
# NICE Appraisal

# Use of Inhaled Corticosteroid (ICS) and Long acting beta2 agonists for the treatment of chronic asthma (adults and children)

Submission from Education for Health

**EXECUTIVE SUMMARY**

1. Education for Health welcomes the development of any guidance that has the potential to improve the care of people with asthma.

2. The majority of asthma care is delivered in primary care settings. Education for Health has collaborated with General Practice in Airways Group (GPIAG) in considering this submission and endorses the GPIAG submission prepared for the NICE appraisals of inhaled corticosteroid (ICS) therapy in Asthma.

3. A large proportion of asthma management in primary care settings is nurse led.

4. The significant costs in asthma occur when the disease is poorly controlled. This appraisal should therefore focus on increasing the appropriate use of inhaled steroids in asthma with the aim of improving overall asthma control and associated quality of life.

5. Non-adherence with ICS therapy is a significant problem in asthma care resulting in increased risk of exacerbation, hospitalisation and potentially death. Any recommendations need to take account of the complex needs of individuals and the importance of patient preference with the overall aim of improving correct usage of ICS treatment.

6. The most favourable outcomes in asthma care are achieved when a person centred approach is adopted and partnership working exists between healthcare professionals and patients.

7. There is considerable heterogeneity within asthma populations and individual response can vary significantly. Clinicians need to have available a range of treatment options in order to select the most appropriate for any individual, taking into account a range of patient characteristics.

8. While NICE has clearly stated that it intends to focus on compounds alone in this appraisal, it is important to acknowledge that the delivery device used may impact significantly on the clinical outcome obtained. In every day practice it is clear that poor inhaler technique is a common problem and the ease with which an individual can use a particular device may influence the choice of ICS prescribed. It will be important therefore that this appraisal acknowledges that in the 'real world' perspective there is an important interplay between the molecule and device used which cannot always be clearly separated.

9. It is important that this appraisal takes into account evidence from 'real world' settings. Many of the studies regarded by NICE for this appraisal as the 'highest grade' evidence may actually exclude the average patient encountered in everyday practice. It is important therefore that studies in milder disease, pragmatic trials and observational data are also considered. These conventionally 'lower grade' sources of evidence may in fact bear more relation to the realities of everyday practice and must be considered alongside those with stricter selection criteria.

10. Some patients and healthcare professionals may have exaggerated and unfounded concerns about the use of ICS which can contribute to reluctance to use appropriate levels of treatment. It is important that any recommendations are carefully presented in order to avoid raising further anxiety which might potentially discourage the use of ICS. Recommendations resulting from this appraisal must be applicable to all healthcare professionals from those with limited respiratory experience through to the most experienced.

## 1. INTRODUCTION

### 1.1 Education for Health

Education for Health is a merger of two of the UK's leading independent educational institutions for health professionals: the National Respiratory Training Centre (NRTC) and Heartsave. It aims to provide a consistent, comprehensive and innovative approach to professional health training across the fields of respiratory and cardiovascular disease, with the ultimate objective of transforming lives worldwide. Education for Health is continually adapting its educational provision to enable health professionals to meet the changing face of the Health Service and has been awarded institutional accreditation by the Open University (OU). Education for Health provides a wide range of training options from basic one-day short courses to a full postgraduate diploma, offering degree and diploma programmes as well as individual modules.

The research department at Education for Health based at the Centre in Warwick is currently undertaking studies to:

- investigate the effects of training on knowledge, practice and patient outcomes
- evaluate methods and delivery of training
- investigate methods of improving the diagnosis and management of patients with respiratory and allergic diseases
- investigate methods of care delivery

Education for Health works collaboratively and in consultation with professional organisations such as British Thoracic Society (BTS), General Practice Airways Group (GPIAG), British Society for Allergy and Clinical Immunology (BSACI) and patient groups such as Asthma UK and British Lung Foundation (BLF). Education for Health has played an important role in the development of national asthma guidelines and in the dissemination of these through its various educational activities.

### 1.2 How Education for Health can contribute to the appraisal

Education for Health acknowledges the importance of appropriate use of inhaled corticosteroids (ICS) as key to good asthma management in all settings and welcomes any initiative that may contribute to improved use of this technology. The organisation has an overall aim of improving patient care and feels strongly that the focus in this assessment must be on improving the lives of people with asthma rather than on containing drug costs.

It is essential that any recommendations that may result from this appraisal reflect the complexities faced by practitioners on a day to day basis. Through its alumni and extensive network of lecturer practitioners Education for Health is able to consult with a wide range of healthcare professionals working across a variety of settings.

