NICE National Institute for Health and Care Excellence

NICE guidance

Inhaled corticosteroids for the treatment of chronic asthma in children under the age of 12 years

Technology appraisal guidance
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Contents

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1 Guidance

This guidance should be read in conjunction with Inhaler devices for routine treatment of chronic asthma in older children (aged 5–15 years), NICE technology appraisal guidance 38, and Guidance on the use of inhaler systems (devices) in children under the age of 5 years with chronic asthma, NICE technology appraisal guidance 10. The future discontinuation of CFC-containing inhaler devices will affect the range of devices available but does not affect the guidance.

1.1 For children under the age of 12 years with chronic asthma in whom treatment with an inhaled corticosteroid (ICS) is considered appropriate, the least costly product that is suitable for an individual child (taking into consideration technology appraisal guidance 38 and 10), within its marketing authorisation, is recommended.

1.2 For children under the age of 12 years with chronic asthma in whom treatment with an ICS and long-acting beta-2 agonist (LABA) is considered appropriate, the following apply.

- The use of a combination device within its marketing authorisation is recommended as an option.
- The decision to use a combination device or the two agents in separate devices should be made on an individual basis, taking into consideration therapeutic need and the likelihood of treatment adherence.
- If a combination device is chosen then the least costly device that is suitable for the individual child is recommended.

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2 Clinical need and practice

2.1 Asthma is a chronic condition that causes symptoms such as shortness of breath (dyspnoea), chest tightness, wheezing, sputum production and cough associated with variable airflow obstruction and airway hyper-responsiveness. There are approximately 5.2 million people with asthma in the UK, nearly 1 million of whom are children. Asthma is the most common chronic disease in children, with a prevalence of between 17% and 23%.

2.2 Diagnosing asthma in children requires excluding other causes of recurrent respiratory symptoms. Persistent respiratory symptoms between acute respiratory attacks are suggestive of asthma, and a personal or family history of atopic conditions such as eczema or hayfever are also linked to asthma. If it is possible to perform lung function tests, bronchodilator responsiveness, peak expiratory flow (PEF) variability and bronchial hyper-reactivity testing may be used to confirm the diagnosis. In addition, allergy testing may be helpful in seeking causal factors.

2.3 Asthma attacks vary in frequency and severity. Many children with asthma are symptom-free most of the time, with occasional episodes of shortness of breath. Some children frequently cough and wheeze and may have severe attacks during viral infections, after exercise, or after exposure to allergens or irritants, including cigarette smoke.

2.4 Although mortality as a result of asthma is rare (38 deaths in children younger than 14 years were reported in the UK in 2004), the condition can have a significant impact on quality of life. One study in Australia suggested that one in five children with asthma did not ride a bike, play at school or play with animals, and one in three did not participate in organised sports. Other effects of asthma can include school absence and night disturbances.

2.5 The aim of asthma management is to control the symptoms, prevent exacerbations and – in school-aged children – to achieve the best possible lung function. Pharmacological management includes drugs

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such as inhaled corticosteroids (ICSs), and short- and long-acting beta-2 agonists (SABAs/LABAs). The latter should be used only in combination with an ICS. A large proportion of children with asthma are managed in primary care, often within nurse-led clinics. Community pharmacists may also play a role in educating children and their carers. General practitioners are encouraged to perform annual reviews on all registered people with asthma as part of the new General Medical Services contract and the Quality and Outcomes Framework in England.

2.6 Current British guidelines from the British Thoracic Society (BTS) and Scottish Intercollegiate Guidelines Network (SIGN) for the management of asthma recommend a stepwise approach to treatment in both adults and children[1]. Treatment is started at the step most appropriate to the initial severity of the asthma, with the aim of achieving early control of symptoms and optimising respiratory function. Control is maintained by stepping up treatment as necessary and stepping down when control is good.

2.7 Mild intermittent asthma (step 1) is treated with inhaled SABAs, as required. The introduction of regular preventer therapy with ICSs (step 2) should be considered when a child has had exacerbations of asthma in the previous 2 years, is using inhaled SABAs three times a week or more, is symptomatic three times a week or more, or is waking at night once a week because of asthma. In children who cannot take an ICS, a leukotriene receptor antagonist is recommended.

2.8 There is no precise ICS dose threshold for moving to step 3 (add-on therapy), in which a third drug is introduced. However, in children aged 5–12 years, the guidelines recommend a trial of add-on therapy before increasing the daily dose of ICS above the equivalent of 400 micrograms of beclometasone dipropionate. The first choice for add-on therapy in children older than 5 years is the addition of a LABA. In children aged 2–5 years, a leukotriene receptor antagonist should be considered. For children younger than 2 years, consideration should be given to referral to a respiratory paediatrician.

2.9 At step 4, further interventions may be considered if control remains inadequate. For children aged 5–12 years this may include increasing the

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daily dose of ICS to the equivalent of 800 micrograms of beclometasone dipropionate, or adding leukotriene receptor antagonists or theophyllines. For children younger than 5 years, step 4 is referral to a respiratory paediatrician (if not already from step 3). At step 5 (for children aged 5–12 years only), continuous or frequent courses of oral corticosteroids are introduced. Before proceeding to this step, referral to a respiratory paediatrician should be considered. The majority of children with asthma are treated at steps 1, 2 or 3, with approximately 10% treated at either step 4 or 5.

2.10 Two important components of asthma management are maintaining adherence to medication and optimising inhaler technique. Studies of adults have suggested that the recommended doses of medication may only be taken on 20% to 73% of days, with average adherence (measured by the ratio of doses taken to doses prescribed) ranging from 63% to 92%. Records from the General Practice Research Database found that, over a 10-year period, only 42% of people obtained a repeat prescription for ICSs within the expected timeframe of the preceding prescription. With regard to inhaler technique, the ability to use an inhaler correctly is important for ensuring the delivery of the desired dose of a drug to the correct part of the lungs. Studies have reported that physicians assess inhaler technique as 'good' in 5–86% of adults. In children, this may be an even greater problem, with repeated education needed to make sure adequate technique is maintained.

2.11 NICE guidance on asthma devices for children aged 5–15 years (NICE technology appraisal guidance 38) recommends that ICSs are delivered using a press-and-breathe pressurised metered-dose inhaler (pMDI) with an appropriate spacer device. However, if a healthcare professional believes a child will be unable to use a press-and-breathe inhaler, other devices should be considered. The guidance also recommends that the child's therapeutic need and their ability and willingness to use a particular inhaler should be taken into account when choosing an inhaler. Guidance for children younger than 5 years (NICE technology appraisal guidance 10) also recommends the use of a pMDI and spacer device, with a face mask if necessary. Again, the choice of a device should take into account the needs of the child and the likelihood of good compliance.

