

15 May 2007

NICE HTA: Corticosteroids for the treatment of chronic asthma in adults and children aged 12 years and over – Appraisal Consultation Document (ACD)

Many thanks for providing the ACD for the above appraisal. AstraZeneca welcomes this opportunity to comment and is generally supportive of the recommendations contained within the ACD. Please find specific further comments below.

ACD recommendations

As stated above AstraZeneca broadly agrees with the preliminary recommendations. However, AstraZeneca is concerned that readers could misinterpret the recommendation in Section 1.2. AstraZeneca suggests the paragraph is amended to clarify the conclusions on the two combination inhalers. AstraZeneca suggest the paragraph is changed to:

1.2 For people in whom treatment with ICSs and long-acting beta-2 agonists (LABAs) is considered appropriate (step 3 of the BTS/SIGN guidelines), the use of a combination device is recommended as an option. The decision about whether to use a combination device or the two agents in separate devices should be made on an individual basis, taking into consideration the likelihood of treatment adherence as well as individual preferences. If both options are considered equally appropriate then the least costly product or combination of products that is suitable for the person is recommended, bearing in mind that no combination inhaler is cheapest in all circumstances.

Adjustable dosing with combinations'

When the technology Assessment Report (TAR) was made available for consultation in January 2007, AstraZeneca commented that as well as comparing fixed dosing regimens of combination inhalers, the TAR should also include a discussion on the use of adjustable dosing which allows treatment to be tailored to individual patient's needs. AstraZeneca is surprised that the assessment groups have not supplied a response to this comment. In addition the ACD does not discuss the availability of flexible dosing with combination inhalers or the advantages they provide. For example, the combination inhaler Symbicort can be administered as Symbicort Adjustable Maintenance Dose (AMD) that maintains asthma control, while reducing exacerbations and drug load compared with fixed dosing. AstraZeneca received UK marketing authorisation for this in May 2001. AstraZeneca suggests that the Final Appraisal Determination (FAD) contains a discussion of the availability and benefit of adjustable dosing.

Cost-effectiveness

In Section 4.2.9 the conclusion is that there is no combination inhaler that is cheapest in all circumstances. AstraZeneca agrees with this, but would like to

highlight three studies that were discussed in our submission of evidence. Firstly, a study of 1719 UK patients who were randomised to either budesonide/formoterol adjustable dosing or budesonide/formoterol fixed dosing demonstrated that adjustable dosing resulted in an annual per patient cost saving of £65.70¹. Secondly, in a randomised study of 1034 patients in Sweden, budesonide/formoterol adjustable dosing compared with budesonide/formoterol fixed dosing was associated with fewer exacerbations, fewer daily inhalations of budesonide/formoterol, and lower costs (six-month saving Euros 98, p<0.001)². Finally, the reduction in exacerbations and reliever medication usage with budesonide/formoterol adjustable dosing compared to budesonide/formoterol fixed dosing was also demonstrated in a study of 658 patients³. This reduction is also likely to lead to budesonide/formoterol adjustable dosing being associated with a lower cost than budesonide/formoterol fixed dosing. In light of these three studies and the potential of the paragraph being misinterpreted, AstraZeneca suggest that the paragraph be amended in the FAD to say:

4.2.9 When comparing the costs of the two combination inhalers budesonide/formoterol and fluticasone propionate/salmeterol there is no combination inhaler that is cheapest in all circumstances, and the difference in cost of the cheapest options is minimal. For example, at the lower dose level the fixed dose 200mcg/6mcg budesonide/formoterol DPI taken one inhalation twice daily costs £231/year. The corresponding cost of fluticasone propionate/salmeterol will vary depending on the device that is prescribed. The fixed dose 100mcg/50mcg fluticasone propionate/salmeterol DPI taken one inhalation twice daily costs £379/year; whereas the fixed dose 50mcg/25mcg pMDI taken two inhalations twice daily costs £221/year. In addition, the use of adjustable dosing can reduce costs compared to fixed dosing.

¹ Price D, et al. (2004) An economic evaluation of adjustable and fixed dosing with budesonide/formoterol via a single inhaler in asthma patients: the ASSURE study. *Curr Med Res Opin.* 20(10):1671-9.

² Stallberg B, et al. (2003) Budesonide/formoterol adjustable maintenance dosing reduces asthma exacerbations versus fixed dosing. *Int J Clin Pract.* 57(8):656-61.

³ Aalbers R, et al. (2004) Adjustable maintenance dosing with budesonide/formoterol compared with fixed-dose salmeterol/fluticasone in moderate to severe asthma. *Curr Med Res Opin.* 20(2):225-40.