When considering recommendations that may significantly impact upon the delivery of asthma care it is important to remember that much of that care is delivered by asthma trained nurses. Having delivered asthma training to over 7,500 primary care nurses in the last ten years, Education for Health has significant experience of the key issues faced by these health professionals in trying to implement measures aimed at improving asthma control; it is well placed to represent their perspective.

In order for any recommendations to become meaningful it will be essential that they are presented in an easily understood and accessible format and that appropriate educational support is given in order to ensure uptake. With almost twenty years of experience in respiratory training and education, Education for Health can provide a valuable perspective on issues surrounding the impact and dissemination of potential recommendations.

## 2. COLLABORATION WITH GENERAL PRACTICE IN AIRWAYS GROUP (GPIAG)

In preparation of submissions for the appraisal of ICS in both children and adults Education for Health has liaised closely with GPIAG and fully supports their detailed submissions. The purpose of this document is to augment and support the information provided by GPIAG and to give an important perspective from an organisation committed to improving asthma care through educational initiatives.

The key issues that will be outlined include:

- the organisation of asthma care and the role of the nurse
- current use of ICS in asthma care
- the contribution of adherence with ICS therapy to effective asthma control
- the importance of inhaler technique in contributing to effective asthma control
- the need for recommendations to be applicable to the complexities faced by health care professionals in every day practice

Throughout the document consideration will be given to the potential impact of any recommendations that may be made as a result of this appraisal process.

## 3. ORGANISATION AND DELIVERY OF ASTHMA CARE

### 3.1 The size of the problem

Asthma affects 5.2 million people in the U|K (Asthma UK 2004a) with 21% of children and 15% of adults having a diagnosis of asthma (BTS 2006). Most people with asthma receive their care in community settings. Less than 1 in 5 visit hospital for treatment of their asthma and more than 9/10 of patients are treated in primary care by their GP or asthma nurse or both (National Asthma Campaign 2001).

### 3.2 The delivery of care

The British Thoracic Society (BTS) and the Scottish Intercollegiate Guidelines Network (SIGN) have produced evidence based guidelines for the management of asthma (BTS/SIGN 2005) which are regularly updated. These provide guidance for clinicians on current best practice on all aspects of asthma care including diagnosis, pharmacological and non-pharmacological treatments and ongoing monitoring and review.

There has been increasing emphasis on the importance of planned proactive care for people with asthma rather than an over reliance on emergency interventions when things go wrong. The new GMS contract (BMA and NHS confederation 2003) encourages as part of the quality outcomes framework (QOF), the identification of people with asthma and the provision of regular asthma reviews.

When considering how asthma care is delivered in the community it is important to recognise that many people with asthma may be reluctant or unable to attend reviews. They may continue to obtain repeat medication without review and may have poorer outcomes. The National Asthma Campaign (2001) found that 1 in 10 people with asthma reported not seeing any healthcare professional in the last three years. Innovative strategies need to be considered in order to meet the needs of such groups and some success with telephone reviews has been achieved (Pinnock et al 2003)

Even those who do attend for review may not reveal the true extent of the problem unless the healthcare professional is able to ask the right questions. Many people with asthma underestimate the impact of their disease assuming that it is normal to have symptoms and without appropriate detailed and direct questions the health professional will not be able to elicit this information (Price et al 1999, Price et al 2002). Without this information appropriate levels of medication may not be instituted and avoidable morbidity will occur.

The involvement of patients in their own care by the use of educational initiatives and negotiated personal asthma action plans has been shown to be important in improving satisfaction and outcomes (Gibson et al 2003, Turner et al 1998). There would appear, however, to be reluctance on the part of some healthcare professionals to engage in these strategies (Jones et al 2000). Appropriate training can significantly improve the use of educational strategies. Education for Health (unpublished data 2006) has found that undertaking diploma level training in asthma care significantly increases the confidence of nurses in delivering appropriate asthma care (see Fig 1)
If optimal outcomes in asthma control are to be achieved it is important that all health professionals delivering such care receive appropriate education so that they are able to implement current guidelines and offer relevant education and opportunities for people with asthma to engage in active partnerships for their care.

### 3.3 The role of nurses and the importance of appropriate education

The role of the asthma nurse has had an important impact on the management of asthma in the community (Morice & Wrench 2001, Kamps et al 2004) and they are frequently responsible for carrying out asthma reviews. With the recent changes to non-medical prescribing (Drug and Therapeutics Bulletin 2006) it is likely that with appropriate asthma training these nurses could become the main prescribers in this field.