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[1] The British Thoracic Society and Scottish Intercollegiate Guidelines Network (2003; updated 2005) British Guideline on the Management of Asthma: a national clinical guideline. SIGN Guideline No. 63. Edinburgh: Scottish Intercollegiate Guidelines Network.

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3 The technologies

3.1 ICSs suppress inflammation in the lungs and are recommended for prophylactic treatment of asthma. In the UK, three ICSs are licensed for use in children: beclometasone dipropionate, budesonide and fluticasone propionate. ICSs are available in both pMDIs and dry powder inhalers (DPIs). pMDIs can either be press-and-breathe or breath actuated, but both contain the drug as either a suspension in a carrier liquid or a solution delivered using a chlorofluorocarbon (CFC) or hydrofluoroalkane (HFA) propellant. It is expected that those using CFC propellants will be phased out in line with the Montreal Protocol[2]. Press-and-breathe pMDIs can be used with spacer devices that enable the drug to be inhaled by breathing normally, thereby removing some of the difficulties with coordinating pressing and inhaling. Spacers also reduce oral deposition of the drug, so they may reduce the likelihood of local adverse effects of corticosteroids such as oral candidiasis. DPIs require less coordination to use, but they require a high flow rate of air through the device to ensure that the drug reaches the lungs.

3.2 Beclometasone dipropionate is licensed for use in children in 10 different products. Three of these products are press-and-breathe pMDIs using a CFC propellant (Beclazone, IVAX Pharmaceuticals; Becotide, GlaxoSmithKline [to be discontinued second quarter 2007]; Filair, 3M Health Care), one of the products is a press-and-breathe pMDI using a HFA propellant (Clenil Modulite, Trinity Chiesi), two products are breath-actuated pMDIs (Aerobec Autohaler, 3M Health Care; Beclazone Easi Breathe, IVAX Pharmaceuticals), and four products are DPIs (Asmabec Clickhaler, UCB; Becodisks Diskhaler, GlaxoSmithKline; Cyclocaps, TEVA; Pulvinal, Trinity Chiesi). The marketing authorisation for beclometasone dipropionate differs depending on the product in which it is available and, within a particular product, not all dose strengths available are recommended for children. The maximum licensed dosage is 400 micrograms per day with no specified lower age limit. Pulvinal and Asmabec are not licensed for children younger than 6 years.

3.3 Budesonide is licensed for use in children in five different products. Two of these products are press-and-breathe pMDIs using a CFC propellant

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(Pulmicort inhaler, AstraZeneca; Pulmicort LS, AstraZeneca) and three of these products are DPIs (Easyhaler, Ranbaxy; Novolizer, Meda Pharmaceuticals; Pulmicort Turbohaler, AstraZeneca). The marketing authorisation for budesonide differs depending on the product in which it is available and, within a particular product, not all dose strengths available are recommended for children. The maximum licensed dosage is 800 micrograms per day. No lower age limit is specified in the marketing authorisation for the three Pulmicort devices, while the lower age limit for the other two products is 6 years.

3.4 Fluticasone propionate is licensed for children in three different products. One of these products is a press-and-breathe pMDI using a HFA propellant (Flixotide Evohaler, GlaxoSmithKline) and two of these products are DPIs (Flixotide Accuhaler, GlaxoSmithKline; Flixotide Diskhaler, GlaxoSmithKline). The marketing authorisation for fluticasone propionate differs depending on the product in which it is available and, within a particular product, not all dose strengths available are recommended for children. The maximum licensed dosage is 400 micrograms per day and none of the products is licensed for the treatment of children younger than 4 years. Fluticasone propionate is considered nominally clinically equivalent to beclometasone dipropionate and budesonide at half the dose (that is, a ratio of 1:2).

3.5 ICSs are also available in combination with a LABA in a single combination device. Budesonide is available in combination with formoterol fumarate in a DPI (Symbicort Turbohaler, AstraZeneca), and fluticasone propionate is available in combination with salmeterol as a pMDI with a HFA propellant (Seretide Evohaler, GlaxoSmithKline) and as a DPI (Seretide Accuhaler, GlaxoSmithKline). The marketing authorisations for combination devices containing corticosteroids and LABAs differ depending on the product in which they are available, but for all products only the lowest dose strength inhalers are recommended for children, and these are not recommended for individuals with severe asthma. Symbicort is licensed for use in children aged 6 years and older with a maximum recommended dosage of 400/24 micrograms (budesonide/formoterol fumarate) per day. Seretide devices are licensed for use in children aged 4 years and older with a maximum recommended dosage of 200/100 micrograms (fluticasone propionate/salmeterol) per day. For

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both Symbicort and Seretide, it is recommended that patients are regularly reassessed by their prescriber so that dosing is titrated to the lowest dose at which effective control of symptoms is maintained. The Seretide Evohaler device is the only combination device currently available as a pMDI, and therefore the only one which can be used with a spacer.

3.6 The side effects of ICSs may be local (following deposition in the upper airways) or systemic (following absorption into the bloodstream). Local adverse effects may include dysphonia, oropharyngeal candidiasis, cough, throat irritation and reflex bronchospasm. Local adverse effects can be minimised by optimising inhaler technique and using a spacer with the inhaler device. Systemic adverse effects may include suppression of the hypothalamic-pituitary-adrenal axis, osteoporosis, skin thinning and easy bruising, cataract formation and glaucoma, and growth retardation in children and adolescents. Systemic adverse effects tend to be associated with higher doses of corticosteroids and can differ depending on both the drug and the delivery system. For full details of side effects and contraindications, see the summaries of product characteristics.

3.7 The costs of ICSs vary depending on the product. The costs also vary depending on the dose strength of the inhaler used (for example, 50 micrograms, 100 micrograms or 200 micrograms) and how the recommended dose is achieved (for example, 200 micrograms could be achieved by either 4 x 50 micrograms, 2 x 100 micrograms or more rarely 1 x 200 micrograms). The annual cost of 200 micrograms beclometasone dipropionate equivalent per day ranges from approximately £10 (£25 following the discontinuation of Becotide devices) to £70. The corresponding costs for budesonide range from approximately £35 to £70 and, for fluticasone propionate, they range from approximately £35 to £90. The annual costs for 200 micrograms beclometasone dipropionate equivalent per day in a combination device are £201 per year for Symbicort Turbohaler, £190 per year for Seretide Accuhaler and £115 for Seretide Evohaler. Costs may vary in different settings because of negotiated procurement discounts.

