CASE AUTH/2006/5/07

PHARMACIST PRACTITIONER v GLAXOSMITHKLINE

Promotion of Seretide

A pharmacist practitioner at a general practice complained about the promotion of Seretide (salmeterol/fluticasone) by GlaxoSmithKline.

Seretide was indicated for the symptomatic treatment of patients with severe chronic obstructive pulmonary disease (COPD) (FEV1 <50% predicted normal) and a history of repeated exacerbations, who had significant symptoms despite regular bronchodilator therapy.

The complainant was at a GlaxoSmithKline meeting where the representatives had displayed a graph, apparently from the Towards a Revolution in COPD Health (TORCH) study showing the mortality outcome. This was annotated in large type highlighting the 16% reduction in mortality, which was not statistically significant. Text below was along the lines of 'Seretide led to a non-statistically significant 16% reduction in mortality'. The complainant's concern was that although factual the graph was unprofessional and misleading, to a passing observer, to which it was targeted, it could be construed as stating Seretide reduced mortality in COPD, which it did not. The outcome was not statistically significant.

The Panel noted that the exhibition display comprised three panels. That described by the complainant was headed 'TORCH 3 YEAR Landmark Study' followed by 'Primary outcome - Seretide 500 Accuhaler survival result'. A graph beneath plotted the probability of death (%) against time to death (years) alongside an emboldened downward arrow and the prominent claim '16.5% risk reduction with Seretide 500 Accuhaler vs control p=0.096'. A highlighted box underneath read 'TORCH shows a trend towards improved survival with Seretide 500 Accuhaler vs control over 3 years which is non-statistically significant - the probability of death at any point over the 3 year study was reduced by 16.5% with Seretide 500 Accuhaler vs control (p=0.096)'.

The Panel considered that overall the exhibition panel detailing the mortality data did not make it sufficiently clear that the data was not statistically significant, particularly given the description of TORCH as a landmark study. The Panel considered that on glancing at the exhibition panel delegates would be struck by the prominent subheading 'Primary outcome - Seretide 500 Accuhaler survival result'. The results were then depicted in the graph which showed a visual difference between Seretide and the control group alongside the emboldened arrow and '16.5%' which was in a larger, bolder typeface than the explanatory text immediately below. A delegate who did not take the time to read the entire exhibition panel would be left with the impression that the 16.5% risk reduction was statistically significant. The Panel considered that graph was misleading and that its content could not be qualified by the text below. Breaches of the Code were ruled.

A pharmacist practitioner at a general practice, complained about the promotion of Seretide (salmeterol/fluticasone) by GlaxoSmithKline UK Ltd.

Seretide was indicated for the symptomatic treatment of patients with severe chronic obstructive pulmonary disease (COPD) (FEV1 <50% predicted normal) and a history of repeated exacerbations, who had significant symptoms despite regular bronchodilator therapy.

COMPLAINT

The complainant explained that he had attended a GlaxoSmithKline meeting where the representatives had had a number of small display boards. The first of these pictured a graph, apparently from the Towards a Revolution in COPD Health (TORCH) study showing the mortality outcome in the study. This was annotated in large type highlighting the 16% reduction in mortality, which was not statistically significant. Text below reinforced the 16% reduction, the complainant could not remember the exact wording but it was along the lines of 'Seretide led to a non-statistically significant 16% reduction in mortality'.

The complainant was concerned that, although factual, the use of such material was unprofessional and misleading. To a passing observer, to which these boards were targeted, they could be construed as stating Seretide reduced mortality in COPD, which it did not. Since the outcome was not statistically significant the complainant saw no place for promoting it or stating other than there was no effect seen.

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

RESPONSE

GlaxoSmithKline noted that the exhibition panel in question was entitled 'Primary Outcome – Seretide 500 Accuhaler survival result' (measured as all-cause mortality). The graph on the exhibition panel plotted the probability of death (%) vs time to death (years) and clearly reflected the non-significant 16.5% risk reduction seen with Seretide Accuhaler vs control. As the TORCH study included a patient group some of whom fell outside the licensed indication for Seretide in COPD, this relative risk reduction represented the sub-group analysis which only included patients within the UK licence for Seretide (FEV1 < 50%). The

p-value [p=0.096] was clearly shown on the graph and also stated in the associated text. It was also made clear that the primary endpoint did not reach statistical significance so as not to mislead. In the TORCH paper the authors suggested that the lower than anticipated number of deaths and the high withdrawal rate in patients receiving placebo (who were free to receive active therapy subsequently, including Seretide), might have contributed to the final results not reaching statistical significance.