The BTS/SIGN guidelines (2005) recommend that people with asthma should receive their care from an appropriately trained healthcare professional. Education for Health (unpublished data 2006) has demonstrated that training significantly increases nurses' confidence in utilising guidelines to select treatment options. It also increased the frequency with which they checked inhaler technique and compliance with treatments (see Fig1).These factors are key to achieving good asthma control and so it must be concluded that it is essential for nurses to receive training if appropriate care is to be delivered and current guidance put into place.

**Fig 1 The effects of diploma level training in asthma care for nurses**
(Unpublished data Education for Health 2006)

| | Pre-training | Post-training |
|---|---|---|
| Never or rarely supplied written asthma action plan | 74% | 19% |
| Usually or very confident in delivering appropriate asthma care and education | 10% | 84% |
| Usually or very confident in using guidelines to select treatment options | 16% | 89% |
| Mostly or always checked inhaler technique | 58% | 91% |
| Mostly or always checked compliance | 62% | 92% |

### 3.4 The cost of asthma care

Asthma has considerable impact functionally and financially both on individuals and society as a whole. Poorly controlled asthma can limit every aspect of an individual's daily life. Of the more than 5 million people with asthma it is estimated that only 500,000 have severe or difficult to control asthma and that the remaining 4.6 million have 'every day' asthma which should be able to be well controlled using current treatment and guidelines (Asthma UK 2004b). Yet approximately 66% of people with asthma report difficulty in running for a bus or enjoying exercise and 50% report disturbed sleep due to their symptoms. These symptoms can result in poor performance or even time off from school or work which can have serious consequences for employment prospects.

Financial costs occur as a result of direct medical costs such as pharmaceutical costs and utilisation of NHS resources and indirect costs such as loss of productivity and the payment of benefits. Analysis of these financial costs has shown that the majority of asthma care costs relate to those associated with poor asthma control. Poor control results in people being unable to perform their normal daily activities including paid work and is the cause of more intensive use of NHS resources including increased consultations and hospital admissions.

As a result improved control should have a major impact on the overall costs of asthma to society. Therefore it would be appropriate for this appraisal to focus on the improvement of asthma control rather than on reducing asthma drug costs as this is likely to have the greatest economic impact.

### 3.5 Potential effects of this review on service delivery

Before any recommendations could be adopted it would be important to ensure that the healthcare professionals were sufficiently educated in the specific technologies and familiar with the complexities surrounding the achievement of good asthma control. If recommendations of this review were to suggest that one molecule was superior to another and should be used in preference this could have a significant impact on the workload of primary care.

If the confidence of patients is to be maintained they need to be involved in any process of change and so it would not be appropriate to simply switch preparations on a repeat prescription. Whilst any switching of preparations could be staged and undertaken at the next review appointment it would clearly increase the length of that consultation. Detailed explanation would be required and potentially a change in inhaler device might be necessary. A period of closer monitoring would be required to ensure good control was maintained or achieved. Those people affected who did not attend for review routinely would need to be contacted and appointments arranged so that the transfer could be properly supervised.

Whilst this impact on workload is important it should not be seen as a reason not to adopt important recommendations but rather as a factor to be taken into account when determining the time frames for implementation.

## 4. ICS PHARMACOTHERAPY FOR ASTHMA

ICS are the recommended treatment for all but the mildest intermittent asthma symptoms and have a good record of efficacy and safety at standard doses (BTS/SIGN 2005). It is now recommended that when symptoms fail to be controlled at normal doses of ICS and that inhaler technique and compliance have been checked and are good that rather than increasing ICS another add on therapy is introduced. There is evidence that in fact these guidelines are not always reflected in prescribing and that both over and under treatment with ICS does occur. High dose and even unlicensed dose treatment is not uncommonly used (Thomas et al 2006) and is particularly significant in children (Turner et al 1998). It has been demonstrated, however, that many patients could have their ICS dose safely reduced without loss of asthma control (Hawkins et al 2003). Conversely there is still evident considerable avoidable asthma morbidity as a result of under treatment with this effective group of drugs (Rabe et al 2000).

Current UK asthma guidelines make clear recommendations about the order in which therapeutic options should be tried but areas of uncertainty can still exist for clinicians. When commencing ICS therapy there is a need to make a decision about not only which ICS molecule to use but also which inhaler device to choose. When increasing therapy and adding in a long acting beta2 bronchodilator there is the need to consider whether to use separate preparations or whether to choose a combination therapy and again which device would be the most suitable.