[2] The Vienna Convention for the Protection of the Ozone Layer and The Montreal

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Protocol on Substances that Deplete the Ozone Layer (2003) The Montreal Protocol on Substances that Deplete the Ozone Layer. Kenya: United Nations Environment Programme.

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4 Evidence and interpretation

The Appraisal Committee (appendix A) considered evidence from a number of sources (appendix B).

4.1 Clinical effectiveness

4.1.1 Submissions were received from four manufacturers. The submissions from Meda Pharmaceuticals and Trinity Chiesi both compared their products with other products delivering the same drug. Such studies were excluded from the systematic review carried out by the Assessment Group because they were outside the scope of the appraisal. The submissions from GlaxoSmithKline and AstraZeneca also focused on their own products but compared these with other available ICSs. However, in both of these submissions, the inclusion criteria differed from those of the Assessment Group, with the result that some of the studies included in the assessment report were excluded from the manufacturers' submissions and vice versa.

4.1.2 The Assessment Group identified evidence on the use of ICSs in six scenarios.

- ICSs were compared with each other at low dose (defined as 200–400 micrograms beclometasone dipropionate or equivalent).
- ICSs were compared with each other at high dose (defined as greater than 400 micrograms beclometasone dipropionate or equivalent).
- Increasing the dose of ICS was compared with adding a LABA to the initial dose using a combination device.
- Remaining on the same dose of ICS was compared with adding a LABA using a combination device.
- ICS/LABA combination devices were compared with the same drugs delivered in separate devices.

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- Different ICS/LABA combination devices were compared with each other.

This section summarises the evidence for each of these scenarios, drawing on evidence included in the assessment report and the manufacturers' submissions.

Comparisons of low-dose corticosteroids

4.1.3 The Assessment Group identified five randomised controlled trials (RCTs) in children that compared ICSs at low doses (200–400 micrograms beclometasone dipropionate or equivalent); one compared beclometasone dipropionate with budesonide, two compared fluticasone propionate with budesonide, and two compared fluticasone propionate with beclometasone dipropionate. The primary aim of three of the studies was to look at differences in adverse effects between the treatments; one of the studies was powered to detect differences in lung function; and one examined whether the two corticosteroids could be considered equipotent.

4.1.4 Reporting of the study data was incomplete in some studies and inconsistent across the different studies. Because of the differences between the studies, they could not be meta-analysed. None of the studies reported any statistically significant differences between treatments in the outcome measures of lung function, symptoms, use of rescue medication, exacerbations and adverse events. Other RCTs were identified in consultees' submissions but were excluded from the Assessments Group's systematic review. In general, these studies supported the conclusions of the studies included in the assessment report, although three studies were identified in the submission from GlaxoSmithKline that suggested a statistically significant difference favouring the use of fluticasone propionate for growth outcomes when compared with budesonide and beclometasone dipropionate. However, this difference was not demonstrated in the low-dose studies included in the assessment report.

Comparisons of high-dose corticosteroids

4.1.5 The Assessment Group identified five RCTs in children that compared

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nominally clinically equivalent doses of ICSs when given at high doses (greater than 400 micrograms beclometasone dipropionate or equivalent); one compared beclometasone dipropionate with budesonide, two compared fluticasone propionate with beclometasone dipropionate, and two compared fluticasone propionate with budesonide. The primary aims were to examine differences in adverse effects (one study) and to examine differences in lung function (three studies). In the fifth study, the primary aim was not reported. The studies were not meta-analysed because they were not considered comparable. In a number of these studies, the doses of ICSs were above the licensed doses for children.

4.1.6 One study identified a statistically significant difference in morning peak expiratory flow rate (PEFR) favouring fluticasone propionate compared with budesonide; two studies identified a statistically significant difference in growth rates favouring fluticasone propionate compared with budesonide; and one study identified a statistically significant difference in cortisol excretion favouring budesonide when compared with beclometasone dipropionate. No further statistically significant differences between ICSs were identified for measures of lung function, symptoms, use of rescue medication, exacerbations or adverse effects.

Comparisons of ICS/LABA and higher dose ICS

4.1.7 One RCT was included in the assessment report that compared budesonide/formoterol fumarate 80/4.5 micrograms daily plus SABA, as required, with higher dose budesonide 320 micrograms daily plus SABA, as required. The primary outcome for this study was time to first severe exacerbation. Of the study participants, 12% (n = 341) were children aged 4–11 years for whom only growth and plasma cortisol outcomes were reported separately from the adult participants. For the population as a whole, no statistically significant differences were reported for the primary study outcome. However, the study identified statistically significant higher growth rates in children receiving budesonide/formoterol fumarate.

4.1.8 No further studies that compared budesonide/formoterol fumarate in a combination device with a higher dose of budesonide alone were

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identified in consultees' submissions. One unpublished RCT was included in the submission from GlaxoSmithKline, which compared fluticasone propionate/salmeterol (as xinafoate) 200/100 micrograms per day with fluticasone propionate 400 micrograms per day. The primary outcome of this study was the combined percentage of symptom-free days and nights. No statistically significant differences between treatments were identified for measures of lung function, symptoms, use of rescue medication, exacerbations or adverse effects.

Comparisons of ICS/LABA and same-dose ICS

4.1.9 The assessment report identified two RCTs that compared the use of ICS and LABA treatment in a combination device with continuing the same dose of ICS alone. The clinical relevance of this situation is limited, because a person whose asthma is not controlled on an ICS alone would either have the dose increased or a LABA added.

4.1.10 One study compared fluticasone propionate/salmeterol 200/100 micrograms per day with fluticasone propionate 200 micrograms per day. The primary aim of this study was to compare the safety profiles of the two treatments. The second study compared budesonide/formoterol fumarate 400/18 micrograms per day with budesonide 400 micrograms per day. The primary outcome of this study was morning and evening PEFR. The studies were not meta-analysed because they were not comparable. The study comparing fluticasone propionate/salmeterol with fluticasone propionate reported safety outcomes, however it stated that the group of participants receiving the fluticasone propionate/salmeterol combination showed greater improvements in lung function and fewer exacerbations than the group receiving fluticasone propionate alone (no significance tests were reported). The study of budesonide/formoterol fumarate identified a statistically significant difference across measures of lung function (forced expiratory volume [FEV], morning and evening PEFR) favouring the use of budesonide/formoterol fumarate over budesonide alone. No other statistically significant differences were identified for lung function, symptoms, use of rescue medication and adverse effects. Exacerbation rates were not reported in the published paper.

