendations in 1.1 should be taken into account when considering the following specific guidance: 1.2.1 A press-and-breathe pressurised metered dose inhaler (pMDI) and suitable spacer device is recommended as the first-line choice for the delivery of inhaled corticosteroids as part of regular planned daily therapy, with the aim of maximising benefits of preventive therapy in attaining good asthma control, and minimising potential systemic absorption. Where clinicians believe that an individual child's adherence to the press-and-breathe pMDI and spacer combination is likely to be so poor as to undermine effective asthma control, other alternative devices (taking account of the factors outlined in 1.1 and evidence of equivalence of clinical effectiveness) should be considered, bearing

	in mind the need to minimise the risks of systemic absorption of corticosteroids. 1.2.2 In the case of other inhaled drugs, primarily bronchodilators, it is recommended that a wider range of devices be considered to take account of their more frequent spontaneous use, the greater need for portability, and the clear feedback that symptom response provides to the device user. In such circumstances the factors outlined in 1.1 are likely to be of greater importance in choosing a device. 1.3 Where more than one device satisfies the considerations outlined above in a particular child, it is recommended that the device with the lowest overall cost (taking into account daily required dose and product price per dose) should be chosen. • On selection of an inhaler device, it is important that consideration is given to other aspects of asthma care that influence the effective delivery of inhaled therapy, including: • individual practical training in the use of the specific device • monitoring of effective inhaler technique and adherence to therapy • regular (i.e. no less than annual) review of inhaler needs, which may change over time with increasing age.
3. Research recommendations from original guidance:	**TA10** 6.1 At present there is insufficient evidence regarding the most clinically and cost effective spacer (e.g. small or large volume). This is reflected in the current lack of standardisation and variations in the usage of these devices. Further research in this area should be carried out in relation to optimising the reproducibility, consistency and acceptability of these delivery systems as well as their overall clinical and cost effectiveness.

	6.2 Well conducted community based trials in the management of asthma in young children and studies to investigate factors determining compliance (including health education and the acceptability of devices) in this group of children would enhance the future evidence base. **TA38** 6.1 Given the scarcity of robust research comparing inhaler devices (including spacers) in older children, decision-making is likely to be substantially improved by adequately powered RCT equivalence studies. Ideally, these would include: 1. treatment of a full spectrum of chronic asthma severity in generalisable clinical settings 2. qualitative assessment of children's experience of devices and factors influencing adherence 3. examination of clinically relevant outcome measures (e.g. symptoms, activities, time away from school) rather than short-term measures of lung function 4. examination of differences in resource use 5. epidemiological investigation of the determinants (e.g. social factors) of adherence, effectiveness and cost effectiveness of treatment. 6.2 The Institute acknowledges that such studies would require large numbers of participants and present a significant challenge to manufacturers and other researchers. A parallel or alternative approach would be to undertake epidemiological and qualitative research on the factors influencing adherence and competence. 6.3 Given that none of the currently available inhaler devices are completely satisfactory for children, manufacturers should consider research into novel

	inhalers that can be used effectively with greater ease by children.
4. Current cost of technology/ technologies:	Able Spacer (spacer device) £4.20; AeroChamber Plus (spacer device) £11.34; Babyhaler (spacer device) £11.34; Optichamber (spacer device) £4.28; Vortex Spacer (spacer device) £6.07; Pocket Chamber (spacer device) £4.18; Volumatic (spacer inhaler) £2.81. Source: BNF63 (March 2012).
5. Cost information from the TA (if available):	No reference to cost in TA10. TA38: Annual costs of spacer devices available on NHS prescription range from £4.28 to £8.56. Cost of inhaler devices in the delivery of one puff of salbutamol are: press and breath pMDI, £3.14; breath activated pMDI, £10.99; DPI, £11.53.
6. Alternative manufacturers:	None.
7. Changes to the original indication:	None.
8. New relevant trials:	Nothing found.
9. Relevant NICE guidance (published or in progress\):	As of July 2012: TA201 Technology appraisal: Omalizumab for the treatment of severe persistent allergic asthma in children aged 6 to 11 years. Issued: October 2010 (replaced by TA278) TA138 Technology appraisal. Inhaled corticosteroids for the treatment of chronic asthma in adults and in children aged 12 years and over. Issued: March 2008. Review date: November 2012. TA133 Technology appraisal. Omalizumab for severe persistent allergic asthma. Issued: November 2007. Reviewed: November (replaced by TA278). TA131 Technology appraisal Inhaled corticosteroids for the treatment of chronic asthma