Many complex factors may need to be taken into consideration when assessing the best option for an individual patient and as a result it is possible that both under and over treatment may occur.

### 4.1 Adherence with ICS treatment for asthma

The effectiveness of treatment with ICS is dependent on the inhaler being used regularly as recommended and yet levels of non-adherence with medication in long term conditions such as asthma are known to be high (Carter et al 2003). Many patients with asthma will only take medication when they feel that they need it rather than as instructed by healthcare professionals (Carter et al 2003) which is a problem because airway inflammation can persist even in periods of low or absent symptoms and the effects of ICS can take several months to become fully apparent (Dollery 1999) . Dasgupta and Guest (2003) estimated that one quarter of asthma patients in the UK had a compliance rate of less than 30%.

The factors affecting adherence with treatment regimes are complex but non adherence may be broadly split into non-intentional and intentional causes. Non-intentional reasons include forgetting, lack of time, complicated regimes, misunderstanding or misinterpretation of instructions. Intentional causes include fears about side effects, lack of confidence in effectiveness of ICS and over estimation of asthma control i.e. feeling well and thinking they don't need ICS. It is important to work with the individual to explore their understanding of the disease and treatments and to find a delivery system that is easy to use, acceptable and fits in with their lifestyle.

When adding another inhaler to an existing regime, for example when stepping up treatment to include use of an inhaled long acting bronchodilator, it is important to consider the impact this may have on the individual. The addition of an extra inhaler potentially complicates the regime and increases the time required for medication use and also imposes increased prescription costs. For this reason there may be difficulties in compliance and it may be preferable to incorporate both treatments into a single inhaler. It is also possible that patients are able to perceive the immediate benefits of the bronchodilator in the combination inhaler more immediately than the delayed effects of the ICS and may have greater confidence and improved compliance based on this perception. A study (Stoloff 2004) examining refill rates for prescriptions in a US health maintenance organisation demonstrated that adherence and persistence with ICS treatment was higher in those prescribed a combination formulation than in those prescribed an ICS alone or those prescribed the two components in separate inhalers.

It will be essential that this appraisal acknowledges the challenges that poor adherence can pose for health professionals and patients when trying to achieve good asthma control.

### 4.2. Inhaler technique and choice

As acknowledged by the NICE technology appraisals NO. 10 (NICE 2000) and No. 38 (NICE 2002) examining the use of inhaler devices by children with asthma the efficacy of asthma treatment depends on the drug being deposited in the correct place and in the right quantity in the airways. It is therefore essential that inhaler technique is optimal as inadequate lung deposition will reduce the effectiveness of treatment. For these reasons current guidelines (BTS/SIGN 2005) recommend that patients should be carefully instructed in the use of the chosen device and technique assessed before issuing and then at regular asthma reviews. Issues that are considered important by trained asthma nurses when selecting a device with a patient include age, level of understanding, manual dexterity, lifestyle factors, acceptability of device (Hardy et al 2003).

Not all molecules are available in all types of device and so inhaler technique may affect the choice of drug. A systematic review of randomised control trials comparing the effectiveness of ICS via different inhaler systems (Brocklebank et al 2001) concluded that there was no benefit with the newer breath actuated devices or dry powder inhalers over the more conventional metered dose inhalers. When considering these findings it is important to understand that entry criteria for many of the studies scrutinised included good inhaler technique and good compliance. In everyday practice, however, it is clear that many patients cannot successfully use some inhaler devices (Duerden and Price 2001) and a range of alternatives needs to be available for these individuals.

It is clear from research (Fletcher et al 2005) that inhaler device characteristics are very important to patients. 75% of respondents in this survey stressed the importance of size and the desire to minimise number of doses required. In another study (Upton et al 2006) embarrassment with using inhalers and lack of knowledge about devices were found to be predictive of increased non adherence. It would seem likely then that any potential change to inhaler device would have a significant impact on patients and could result in a decrease in adherence.

Although NICE intends to focus solely on molecules alone in this appraisal it is clear that delivery device and compound are closely related. Using the same molecule in different devices may result in different outcomes. Whatever the proven clinical effectiveness of any molecule it will only achieve a good outcome in an individual if that individual is sufficiently able to achieve adequate deposition in the lungs (i.e. is able to use the chosen inhaler correctly).