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4.1.11 Two further studies were included in manufacturers' submissions, but these were excluded from the review by the Assessment Group. The first compared fluticasone propionate 200 micrograms per day with fluticasone propionate/salmeterol 200/100 micrograms per day. This study identified no statistically significant differences for lung function, symptoms, use of rescue medication and adverse effects. A second study compared budesonide 400 micrograms per day with budesonide/formoterol fumarate 400/18 micrograms per day. This study identified a statistically significant difference favouring the budesonide/formoterol fumarate group for lung function outcomes, but not for other measures of symptoms, use of rescue medication or adverse events. Exacerbation rates were not reported in the published paper.

Comparisons of ICS/LABA administered in separate or combination devices

4.1.12 One RCT was included in the assessment report that compared fluticasone propionate/salmeterol 200/100 micrograms per day delivered using either a combination device or two separate devices. The aim of the study was to compare the safety and efficacy of the two methods of delivery. No statistically significant differences were identified for outcomes in lung function, symptoms, use of rescue medication and adverse effects. Exacerbation rates were not reported.

4.1.13 A second RCT was included in the AstraZeneca submission, but it was published after the cut-off date for inclusion in the assessment report. This study compared budesonide/formoterol fumarate delivered using either a combination device or separate devices. The primary outcome for the study was morning PEFR. The study identified no statistically significant differences in lung function, symptoms, use of rescue medication or adverse effects. Exacerbation rates were not reported in the published paper. Because these studies used a double-blind double-dummy design – the patients taking a combination device also received a placebo dummy – they may not capture the benefits of improved treatment adherence with a combination device.

Comparisons of budesonide/formoterol fumarate and fluticasone

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propionate/salmeterol combination devices

4.1.14 No RCTs were identified in either the assessment report or in consultees' submissions that compared budesonide/formoterol fumarate with fluticasone propionate/salmeterol.

4.2 Cost effectiveness

4.2.1 Submissions were received from four manufacturers and each was specific to the manufacturer's product(s). The submissions from Trinity Chiesi and Meda Pharmaceuticals specifically compared their products with devices containing the same drug, whereas the submissions from AstraZeneca and GlaxoSmithKline compared their products with different ICSs. All submissions included some analyses that assumed equal efficacy between drugs and products and compared the costs of different products. Two of the submissions also included cost–utility analyses (AstraZeneca and GlaxoSmithKline). The Assessment Group did not model the cost–utility of ICSs because of incomplete trial evidence; it carried out cost-comparison analyses if it was considered appropriate to assume equal efficacy between the drugs, and it otherwise conducted exploratory cost-offset analyses.

4.2.2 Neither the Assessment Group nor consultees identified any existing published cost-effectiveness studies with the relevant comparator for the population of children younger than 12 years with chronic asthma.

AstraZeneca submission

4.2.3 The submission from AstraZeneca included analyses to support the use of the AstraZeneca products Pulmicort (budesonide delivered by either a pMDI or a DPI) and Symbicort (budesonide/formoterol fumarate delivered by a DPI). The cost–utility of Symbicort was modelled firstly as a comparison between fixed dose and adjusted maintenance dosing. Secondly, Symbicort fixed dose was modelled in comparison with remaining on the same dose of ICS alone or adding a LABA, and thirdly in comparison with providing an ICS and a LABA in separate devices. Cost–utility analyses were not carried out comparing the different ICSs or comparing Seretide and Symbicort. Instead, analyses of costs assuming

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equal efficacy were completed.

4.2.4 The submission included a Markov-type model designed to capture the differences in exacerbations between the different treatments and the difference in time spent without exacerbations. The model had four health states: non-exacerbation, mild exacerbation, severe exacerbation and treatment change. Treatment changes were modelled in line with BTS/SIGN guidelines. The model had a cycle length of 4 weeks and a time horizon of 1 year. Transition probabilities were based on data from clinical trials. EuroQol-5D (EQ-5D) was used to produce utility values for children with asthma.

4.2.5 With regard to Pulmicort, the submission concluded that the costs of Pulmicort, either as a DPI or a pMDI, were within the range of costs of other corticosteroids. With regard to Symbicort, the submission concluded that fixed-dose Symbicort was dominated by Symbicort adjusted maintenance dosing. Fixed-dose Symbicort was also dominated by remaining on the same high-dose ICS alone (Symbicort was associated with greater costs and fewer quality-adjusted life years [QALYs]) and by Seretide (equal efficacy was assumed between the combination devices and Symbicort was associated with greater costs). Symbicort was dominant over ICS and LABA delivered using separate devices (it was associated with equal efficacy and lower costs).

GlaxoSmithKline submission

4.2.6 The submission from GlaxoSmithKline included analyses to support the use of three GlaxoSmithKline products: Becotide (beclometasone dipropionate delivered by a pMDI), Flixotide (fluticasone propionate delivered by either a DPI or a HFA-propelled pMDI) and Seretide (containing fluticasone propionate and salmeterol delivered by either a DPI or a HFA-propelled pMDI). The submission modelled the cost–utility of Seretide in comparison with the same dose of ICS, a higher dose of ICS, and the same dose of ICS and a LABA delivered using separate devices. Cost–utility analyses were not carried out comparing the different ICSs or comparing Seretide and Symbicort. Instead, analyses of costs assuming equal efficacy were completed.

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4.2.7 A common model was developed for both adults and children. The model had two states, in which people with asthma could be either with or without symptoms. The model was not a disease-progression model and did not involve transitions between the two health states. Effectiveness data for symptom-free days were taken from clinical trial data. Utility values, sourced from adults enrolled in the Gaining Optimal Asthma controL (GOAL) study, were 0.97 for the 'symptom-free' and 0.85 for 'with symptoms' health states.

4.2.8 The estimates of incremental cost effectiveness for Seretide compared with using the same dose of fluticasone propionate alone were £31,388 (using Evohaler cost) and £65,957 (using Accuhaler cost) per QALY gained. When Seretide was compared with a higher dose of fluticasone propionate alone, the estimates of incremental cost effectiveness were £15,739 and £63,736 per QALY gained, using Evohaler and Accuhaler costs, respectively. When comparing Seretide with the same dose of ICS and a LABA in separate devices, Seretide was dominant (that is, it was associated with a greater effect and was less costly). When the costs of Seretide and Symbicort were compared, Seretide was less costly (assuming equal effect).

