NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Appeal Hearing

Inhaled corticosteroids for the treatment of chronic asthma in adults and in children aged 12 years and over.

Decision of the Appeal Panel

Introduction

1. An Appeal Panel was convened on 9th January 2008 to consider an appeal against the Institute's Final Appraisal Determination (FAD), to the NHS, on the use of inhaled corticosteroids for the treatment of chronic asthma in adults and in children aged 12 years and over.

2. The Appeal Panel (the 'Panel') consisted of Mr. Jonathan Tross (non-executive director of the Institute and chair of the Panel), Professor Sir Michael Rawlins (chair of the Institute), Ms. Jenny Griffiths (non-executive director of the Institute), Professor Peter Stonier (Industry representative), and Mrs. Alison Hawdale (Lay Member). All members confirmed they had no interest to declare in respect of the appeal under consideration.

3. The Panel considered an appeal submitted by TEVA UK Limited.

4. There are three grounds on which an appeal can be lodged:

1. The Institute has failed to act fairly and in accordance with the published procedures as set out in the Institute's Guide to the Technology Appraisal Process;
2. The Institute has prepared guidance that is perverse in light of the evidence submitted;
3. The Institute has exceeded its legal powers.

4. The chair of the Appeals Committee (Mr Mark Taylor), in preliminary correspondence, had confirmed that the appellant had potentially valid grounds of appeal in relation to Ground 2 (perverse guidance).

5. However, in view of the nature of the appeal, the chair of the Appeals Committee proposed that, rather than an oral hearing, the Panel should reach a decision on the written evidence. That is, the letter of appeal would be passed to the appraisal committee for comment. Further comments on that response from the company would go with the original appraisal documents to the Appeal Panel for consideration. The company confirmed that they were content with this process.

6. Given this process, neither the appellant nor the Appraisal Committee were represented at the consideration of the appeal by the Panel. Nor were members of the public or a legal adviser present. Two members of the Panel were present at NICE's offices in High Holborn; the remaining members took part simultaneously by teleconference.

7. The Final Appraisal Determination considered at this Appeal provided guidance on the use of corticosteroids for the treatment of asthma in adults and in children aged 12 years and over.

Ground of Appeal

8. The Company's specific argument that the guidance was perverse in the light of the evidence focused on the impact of cost comparisons presented in Sections 4.2.5 and 4.2.6 of the FAD. The passages objected to concern comparisons of two dosage ranges between particular drugs in the inhaled corticosteroid (ICS) class of drugs. The company argued that the presentation of weighted averages in the appraisal, which suggested that when products containing a chlorofluorocarbon (CFC) propellant are excluded (because such products are being phased out) then fluticasone propionate (FP) is on average cheaper than beclometasone dipropionate (BDP), was perverse.

9. More particularly, the company argued that the conclusion reflected flaws in the calculations arising from: a) combining data for BDP products administered by metered dose inhaler (pMDI, some of which contain CFC and some not) with data for BDP administered as a dry powder inhaler (DPI, which was more expensive); b) assumptions about future prescribing patterns after

the withdrawal of CFC-using products; c) weaknesses in the Prescription Costs Analysis ('PCA') data on quantities prescribed; and d) assumptions about clinical patterns of prescription.

10. In a written response the Chair of the Appraisal Committee had argued: a) that the paragraphs appealed against were in the evidence section of the FAD not the formal guidance (which had not been challenged); b) that the comparisons were not obviously and unarguably wrong; and c) that the Committee was conscious that use of both weighted and unweighted averages for particular drugs concealed individual variations. He argued that this was properly reflected in the non-specific formal recommendation (FAD paragraphs 1.1 and 1.2) that the least costly product that is suitable for the patient should be used. While not accepting that the two paragraphs were factually inaccurate, he proposed revised versions of both to clarify that the cheapest product may not be a product containing the corticosteroid drug that was cheapest on average.

11. The company in a further written submission continued to challenge the specific calculations for BDP distributed through pMDI devices. While welcoming the suggested changes to the two paragraphs, the company argued that this did not sufficiently address their concern at the implications of the overall average price comparisons when CFC products are removed from the comparisons.

Consideration by the Appeal Panel

12. The Appeal Panel noted that the substantive recommendation in the formal guidance – that the least costly inhaled corticosteroid suitable for the individual should be used – was not challenged. Nor was the Appraisal Committee finding that there was no persuasive evidence of significant differences in effectiveness between drugs in the ICS class. That is, the choice is essentially to do with which product suits the individual patient and the price. Therefore, what was at issue was the technical comparison of costs of different products and whether flaws in the calculation had the effect of undermining the formal guidance in a way that rendered that guidance perverse in the light of the evidence.

13. As the economic analysis undertaken for the Appraisal Committee records, the Panel noted that cost comparisons of ICS drugs are far from straightforward. This is because: a) there are a number of ICS products available from different manufacturers at different prices; b) the ICS products use different delivery mechanisms (in particular there is a choice between pMDI and

DPI devices); c) ICS products are available in different strengths with different equivalence in terms of the amount of active ingredient needed for a given effect (linked to particle size and the delivery mechanism); and d) products with different strengths are used in relation to the various steps in the treatment of asthma.