### 4.3 Potential effects of this review on adherence

There is the potential that any review of a technology such as ICS will arouse increased anxiety about the safety and effectiveness of that technology among the general public and health professionals. This may be particularly true of ICS as there already exists among some people an exaggerated fear of the treatment. If the recommendations are not sensitively handled then it is possible that many people who have already had doubts will feel them to be confirmed and reduce or stop treatment altogether. If switching of compounds is recommended then it will be important to ensure that a feeling that people have been on unsafe or ineffective treatments previously is not created. It would seem likely that recommendations may suggest that certain molecules may be better suited to certain situations than others and this will need to be clearly understood by the public and healthcare professionals. If a change in molecule also results in a change in inhaler device, care must be taken to ensure that individuals are able to use the new device effectively and that they are willing to do so or poor adherence to therapy and loss of control could result. The most important overall message must be that ICS are key to achieving good asthma control although in some situations there may be benefits using one over another. The most effective ICS for any individual must surely remain the one that they can and will use.

## 5. APPLYING THE EVIDENCE

Whilst it is important that this NICE evaluation is based on evidence-based recommendations, it is important to acknowledge that may be certain limitations if only evidence from randomised controlled trials (RCTs) and systematic reviews is considered. RCTs are designed in such a way as to limit possible sources of bias and strict entry criteria often mean that patients participating may not be typical of the broader demographic range encountered in every day practice. When applying the results of RCTs to wider patient populations it is important to establish that the study population is broadly similar to the general population for whom the guidance is intended.

A study (Herland et al 2005) to investigate if patients attending GP or hospital outpatient clinics would meet the typical entry criteria (absence of co-morbidity, FEV1 50-85% predicted, present or history of reversibility in the last year, non smoker, or ex smoker of less than 10 pack years) for many asthma trials demonstrated that in fact only 5% of 334 consecutive patients would have been eligible. When other criteria such as being symptomatic or regular use of inhaled steroids were included then the number of eligible patients fell even further to 3.3%. This must raise questions as to how widely results from such trials can be applied to the asthma population at large. Such trials are designed to demonstrate specific benefits and so inclusion and exclusion measures may be chosen with this specifically in mind.

Given the complex nature of asthma it is unlikely that any one outcome measure can fully measure the impact of any intervention in asthma. (Barnes 2000) Relevant outcome measures in the assessment of asthma control include lung function, symptoms, health status, exacerbations, lung function and measures of airways inflammation and hyper-reactivity. No single outcome measure can give sufficient information in isolation on asthma control; there is for example a poor relationship between symptoms and lung function (Teeter and Bleecker 1998). It has been increasingly recognised that the duration of asthma studies may be important when examining outcomes. Whilst trials of 12 weeks duration may be sufficient to demonstrate a change in lung function, they may not capture the effect on events such as exacerbation and may not reflect the broader aspects of asthma control. Longer term studies also enable assessment of the impact of issues such as adherence on asthma outcomes related to different technologies.

For these reasons it is possible that healthcare professionals may view the result of some trials with scepticism about how they apply to the patient populations they treat. Qualitative studies of UK GPs (Tomlin et al 1999, Freeman and Sweeney 2001) suggest that their views of effective care were based not only on the objective clinical factors found in RCTs but also took account of individual patient features and the resource implications that play a role in every day practice.

It is important therefore that this appraisal takes account of good quality data from ‘real-world’ settings including studies in milder disease, pragmatic trials and observational studies as well as RCTs. In this way any recommendations that result should reflect more closely the day to day context in which most healthcare professionals practice and should be more readily accepted by them as relevant to their practice.

## 6. CONCLUSION

Education for Health supports the review of the use of ICS technologies in the treatment and management of asthma. It is important that this review arrives at recommendations that can be easily applied by all healthcare professionals across the wide range of settings in which people with asthma are treated. The recommendations must stress the importance of the overall approach in using ICS therapy to achieve good asthma control whilst acknowledging the circumstances in which specific molecules may be more appropriate. Within the scope of the recommendations there needs to be recognition that the complexities surrounding individual cases may require clinical judgement to be applied so that the needs of the individual can be optimally met. The issues of adherence to therapy and inhaler technique are frequently the key to achieving good asthma control and this review should therefore take account of this. When weighing the evidence it will be important to look wider than the evidence from randomised control trials alone and essential to consider how this RCT data applies to everyday situations. The variability of response by individuals to ICS therapy and the complex issues surrounding asthma management makes this a challenging area of disease management which means that a simple recommendation of one molecule over another may not result in improved patient outcomes or quality of life.

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