Meda Pharmaceuticals submission

4.2.9 The submission from Meda Pharmaceuticals included a cost-minimisation analysis for Novolizer (budesonide delivered by a DPI) compared with Pulmicort Turbohaler (the main budesonide DPI competitor). The submission calculated the costs of providing both devices at 400 micrograms per day over a 1-year period. The annual cost of Novolizer was estimated at £75.28 compared with £135.05 for Turbohaler, making a saving per person of £59.77. The submission concluded that, if all people (both adults and children) with asthma currently on Turbohaler were switched to Novolizer, there would be cost savings to the NHS of £3.7 million per year.

Trinity Chiesi submission

4.2.10 The submission from Trinity Chiesi included a cost-minimisation analysis for Clenil Modulite (beclometasone dipropionate delivered by a CFC-free

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pMDI). The submission was in the context of the Montreal Protocol and the likely removal of CFC-containing devices such as Becotide (beclometasone dipropionate delivered by a pMDI). It calculated the annual cost of Clenil Modulite and two other commonly used non-CFC-containing devices, Asmabec and Becodisks. It compared the costs for these devices with those of Becotide at both 200 micrograms and 400 micrograms per day. Data were provided that demonstrated clinical equivalence with Becotide, but clinical equivalence was assumed for the other two products. The annual cost of Becotide 200 micrograms per day was calculated to be £10.18. This was compared with annual costs of £28.18 for Clenil Modulite, £35.81 for Asmabec and £73.00 for Becodisks. The annual costs for 400 micrograms per day were £29.71 for Becotide compared with £61.43 for Clenil Modulite, £71.61 for Asmabec and £139.13 for Becodisks. The submission concluded that, after the removal of CFC-containing devices, Clenil Modulite may be cost saving compared with alternatives, although overall the cost to the NHS would increase.

The Assessment Group economic assessment

4.2.11 To compare the different ICSs, the Assessment Group calculated the mean annual treatment cost per child for each specific preparation. The doses of each ICS were calculated based on 200 micrograms per day, 400 micrograms per day and 800 micrograms per day of CFC-containing beclometasone dipropionate (or equivalent). For each of the above, an unweighted average (based on the number of products) and a weighted average (based on annual quantities sold) were calculated. Products were categorised as pMDI with CFC, pMDI with HFA, or DPI, with separate analyses including and excluding CFC-propelled products.

4.2.12 Overall, beclometasone dipropionate was identified as the cheapest group of ICS products, with an average annual cost of £32 for the equivalent of 200 micrograms per day (unweighted). Excluding CFC-containing preparations increased the annual cost to an average of £42 (unweighted). The unweighted average annual costs of budesonide were calculated to be £61, including CFC-containing preparations, and £68, excluding CFC-containing preparations. The unweighted average annual cost of fluticasone propionate was calculated to be £68 and was unaffected by the exclusion of CFC-containing products. These analyses

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did not include two budesonide products (Novolizer and Easyhaler) that have comparatively low annual costs of approximately £40 and £34 for 200 micrograms per day, respectively.

4.2.13 At an equivalent of 400 micrograms per day, beclometasone dipropionate remained the cheapest group of ICS products, with an average annual cost of approximately £68 (unweighted). Excluding CFC-containing preparations increased the annual cost to an average of £92 (unweighted). The unweighted average annual costs of budesonide were calculated to be £106, including CFC-containing preparations, and £113, excluding CFC-containing preparations. The unweighted average annual cost of fluticasone propionate was calculated to be £128 and was unaffected by the exclusion of CFC-containing products. In general, the average figures concealed a wide variation in cost of the different products using the same drugs.

4.2.14 To examine the cost implications of switching a person with uncontrolled asthma from an ICS alone to either a higher dose of ICS (400 micrograms beclometasone dipropionate or equivalent) or adding a LABA to a lower dose of ICS (200 micrograms beclometasone dipropionate or equivalent), the Assessment Group calculated the cost of a GP-managed (£24) and hospital-managed (£1056) exacerbation and then identified the number of exacerbations that would need to be avoided to offset any additional costs. The Assessment Group calculated that Seretide Evohaler is currently cheaper than budesonide and fluticasone propionate at higher doses when the comparison is based on a weighted mean average cost (including CFC-containing products). However, in comparison with the weighted mean average cost of beclometasone dipropionate (including CFC-containing products), Seretide Evohaler was calculated to be £52 more expensive. This would mean that one hospital-managed exacerbation (costing £1056) would need to be averted for every 20 people using the combination devices.

4.2.15 Both Seretide Accuhaler and Symbicort Turbohaler are currently more expensive than doubling the dose of ICS. The additional costs in comparison with the weighted mean average cost of beclometasone dipropionate are £127 and £138 per year, respectively, in comparison with budesonide are £70 and £81, respectively, and in comparison with

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fluticasone propionate are £57 and £68, respectively (all including CFC-containing products). The Assessment Group concluded that the extra annual cost to the NHS of combination devices, compared with an increased dose of the different ICS drugs as monotherapy, can vary enormously depending on the exact ICS product used. It is difficult to interpret these results within the context of the clinical data available because of the lack of studies making the comparison between combination devices and increasing the dose of ICS alone. It is also unclear how additional costs would translate into estimates of incremental cost effectiveness.

4.2.16 The costs of separate ICSs and LABAs in different devices were compared with the costs of a corticosteroid and LABA in a single combination device. The analyses were based on the person receiving the manufacturers' corresponding separate ICS product (for example, the costs of separate devices in comparison to Symbicort were calculated using the price of Pulmicort Turbohaler rather than the price of budesonide Novolizer). For the budesonide/formoterol fumarate combination (Symbicort), the Assessment Group identified an annual saving per person of between £35 and £190 when the drugs were given in a combination device as opposed to separate devices. Cost savings were dependent on the daily dose of ICS required (for example, 200 or 400 micrograms) and the LABA preparation used. The annual cost savings associated with fluticasone propionate/salmeterol (Seretide) were between £132 and £274 using a combination device. Cost savings were dependent on the type of device used (for example, Accuhaler versus Evohaler) and the daily dose of ICS required (for example, 100 or 200 micrograms). However, Seretide Evohaler was associated with greater cost savings than Seretide Accuhaler.

4.2.17 Finally, the Assessment Group compared the annual costs associated with providing a fixed dose of ICS with the different combination devices. For 200 micrograms per day beclometasone dipropionate equivalent, the cost of Symbicort was £201, compared with £190 and £115 for Seretide Accuhaler and Evohaler, respectively. The corresponding figures for 400 micrograms per day beclometasone dipropionate equivalent were £402, £379 and £233 per year. The Assessment Group concluded that, assuming equal efficacy, Seretide is currently less expensive than

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Symbicort, although this is based on a relatively crude assumption of clinical equivalence at a dose ratio of 1:2.