As mentioned above, the mortality data represented the primary outcome of this landmark study. GlaxoSmithKline noted that it also presented a secondary endpoint [quality of life] from the study in another exhibition panel displayed at the meeting. To be able to present the secondary endpoint of this study it was important to clearly inform health professionals that the primary endpoint was statistically not significant to enable all the available evidence from the study to be put in context in a transparent manner. GlaxoSmithKline had not made any mortality claims. The need to present study data in the context of its primary parameter had been considered in a previous case (AUTH/1579/4/04) which GlaxoSmithKline took into consideration in preparing these materials to ensure balance and so as not to mislead.

The TORCH study was the first and largest study to prospectively investigate the potential for medicines to impact survival in patients with COPD and had been considered a landmark COPD study. It would be misleading, unprofessional and unethical to talk to health professionals about a clinically important study without reporting the primary endpoint or saying 'no effect seen' as suggested. Even though the primary endpoint was statistically not significant it was of clinical interest given the landmark nature of the study.

GlaxoSmithKline disagreed with the complainant's submission that the exhibition panel was 'targeted at' a 'passing observer'. It was exhibited at a meeting for health professionals capable of interpreting the relative importance of this data; if they had any questions they could have discussed these with a representative on the stand.

GlaxoSmithKline believed that the material presented in the exhibition panel was accurate, balanced, objective and unambiguous and based on an up-to-date evaluation of the evidence. It was clearly substantiated and the finding of a statistically non-significant primary endpoint was prominently stated. Therefore GlaxoSmithKline firmly believed that the exhibition panel reflected the TORCH primary outcome result and was thus not in breach of either Clause 7.2 or Clause 7.4.

PANEL RULING

The Panel noted that the exhibition display comprised three panels. That described by the complainant was headed 'TORCH 3 YEAR Landmark Study' followed by 'Primary outcome - Seretide 500 Accuhaler survival result'. A graph beneath plotted the probability of death (%) against time to death (years) alongside an emboldened downward arrow and the prominent claim '16.5% risk reduction with Seretide 500 Accuhaler vs control p=0.096'. A highlighted box underneath read 'TORCH shows a trend towards improved survival with Seretide 500 Accuhaler vs control over 3 years which is non-statistically significant - the probability of death at any point over the 3 year study was reduced by 16.5% with Seretide 500 Accuhaler vs control (p=0.096)'. One accompanying exhibition panel featured a photograph of a man and a boy and the claim 'Seretide is for patients who still have so much to live for'. The third presented the 3 year quality of life data, a secondary outcome wherein Seretide patients demonstrated a 2.7 improvement in their adjusted mean 3 year quality of life score vs a 0.7 decline in the control group; p<0.001.

The Panel noted GlaxoSmithKline's explanation that to be able to present the secondary endpoint data it was important to tell health professionals that the primary endpoint was not statistically significant. The Panel noted that nonetheless each exhibition panel had to be capable of standing alone as regards the requirements of the Code. The Panel considered that overall the exhibition panel detailing the mortality data did not make it sufficiently clear that the data was not statistically significant particularly given the description of TORCH as a landmark study. The Panel considered that on glancing at the exhibition panel delegates would be struck by the prominent subheading 'Primary outcome - Seretide 500 Accuhaler survival result'. The results were then depicted in the graph which showed a visual difference between Seretide and the control group alongside the emboldened arrow and '16.5%' which was in a larger, bolder typeface than the explanatory text immediately below. A delegate who did not take the time to read the entire exhibition panel would be left with the impression that the 16.5% risk reduction was statistically significant. The Panel considered that graph was misleading and that its content could not be qualified by the text below. This initial impression of the exhibition panel was misleading and could not be substantiated. Breaches of Clauses 7.2 and 7.4 were ruled.

Complaint received **30 May 2007**

Case completed **26 July 2007**