National Institute for Clinical Excellence

Appraisal of the use of inhaler devices for routine treatment of chronic asthma in older children (aged 5-15years)

Decision of the Appeal Panel

1. Introduction

1.1 The Appeal Panel convened a hearing on the 13th February 2002 to consider an appeal against the Institute's Guidance to the NHS on the use of inhaler devices for routine treatment of chronic asthma in older children (aged 5-15 years) as set out in the Final Appraisal Determination of the Appraisal Committee (the "FAD").

1.2 The Appeal Panel comprised Professor Sir Michael Rawlins (Chair of the Panel and Chair of the Institute), Mercy Jeyasinham (non-executive director of the Institute), Roy Luff (non-executive director of the Institute), Dr Robert Donnelly (industry representative) and Mrs Joan Hansford (patient representative).

1.3 An appeal had been lodged by IVAX Pharmaceuticals UK ("IVAX")

1.4 The following individuals from the Institute who were involved in the appraisal were present to answer questions from the Appeal Panel: Andrew Dillon (Chief Executive and Executive Lead); Professor David Barnett (Chair, Appraisals Committee); Dr Carol Longson (Appraisals Programme Director); Nina Pinwill (Appraisals Co-ordinator).

1.5 The three grounds upon which the Appeal Panel can hear an appeal are:-

(1) The Institute has failed to act fairly and in accordance with the Appraisal Procedure set out in the Interim Guidance for Manufacturers and Sponsors;

(2) The Institute has prepared guidance which is perverse in the light of the evidence submitted

(3) The Institute has exceeded its powers.

IVAX submitted an appeal under ground (2), which they characterised as also being under 3.

2. Appeal Ground Two: The Institute has prepared guidance which is perverse in the light of the evidence submitted.

2.1 The recommendation in paragraph 1.2.1 of the FAD was perverse.

IVAX's submissions

IVAX contended that the Appraisal Committee's guidance, rcommending a press-and-breathe pressurised metered dose inhaler (pMDI) and suitable spacer device for the delivery of inhaled corticisteroids, was irrational and unsupported by proper evidence. In coming to this conclusion, the Committee had failed to take account of relevant evidence and had relied on irrelevant evidence.

IVAX alleged that the Appraisal Committee appeared to have based its conclusions on the balance of the available evidence, clinical opinion and pharmacological considerations, but that the Committee had failed to strike the right balance. In paragraph 4.14 of the FAD, the Committee stated that the available evidence fails to distinguish adequately between devices to suggest significant advantage in clinical effectiveness for one single delivery system. Moreover, expert clinical opinion appeared to emphasise the importance of patient choice rather than the superiority of one particular delivery system. Finally, the Easi-Breathe device avoids the co-ordination problems inherent with the press and breathe pMDIs, and the small volume spacer (which is routinely included) reduces oropharyngeal deposition of active drug.

Appraisal Committee's submissions

In response to questions from the Panel Professor Barnett explained that both the clinical experts, and the patient representatives, emphasised the overiding importance of individual preference in choosing inhaler devices for children. The clinical experts also emphasised that, in this age group, there was a greater imperative for the regular use of preventative treatments (anti-inflammatory products such as inhaled corticosteroids) rather than symptomatic treatments (bronchodilators). For these reasons the FAD stresses, in paragraph 1.1, the importance of individual preference and acceptability; and in paragraphs 1.2.1 and 1.2.2, the FAD distinguishes between devices delivering anti-inflammatory agents from those delivering bronchodilators.

Professor Barnett continued by explaining that expert clinical opinion, expressed orally to the Appraisal Committee, supported the use of press-and-breathe pMDIs with a spacer. The Committee considered that the acceptability of press-and-breathe pMDIs was greater for inhaled corticosteroids than for inhaled bronchodilators because the former only required twice daily administration. Children did not, therefore, need to take press-and-breathe pMDIs delivering corticosteroids to school; thus embarrasment was avoided. On the other hand, the more frequent use of inhaled bronchodilators required a greater choice of delivery devices to be considered and paragraph 1.2.2 was intended to reflect this. Professor Barnett also confirmed that the Committee had given full consideration to the potential benefits of Easi-Breathe; they were aware that the device was routinely supplied with a small volume spacer and that it was quieter when operated. Nevertheless, expert opinion proposed that press-and-breathe pMDIs with a suitable spacer should be the first choice for the administration of inhaled corticosteroids. The pharmacological considerations that the Committee had considerd were primarily related to the extent of deposition of corticosteroids in the oropharynx and hence the potential for systemic absorption.

Professor Barnett stated that the Appraisal Committee was cognisant of the evidence submitted by IVAX. He said that the Appraisal Committee had taken IVAX's evidence fully into account. Paragraph 1.2.1 of the FAD states that whilst press-and-breathe pMDIs are recommended as the first choice, they may not be suitable in a particular case; and that the general guidance as to choice in paragraph 1.1 must take precedence.

Professor Barnett said that the Appraisal Committee took into account that published evidence was not strongly indicative of one device over another, but also took account of the witness and oral submissions at the Appraisal Committee meeting, which did support the recommendation made in paragraph 1.2.1.

Appeal Panel's decision

The Appeal Panel noted that there was a lack of good quality published evidence indicating that one device rather than another should be preferred for the delivery of inhaled corticosteroids. The Appeal Panel noted that the Appraisal Committee had therefore given primacy in its guidance to a statement that factors relating to the individual patient should be taken into account. The Appeal Panel did not consider that the Appraisal Committee had acted perversely in basing its guidance, in paragraph 1.2.1, on clinical opinion, in the absence of good quality published evidence. Whilst the Panel would

normally expect the Committee to base its advice on the results of formal studies, such an approach was impossible in this instance, but the opinions of experts in the field could properly be given weight and published, in the form of a suitably worded recommendation, to the health profession at large. The Panel also noted that whilst the Guidance was not supported by good quality published studies, it was not contradicted by any such studies either. The Panel therefore considered that the Committee had not acted perversely in making the qualified recommendation in paragraph 1.2.1.

The Appeal Panel also observed that the Guidance had to be read as a whole, and that the recommendations taken together with the analysis contained in the rest of the document did not constitute perverse guidance.

The Panel therefore rejected the appeal on this point.

2.2 Appeal Ground Three: The Institute has exceeded its powers

The Appeal Panel did not consider that describing the basis of the appeal on this alternative ground introduced any considerations which had not been addressed under ground two. For the reasons set out in the Appeal Panel's decision on appeal ground two, the Appeal Panel did not consider that the Institute has exceeded its powers.

The Panel therefore rejected the appeal on this point.

3. Outcome of Appeal

The Panel dismissed the appeal on the point put forward by IVAX. The Guidance will therefore be issued to the NHS without amendment.

There is no possibility of a further appeal within the Institute against this decision of the Appeal Panel. However, the decision of the Appeal Panel and the Institute's decision to issue the Guidance may be challenged by an interested party through an application to the High Court for permission to apply for judicial review. Any such application must be made promptly and in any event within three months of this Decision or the issue of the Guidance.