4.3 Consideration of the evidence

4.3.1 The Appraisal Committee reviewed the data available on the clinical and cost effectiveness of ICSs (including combination devices) for the treatment of chronic asthma in children under the age of 12 years, having considered evidence on the nature of the condition and the value placed on the benefits of ICSs by children with chronic asthma (and their parents), those who represent them, and clinical specialists. It was also mindful of the need to take account of the effective use of NHS resources.

4.3.2 The Committee heard from clinical specialists that they were in general agreement with the dose-equivalent estimates for the effectiveness of CFC-containing preparations of ICSs, as given in the BTS/SIGN guidelines. However, they noted that this was open to some disagreement, specifically when considering comparisons between different inhaler devices. The Committee concluded that it was appropriate to examine studies in which the dose of fluticasone propionate was half that of budesonide and beclometasone dipropionate, but it understood that there was some uncertainty regarding equivalence.

4.3.3 The Committee heard from clinical specialists that when considering the management of asthma there was a need to distinguish between pre-school children and school-aged children with asthma, and that the evidence for the appropriate management of pre-school children was still emerging. The Committee heard from the clinical specialists that the BTS/SIGN guidelines were at present the most appropriate starting point for considering the management of children with asthma, but that future revisions to the guidelines may make further distinctions between different types of asthma that may have implications for management. The Committee was aware that uncertainties existed in the management of asthma and its diagnosis, but it recognised that within the scope of the appraisal, the evidence on the clinical effectiveness of ICSs and their use should be considered within the context of the BTS/SIGN guidelines

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on the management of asthma.

4.3.4 The Committee noted that the different ICSs were available in a range of devices and recognised that there was already NICE guidance on the use of inhaler devices in children younger than 5 years (TA10) and in children aged 5–12 years (TA38). The Committee heard from clinical specialists that for younger children it was considered appropriate to use a pMDI with a spacer as a first choice, but that as children grow older it may be necessary to consider a wider range of products to maintain adherence. The Committee heard from patient experts that giving the child a choice of device could improve adherence to treatment, which may help to achieve and maintain efficacy and to set a pattern for adherence later in life. The Committee also heard from clinical specialists that there were benefits to maintaining technique if a child could use the same device type for their SABA as for their ICS. The Committee concluded that the guidance issued in NICE technology appraisal guidance 10 and 38 was still relevant and that the issues around choosing a suitable product to maximise adherence still applied.

4.3.5 The Committee noted that the marketing authorisations for the ICSs differed for the drugs and the type of device within which a drug was available. The Committee was aware that these differences were important, and included recommended age groups for which the products were approved, dose delivered per actuation and the maximum daily dose. The Committee recognised that there could be difficulties in prescribing because the marketing authorisations may not always adequately cover the clinical needs of children, but it also understood that the recommendations should not contradict the marketing authorisations for the individual products.

4.3.6 The Committee considered the implications of phasing out CFC propellants in accordance with the Montreal Protocol and the impact that this would have on the availability of devices. The Committee heard from clinical specialists that the Montreal Protocol had not yet been put into effect for ICSs because of the limited number of pMDIs using HFA propellants that had been developed. However, it stated that the manufacture of CFC-containing devices was being reduced and that it was expected that such devices would soon be phased out. The

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Committee concluded that it was unclear exactly when CFC-containing devices would become unavailable, but that this would impact on the range and type of devices that prescribers would have access to, and it would have an impact on device cost.

4.3.7 The Committee noted that there were few studies comparing the different ICSs in children within the steps of the BTS/SIGN guidelines and that studies in children were often underpowered and poorly reported. The Committee noted that, in particular, the evidence base for ICS/LABA combination devices was limited to a small number of studies. The Committee noted concerns from consultees that participants in the studies may not reflect those typically seen in general practice, and that no studies included any children younger than 4 years. The Committee heard from clinical specialists that ICSs were prescribed to pre-school children. Therefore, it considered that recommendations should not exclude pre-school children, but that owing to the lack of evidence, specific recommendations could not be made for children younger than 4 years. However, the Committee noted uncertainties in diagnosis and management faced by physicians when deciding whether the prescription of an ICS was appropriate in very young children.

4.3.8 The Committee considered the comparative clinical evidence included in the submissions from consultees and the assessment report. It also noted the evidence that had been available in the technology appraisal for ICSs for the treatment of chronic asthma in adults and in children aged 12 years and over (publication expected November 2007). The Committee concluded that the evidence available suggested that there were no clinically relevant differences in efficacy between the different ICSs but that, at present, the evidence base upon which to draw conclusions about the comparative efficacy of ICS/LABA combination devices was limited.

4.3.9 The Committee considered the adverse event profiles of the different ICSs. It was aware that parents were often concerned about possible adverse events associated with ICSs, including growth and adrenal suppression. The Committee noted that some studies had suggested that, in the short term, fluticasone propionate may be associated with less impact on growth than other ICSs. However, the Committee did not

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consider that this effect had been shown to be consistent across studies. In addition, the Committee heard from clinical specialists that they considered that such adverse events were more frequently associated with higher than licensed doses and that the long-term evidence for an impact on growth and final height was inconclusive. The Committee heard from clinical specialists that, in clinical practice, other factors such as choosing the most appropriate device were considered to be more important when selecting an ICS than the possible differences in the impact on growth, so this was not seen to be an overriding factor in considering which product to use. The Committee concluded it was not appropriate to distinguish between the different ICSs on the basis of adverse events.

4.3.10 The Committee considered the cost effectiveness of the ICSs. It noted that consultees had used a similar approach to considering this question and had assumed equal efficacy when comparing costs. The Committee heard from the Assessment Group that it had not been possible to model the cost effectiveness of ICSs. Therefore, the Committee accepted that, based on the evidence before it, a decision would be necessary based on the cost comparisons. The Committee noted that, although the Assessment Group had identified that beclometasone dipropionate was currently the least expensive drug on average, there was a wide variation in costs of products containing the same drug. Therefore, the Committee concluded that it would not be appropriate to name a specific product as more cost effective but that, if different products were available and were considered equally appropriate for an individual child, the least expensive should be used.