	in children under the age of 12 years. Issued: November 2007. TA278 Technology Appraisal: Omalizumab for the treatment of severe persistent allergic asthma in children aged 6 and over and adults (review of TA133 and TA201). Issued April 2013
10. Relevant safety issues:	Nothing found.
11. Any other additional relevant information or comments:	BTS/SIGN Asthma Guideline: 2011 (Update of the 2008 edition) – recommendations are unchanged from 2004 edition referred to in 2005 RPP for TA10 and TA38. Global Initiative for Asthma (GINA) (2009) Global Strategy for the Diagnosis and Management of Asthma in Children 5 Years and Younger – recommendation on inhalers (page 5) matches that given in TA 10. The Cochrane Collaboration (2009) Pressurised-metered dose inhalers versus other hand-held inhalation devices for the delivery of inhaled corticosteroid therapy in children with non-acute asthma – Intervention protocol. No publication date for final review.
12. Technical Lead comments and recommendation:	Searches in the clinical trials data base using term 'asthma' and children joined by Boolean operative AND resulted in 78 hits. We followed the same inclusion strategy as the original appraisals; that is studies comparing the same drug at an equivalent dose in different devices, and shortlisted 6 trials for further consideration. All trials were reported to be completed but no published results could be identified. Three trials (NCT01360021, NCT00862394 and NCT00163436) compared the efficacy of different inhaler devices in a population of 12 years and above and were considered to have limited relevance in the review decision for these appraisals. One trial (NCT00530062) compared single-dose effectiveness of albuterol-HFA-BAI (breath activated inhaler) and albuterol-HFA-MDI (metered dose inhaler) in asthmatics with poor inhaler coordinating abilities. The included population were between 7 to 70 years of age. It is not clear whether a subgroup analysis for younger patients (7-15

	years) was planned or not. A phase 4 single group pharmacokinetic study in children 1-18 yr, with adequately controlled persistent asthma was carried out to determine the effect of age and device on delivery of HFA-Fluticasone Propionate (NCT00308932). In this study, 60 children with well-controlled persistent asthma received two actuations of 110 mcg twice daily for at least 3 days. Blood sample were collected one hour after the last dose when 100% adherence was documented by electronic monitor. Five groups of equal size (n=12) were studied: 1) 12-18 yr by actuator alone; 2) 5-9 yr by actuator alone; 3) 5-9 yr by antistatic VHC/mouthpiece; 4) 5-9 yr by antistatic VHC/mask and 5) 1-4 yr by antistatic VHC/mask. Fluticasone plasma concentration between groups was compared. The study has been reported to be completed results could not be identified. Another very small open label phase 4 study (NCT00307970) with estimated enrolment of 12 children of 1-6 years old who have adequately controlled persistent asthma and currently receiving fluticasone propionate (a corticosteroid) delivered by CFC MDI attached to valved-holding chamber/mask. This study compared lung delivery of drug by conventional chamber/mask device to anti-static chamber/mask device. The study has been reported to be completed but results are not available. In summary no published study was identified which could have an impact the decision regarding review of the previous TA guidance (10 and 138). A few unpublished trials were identified which have very limited relevance to the guidance. There has been no change in the evidence to warrant a review proposal, but there is an ongoing Cochrane review on pressurised-metered dose inhalers versus other hand-held inhalation devices for the delivery of inhaled corticosteroid therapy in children, the result of which may affect the recommendations in the future.

Appendix 1 – explanation of options

Options	Consequence	Selected – 'Yes/No'
The guidance will remain on the 'static guidance list'	The guidance will remain in place, in its current form, unless NICE becomes aware of substantive information which would make it reconsider. Literature searches are carried out every 5 years to check whether any of the Appraisals on the static list should be flagged for review.	Yes
The decision to review the guidance will be deferred to specify date or trial	NICE will consider whether a review is necessary at the specified date. NICE will actively monitor the evidence available to ascertain when a consideration of a review is more suitable.	
A full consideration of a review will be carried out through the Review Proposal Process	There is evidence that could warrant a review of the guidance. NICE will schedule a consideration of a review, including a consultation with relevant consultees and commentators.	
The guidance will be withdrawn	The guidance is no longer relevant and an update of the existing recommendations would not add value to the NHS. NICE will schedule a consideration of a review, including a consultation with relevant consultees and commentators.	

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