14. There is therefore a variety of options for treatment by a corticosteroid, particularly for a long-established drug like BDP available in multiple versions.

15. The analysis produced for the Appraisal Committee calculated a mean annual patient cost of taking each preparation of each drug to achieve an equivalent given level of effective treatment. It looked at low and high dosage levels relating to different steps in the treatment of asthma. It did so using alternative presentations of the results:

1. Taking the annual equivalent cost for achieving an equivalent treatment effect , simply summing the available products and dividing by the number of those products;
2. Weighting the average by the relative quantity of the drug prescribed as recorded by the PCA.

16. There is a further complication on which the Appraisal Committee sought to reflect. A significant proportion of BDP pMDI products contain CFC which is being phased out. Therefore the analysis sought to anticipate this by making cost comparisons both with and without the products containing CFC propellants.

17. The issue is the effect of the comparisons which seek to capture an average for the separate individual corticosteroids; and which combine within the calculation for each ICS what can be numerous product permutations. To illustrate (and simplify) in relation to the issue underlying the appeal:

- When the averages are not weighted for usage, BDP is a cheaper ICS than FC.
- The cheapest individual ICS products typically contain BDP delivered through a pMDI device using CFC.
- There is a price differential between BDP delivered through a pMDI device and BDP delivered through a DPI device, which is more expensive.

- Because a significant proportion of prescriptions are for cheaper BDP CFC-using products, excluding CFC-using products increases the average price.
- FC products do not use CFC so the effect of excluding such products has no impact on the average cost of FC.
- When the averages anticipate the phasing out of CFC by excluding the relevant products and are weighted to reflect assumptions about future quantities prescribed, then the effect of the more expensive DPI versions of BDP and the way the PCA records volumes of DPI products tip the price comparison adversely against BDP products in favour of FC.

18. On the issue of the cost comparisons the Panel concluded the following.

- It would be unusual and unhelpful, given NICE's remit, to give no discussion of cost comparisons in guidance to the NHS, particularly given that there was no persuasive evidence on differential effectiveness between drugs in the ICS class.
- It is inescapable, for the reasons given above, that cost comparisons are complicated and that the results when taken as averages may be sensitive to the basis and assumptions of the calculations.
- To help the NHS assess the overall cost impact, it is reasonable to adjust for equivalence in effect and to seek to reflect relative quantities of products.
- It is also sensible to calculate comparisons which seek to anticipate the phasing out of products using CFC. Otherwise the information could be rapidly out of date.
- As the cost comparisons are expressed in overall average terms and expressed in a qualified manner, these do not state that one drug within the class of ICS drugs is automatically cheaper than another irrespective of the dosage and delivery mechanism.
- So which corticosteroid is the cheapest option, depends essentially on the particular product chosen and the delivery mechanism which is in turn linked to what suits the patient.
- That is what the formal guidance says. The more detailed cost comparisons provide more information but do not alter that formal recommendation

19. The Panel concluded that the way the cost comparisons were handled was not unreasonable, given the complications of doing so. The simplest alternative would have been to contain no cost comparison evidence, leaving only the non-specific recommendation. That would have had the effect of excluding the positive references to BDP as well as the specific reference that was the

source of the appeal. It is possible that different assumptions or weightings on usage might produce some variation in the detailed cost comparisons. However the Panel concluded this would not invalidate the formal recommendation in the guidance itself, which has not been challenged.

20. In conclusion the Panel did not uphold the appeal that the guidance in the FAD is perverse. The Panel gave particular weight to the following.

- The formal recommendation is not product or delivery mechanism specific. It recommends the '… least costly product that is suitable for an individual within its marketing authorisation…'. That is the substantive advice to the NHS, which has not been challenged.
- The material that was the trigger for the appeal is clearly in a section dealing with the consideration of the evidence, separate from the formal recommendation in the guidance.
- The amendments to Sections 4.2.5 and 4.2.6 proposed by the Appraisal Committee, in the further exchanges before the Panel's consideration, make it clear that 'the weighted and unweighted mean costs for each drug conceal variation in the costs of individual generic or branded inhalers, and the cheapest product may not be a product containing the corticosteroid drug that was cheapest on average.'

The Panel considered that the Appraisal Committee's response appropriate and proportionate in relation to the concerns of the appellant.

Conclusion

21. The Appeal Panel rejects this appeal on the points put forward by the Appellants. It does, however, in doing so, endorse the inclusion in the FAD of the suggested amendments to Sections 4.2.5 and 4.2.6 which further clarify that overall averages may not signify the cheapest ICS product in a particular dosage strength or delivery mechanism.

22. There is no possibility of further appeal within the Institute against this decision of the Appeal Panel. However, the decision of the Appeal Panel 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 issuing of the Guidance.