4.3.11 The Committee heard from clinical specialists that, according to the BTS/SIGN guidelines, if a child with asthma was uncontrolled on a low-to-moderate dose of ICS alone then either the dose of ICS would be increased or another agent such as a LABA added. The Assessment Group explained that it had tried but had not been able to model the cost effectiveness of increasing the dose of an ICS versus adding a LABA to half the dose of ICS in a combination device. The Committee heard from the Assessment Group that it had not modelled the cost effectiveness of remaining on the same dose of ICS or adding a LABA because it appeared to be outside of the BTS/SIGN guidelines. The Committee

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noted that such a comparison had been made by two of the manufacturers. The Committee considered that combination devices could, in some circumstances, be cost saving in comparison to doubling the dose of ICS, but that this depended on a range of factors including the combination device, the ICS device, and the amount of ICS required. On balance, the Committee was persuaded that if it was considered appropriate to either increase the dose of an ICS or add a LABA for an individual child, then adding a LABA using a combination device should be considered an option, as specified in the BTS/SIGN guideline.

4.3.12 The Committee considered the evidence on the cost effectiveness of ICS plus LABA treatment when using a single combination device or separate devices. The Committee noted that both the Assessment Group and the manufacturers came to a similar conclusion that the use of a combination device (ICS plus LABA) could be cost saving compared with using separate devices. The Committee heard from clinical specialists that there may be additional benefits from using a combination device not reflected in the trial data, in terms of adherence to medication from using a single device. However, they cautioned that combination devices may discourage patients from stepping down treatment and in particular stopping LABA treatment in periods when they were symptom free. The Committee recognised that there were important safety considerations if a LABA was used without an ICS, so the combination device may be preferred in some individuals to reduce the risk of the ICS being omitted. However, the flexibility associated with being able to increase the dose of ICS without also having to increase the dose of LABA may also mean that in some circumstances separate devices could be more appropriate. The Committee therefore concluded that combination devices should be recommended as a treatment option.

4.3.13 The Committee recognised that the range of ICS and LABA products may change and considered that future changes in the availability and relative cost of generic ICSs, LABAs and combination devices (ICS plus LABA in a single device) might alter the relative cost effectiveness of delivery using a single combination device compared with separate devices. The Committee considered that in the future, delivery via separate devices may become the most cost-effective option in fully compliant individuals. However, based on the current availability and relative pricing of

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combination devices, the Committee considered that, at present, combination devices were the least costly option.

4.3.14 The Committee was aware that there were two combinations of ICS and LABA available within a number of different types of single combination devices. It noted that comparisons of costs carried out by the manufacturers and the Assessment Group concluded that for a fixed dose of ICS the combination of fluticasone propionate/salmeterol was currently the least costly. The Committee recognised that this was the only combination available as a pMDI and so was the only one that could appropriately be used with a spacer. However, it was aware that the other combination, budesonide/formoterol fumarate, could be considered appropriate for some children as dosing may be more flexible. Taking into consideration the different profiles of the products and the need to maximise adherence with medication, the Committee concluded that it would not be appropriate to specify a particular combination product or device. However, if more than one combination device was considered appropriate for an individual child, the least costly product should be used.

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5 Implementation

5.1 The Healthcare Commission assesses the performance of NHS organisations in meeting core and developmental standards set by the Department of Health in 'Standards for better health'issued in July 2004. The Secretary of State has directed that the NHS provides funding and resources for medicines and treatments that have been recommended by NICE technology appraisals normally within 3 months from the date that NICE publishes the guidance. Core standard C5 states that healthcare organisations should ensure they conform to NICE technology appraisals.

5.2 'Healthcare Standards for Wales' was issued by the Welsh Assembly Government in May 2005 and provides a framework both for self-assessment by healthcare organisations and for external review and investigation by Healthcare Inspectorate Wales. Standard 12a requires healthcare organisations to ensure that patients and service users are provided with effective treatment and care that conforms to NICE technology appraisal guidance. The Assembly Minister for Health and Social Services issued a Direction in October 2003 which requires Local Health Boards and NHS Trusts to make funding available to enable the implementation of NICE technology appraisal guidance, normally within 3 months.

5.3 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraph above. This means that, if a child under the age of 12 years has chronic asthma and the doctor responsible for their care thinks that inhaled corticosteroids are the right treatment, they should be available for use, in line with NICE's recommendations.

5.4 NICE has developed tools to help organisations implement this guidance (listed below).

- Audit criteria to monitor local practice.
- A costing statement explaining the resource impact of this guidance.

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6 Recommendations for further research

6.1 ICSs are a well-established therapeutic intervention. Therefore, research on ICSs tends to be done when new devices are developed. There is an ongoing programme of postmarketing research in relation to combination devices.

6.2 The Committee recognised the need for some larger and longer term comparative trials of ICSs in children younger than 12 years, with full assessment of side effects including growth and other effects on adrenal suppression.

6.3 The Committee also recommended further research that focused on comparisons of ICSs in children younger than 5 years, and that compared the effectiveness of remaining on the same dose of ICS, increasing the dose of ICS and adding a LABA.

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7 Related NICE guidance

- Inhaler devices for routine treatment of chronic asthma in older children (aged 5–15 years). NICE technology appraisal guidance 38 (2002).
- Guidance on the use of inhaler systems (devices) in children under the age of 5 years with chronic asthma. NICE technology appraisal guidance 10 (2000).
- Inhaled corticosteroids for the treatment of chronic asthma in adults and children aged 12 years and over. NICE technology appraisal guidance 138 (2008).

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8 Review of guidance

8.1 The review date for a technology appraisal refers to the month and year in which the Guidance Executive will consider whether the technology should be reviewed. This decision will be taken in the light of information gathered by the Institute, and in consultation with consultees and commentators.

8.2 The guidance on these technologies will be considered for review in November 2012. A 5-year review date is proposed because it is not expected that further research will substantially change the recommendation of this appraisal.

