CASE AUTH/1853/6/06

ANONYMOUS HOSPITAL CONSULTANT v ASTRAZENECA

Symbicort journal advertisement

An anonymous hospital consultant complained about a journal advertisement for Symbicort (budesonide/formoterol), issued by AstraZeneca. The advertisement was headed 'Improving survival in COPD' and consisted of two columns of text. At the top of the right hand column, and thus immediately below the heading, was a diagram showing that treating 100 patients with Symbicort for 1 year vs formoterol alone could prevent 47 exacerbations. The prescribing information for Symbicort was provided at the bottom of the page.

The complainant was concerned that AstraZeneca appeared to be claiming that Symbicort improved survival in COPD without any evidence other than a study with an alternative medicine.

The Panel noted AstraZeneca's submission that there were data to show a link between frequent exacerbations and increased mortality and that combination therapy of the same type as Seretide as a class, was associated with reduced mortality. The Panel considered, however, that the advertisment implied that Symbicort in particular had been shown to improve survival in COPD and this was not so. The claim was misleading and could not be substantiated. The Panel ruled a breach of the Code.

An anonymous hospital consultant with an interest in respiratory diseases complained about a journal advertisement (ref SYM 06 18758) for Symbicort (budesonide/formoterol), issued by AstraZeneca UK Limited and published in the BMJ.

The advertisement was headed 'Improving survival in COPD' and consisted of two columns of text. At the top of the right hand column, and thus immediately below the heading, was a diagram showing that treating 100 patients with Symbicort for one year vs formoterol alone could prevent 47 exacerbations. The prescribing information for Symbicort was provided at the bottom of the page.

COMPLAINT

The complainant stated that AstraZeneca appeared to be claiming that Symbicort improved survival in COPD without any evidence other than a study with an alternative medicine.

Was this permitted? The complainant would be grateful if it was investigated as it was typical of pharmaceutical company activity where a class action was claimed for efficacy but never for safety.

When writing to AstraZeneca the Authority asked it to respond in relation to Clauses 7.2 and 7.4 of the Code of Practice.

RESPONSE

AstraZeneca accepted in hindsight that the juxtaposition of the advertisement's title 'Improving Survival in COPD' to the diagram indicating the data for Symbicort on exacerbation reduction could be potentially misconstrued as Symbicort having demonstrated a direct effect on mortality which was not what it had intended. AstraZeneca accepted a breach of Clause 7.2. However, the company denied a breach of Clause 7.4 since the data presented was valid and capable of substantiation.

The advertisement described how the inhaled corticosteroid and long-acting beta 2 agonist (ICS/LABA) class had several beneficial effects including reducing severe COPD exacerbations and overall COPD mortality.

The introduction stressed the serious clinical consequences of COPD and the burden it placed on the health service. In fact, COPD was the only major disease in the developed countries for which mortality was increasing. Of particular relevance was the prediction that it would become the third leading cause of death by 2020.

The strong link between frequent exacerbations and increased mortality was well established (as described in the first section of the article). The study cited in the advertisement (Soler-Cataluna *et al* 2005) demonstrated that, over a 5-year period, patients with 3 or more exacerbations per year had a four times greater risk of dying compared with those with no exacerbations. More frequent exacerbations were also associated with a greater deterioration in lung function, which in turn left patients more vulnerable to further exacerbations. And lastly, more frequent exacerbations were associated with greater reductions in quality of life, which in turn was an independent predictor of mortality.

Taking all this together, reducing the frequency of COPD exacerbations was a clear treatment goal that in turn reduced the decline in lung function, improved quality of life, and (of most relevance to the advertisement) decreased mortality associated with COPD. Thus, a key goal in COPD management was the prevention of exacerbations as reflected in COPD treatment guidelines.

The second section 'Managing exacerbations with combination treatment' emphasised the efficacy of Symbicort at reducing the frequency of exacerbations and improving health-related quality of life in comparison to LABA monotherapy in two Symbicort pivotal trials. This added to the substantial body of evidence that ICS/LABA combination therapy reduced COPD exacerbations and improved quality of life. This evidence formed the basis of both international (GOLD) and national (NICE and BTS) evidence-based treatment guidelines regarding the use of ICS/LABA to reduce the exacerbation rate in patients with severe COPD.

There were also extensive data relating to a class effect in reducing mortality. Firstly, ICS monotherapy reduced mortality in the majority of observational studies. ICS was the component of the ICS/LABA combination that was thought to have the greatest effect in this regard. Secondly, ICS/LABA combination therapy itself reduced mortality in both retrospective observational studies and in a recently published post-hoc pooled analysis of the two previously mentioned Symbicort COPD pivotal trials. This pooled data showed that treatment for severe COPD patients treated with budesonide added to formoterol (Symbicort) or terbutaline alone; a short acting bronchodilator (SABA) reduced the risk of mortality compared with patients treated with only a LABA (formoterol) and/or SABA (terbutaline). The results showed fewer deaths in the combined budesonide and budesonide plus formoterol (Symbicort) group compared with the bronchodilator group (p=0.037). This represented a 44% reduction in all-cause mortality over one year for patients treated with budesonide-containing therapy. This new data from the same author of the TORCH study corroborated the findings of the TORCH study and whilst these abstracts were not published when the advertisement was published, the data was available on request. Thus in consideration of this pool of clinical data, it was justifiable to claim that ICS/LABA as a class was associated with a reduction in mortality.

Finally the complainant was concerned that AstraZeneca was claiming a class effect without consideration for safety. In fact combination ICS/LABA products had a good risk benefit profile as indicated in the available evidence for these products in patients with COPD. There were no specific safety issues other than those noted in the prescribing information for Symbicort. The prescribing information was included in the advertisement along with all the relevant safety information.

PANEL RULING

The Panel noted AstraZeneca's submission that there were data to show a link between frequent exacerbations and increased mortality and that ICS/LABA as a class was associated with a reduction in mortality. The Panel considered, however, that the advertisment implied that Symbicort in particular had been shown to improve survival in COPD and this was not so. The claim was misleading and could not be substantiated. The Panel ruled breaches of Clauses 7.2 and 7.4 of the Code.

Complaint received **27 June 2006**

Case completed **18 August 2006**