Andrew Dillon
Chief Executive
November 2007

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Appendix A. Appraisal Committee members and NICE project team

A. Appraisal Committee members

The Appraisal Committee is a standing advisory committee of the Institute. Its members are appointed for a 3-year term. A list of the Committee members who took part in the discussions for this appraisal appears below. The Appraisal Committee meets three times a month except in December, when there are no meetings. The Committee membership is split into three branches, each with a chair and vice-chair. Each branch considers its own list of technologies and ongoing topics are not moved between the branches.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

The minutes of each Appraisal Committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

Dr Jane Adam
Radiologist, St George's Hospital, London

Professor AE Ades
MRC Senior Scientist, MRC Health Services Research Collaboration, Department of Social Medicine, University of Bristol

Anne Allison
Nurse Clinical Adviser, Healthcare Commission

Dr Tom Aslan
General Practitioner, Stockwell, London

Professor David Barnett (Chair)
Professor of Clinical Pharmacology, University of Leicester

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Mrs Elizabeth Brain
Lay Member

Dr Karl Claxton
Health Economist, University of York

Dr Richard Cookson
Senior Lecturer in Health Economics, School of Medicine Health Policy and Practice, University of East Anglia

Mrs Fiona Duncan
Clinical Nurse Specialist, Anaesthetic Department, Blackpool Victoria Hospital, Blackpool

Professor Christopher Eccleston
Director Pain Management Unit, University of Bath

Dr Paul Ewings
Statistician, Taunton & Somerset NHS Trust, Taunton

Professor John Geddes
Professor of Epidemiological Psychiatry, University of Oxford

Mr John Goulston
Director of Finance, Barts and the London NHS Trust

Mr Adrian Griffin
Health Outcomes Manager, Johnson & Johnson Medical Ltd

Ms Linda Hands
Clinical Reader in Surgery, University of Oxford

Dr Rowan Hillson
Consultant Physician, Diabeticare, The Hillingdon

Professor Philip Home (Vice Chair)
Professor of Diabetes Medicine, University of Newcastle upon Tyne

Dr Terry John

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General Practitioner, The Firs, London

Professor Richard Lilford
Professor of Clinical Epidemiology, Department of Public Health and Epidemiology, University of Birmigham

Dr Simon Maxwell
Senior Lecturer in Clinical Pharmacology and Honorary Consultant Physician, Queens Medical Research Institute, University of Edinburgh

Dr Alec Miners
Lecturer in Health Economics, London School of Hygiene and Tropical Medicine

Ms Judith Paget
Chief Executive, Caerphilly Local Health Board, Wales

Dr Ann Richardson
Lay Member

Mr Mike Spencer
General Manager, Clinical Support Services, Cardiff and Vale NHS Trust

Dr Simon Thomas
Consultant Physician, General Medicine and Clinical Pharmacology, Newcastle Hospitals NHS Trust

Mr David Thomson
Lay Member

Dr Norman Vetter
Reader, Department of Epidemiology, Statistics and Public Health, School of Medicine, Cardiff University, Cardiff

Dr Paul Watson
Director of Commissioning, East of England Strategic Health Authority

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B. NICE project team

Each technology appraisal is assigned to a team consisting of one or more health technology analysts (who act as technical leads for the appraisal), a technical adviser and a project manager.

Zoe Garrett
Technical Lead

Janet Robertson
Technical Adviser

Alana Miller
Project Manager

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Appendix B. Sources of evidence considered by the Committee

A. The assessment report for this appraisal was prepared by Peninsula Technology Assessment Group (PenTAG), Peninsula Medical School and Southampton Health Technology Assessments Centre (SHTAC), Wessex Institute for Health Research and Development (WIHRD), University of Southampton.

- Main C, Shepherd J, Anderson R, et al, Inhaled corticosteroids and long-acting beta2-agonists for the treatment of chronic asthma in children under the age of 12 years: systematic review and economic analysis, December 2006

B. The following organisations accepted the invitation to participate in this appraisal. They were invited to comment on the draft scope, assessment report and the appraisal consultation document (ACD). Organisations listed in I and II were also invited to make written submissions and have the opportunity to appeal against the final appraisal determination.

Manufacturers/sponsors:

- AstraZeneca UK Ltd
- GlaxoSmithKline UK Ltd
- IVAX Pharmaceuticals UK Ltd
- TEVA UK Ltd
- Ranbaxy UK Limited
- Trinity-Chiesi Pharmaceuticals Ltd (Trinity Pharmaceuticals Ltd)
- Meda Pharmaceuticals Ltd

Professional/specialist and patient/carer groups:

- Action Against Allergy (AAA)
- Action for Sick Children

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- Allergy UK
- Asthma UK
- British Paediatric Respiratory Society
- British Thoracic Society
- Cochrane Airways Group
- Department of Health
- Education for Health
- General Practice Airways Group (GPIAG)
- Knowsley PCT
- Royal College of General Practitioners
- Royal College of Nursing
- Royal College of Paediatrics and Child Health
- Royal College of Physicians
- Royal College of Physicians of Edinburgh
- Welsh Assembly Government

Commentator organisations (without the right of appeal):

- Asthma And Allergy Research Group, University of Dundee
- AstraZeneca UK Ltd
- British National Formulary
- GlaxoSmithKline UK Ltd
- IVAX Pharmaceuticals UK Ltd
- Meda Pharmaceuticals Ltd
- Medicines and Healthcare products Regulatory Agency (MHRA)

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- National Coordinating Centre for Health Technology Assessment
- NHS Quality Improvement Scotland
- Peninsula Technology Assessment Group (PenTAG)
- Ranbaxy UK Limited
- Respiratory Research Group, University of Glasgow
- Southampton Health Technology Assessment Centre (SHTAC), University of Southampton
- TEVA UK Ltd
- Trinity – Chiesi Pharmaceuticals Ltd (Trinity Pharmaceuticals Ltd)

C. The following individuals were selected from clinical specialist and patient advocate nominations from the non-manufacturer/sponsor consultees and commentators. They participated in the Appraisal Committee discussions and provided evidence to inform the Appraisal Committee's deliberations. They gave their expert personal view on corticosteroids for the treatment of chronic asthma in children under 12 years by attending the initial Committee discussion and/or providing written evidence to the Committee. They were also invited to comment on the ACD.

- Dr Jonathan Grigg, Professor of Paediatric and Respiratory Medicine, nominated by Royal College of Paediatrics and Child Health – clinical specialist
- Dr Mike Thomas, External Affairs Liaison nominated by General Practice Airways Group – clinical specialist
- Ms Sally Rose, Asthma Nurse Specialist, nominated by Asthma UK – patient expert

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Changes after publication

March 2014: implementation section updated to clarify that inhaled corticosteroids are recommended as an option for treating chronic asthma in children under the age of 12 years. Additional minor maintenance update also carried out.

March 2012: minor maintenance

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About this guidance

NICE technology appraisal guidance is about the use of new and existing medicines and treatments in the NHS in England and Wales.

This guidance was developed using the NICE multiple technology appraisal process.

We have produced a summary of this guidance for patients and carers. Tools to help you put the guidance into practice and information about the evidence it is based on are also available.

Your responsibility

This guidance represents the views of NICE and was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to avoid unlawful discrimination and to have regard to promoting equality of opportunity. Nothing in this guidance should be interpreted in a way which would be inconsistent with compliance with those duties.

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