ASTRAZENECA V TRINITY-CHIESI

Fostair cost comparison chart

AstraZeneca complained that a cost comparison chart used by Trinity-Chiesi to promote Fostair (beclometasone 100mcg formoterol 6mcg) inhaler for asthma was incomplete, unfair and misleading. The chart compared the cost of Fostair, two puffs twice daily, with Seretide (GlaxoSmithKline's combination inhaler) two puffs twice a day, and AstraZeneca's combined corticosteroid/long-acting ß-agonist inhaler Symbicort. Symbicort was available in three strengths but only one (budesonide 200mcg plus salmeterol 6mcg (Symbicort 200/6)) was included in the chart – also at a dose of two puffs twice daily. For each inhaler the chart gave the NHS price for 30 days, the NHS price per patient per year, the annual NHS inhaler cost saving per patient with Fostair and the percentage annual inhaler cost saving per patient with Fostair. It was stated that there was a 23% annual saving if Fostair (two puffs bd) was used instead of Symbicort 200/6 (two puffs bd), and a 20% annual saving compared with Seretide. Despite ongoing inter-company correspondence about it, the chart appeared in a detail aid which had been prepared in April 2008, and contrary to assurances that it would be amended, in an advertisement in Pulse in June 2008

The cost comparison in Pulse was headed 'Fostair is less expensive than comparable doses of Symbicort or Seretide' referenced to Papi *et al* (2007a/b). Papi *et al* (2007a) compared Fostair with Symbicort 200/6. The claim was also referenced to MIMS May 2008. The cost comparison in the detail aid was headed '20% less expensive than other fixed combinations' and referenced to MIMS, March 2008.

The chart showed that Fostair was 23% cheaper than Symbicort in the doses chosen over a year. AstraZeneca considered that the chart was incomplete and misleading as it only showed one presentation and one dosing regimen for Symbicort, which happened to be more expensive than the Fostair comparator dose. Readers would be unaware that Symbicort was available in different presentations (eg 100/6 and 400/12) or that there were other dosing regimens including using Symbicort as maintenance and reliever therapy and that some of these regimens or presentations were cheaper than Fostair.

The detail aid produced in April 2008 contained the disputed chart when inter-company discussions about it were ongoing. The detail aid was not withdrawn as agreed as a representative gave it to a GP in mid-June 2008. The advertisement was not published until 25 June 2008 which gave Trinity-Chiesi ample time to change the chart before final copy was required. However it seemed that Trinity-Chiesi failed to do so and the chart was reproduced unaltered. AstraZeneca considered that this illustrated, at best, systematic failure of internal recall procedures and processes within Trinity-Chiesi to update material, or at worst, a blatant disregard for inter-company dialogue and failure to adhere to agreed undertakings.

The detailed response from Trinity-Chiesi is given below.

The Panel noted that the advertisement in Pulse had appeared as a double page spread. The left-hand page detailed the results of Papi *et al* (2007a) and showed that at a dose of two puffs twice daily Fostair and Symbicort (200/6), over a twelve week treatment period, resulted in comparable morning peak expiratory flows. The published paper concluded that the two products produced equivalent benefits in lung function and clinical symptoms and led to a significant decrease in the use of rescue medicines. No significant differences were observed in terms of rates of asthma exacerbations and/or the need for additional prevention therapy. The cost comparison chart appeared on the right-hand page under the heading 'Fostair is less expensive than comparable doses of Symbicort or Seretide' which was referenced to Papi *et al* (2007a/b) and to MIMS, May 2008. The strengths and doses cited in the chart were the same as those used in Papi *et al* (2007a).

The Panel considered that in the context of an advertisement which had discussed the results of Papi *et al* (2007a), it was not unreasonable to use a cost comparison chart based on those results. In that regard the Panel did not consider it was necessary to include other strengths or dosage regimens for Symbicort. The Panel noted AstraZeneca's submission with regard to Symbicort SMART (Symbicort as maintenance and reliever therapy). The Symbicort (200/6) summary of product characteristics (SPC) stated that SMART treatment should be especially considered for, *inter alia*, asthmatics with exacerbations in the past requiring medical intervention. One of the exclusion criteria in Papi *et al* (2007a) was three or more courses of oral corticosteroids or hospitalisation due to asthma in the previous 6 months. The Panel did not consider that, given the context in which it appeared, the chart was incomplete, unfair or misleading as alleged; it was clear that the figures cited were based on the results of Papi *et al* (2007a). The Panel ruled no breach of the Code.

With regard to the detail aid, the Panel noted that it

had detailed the results of the Papi *et al* studies. The Panel noted its comments regarding the cost comparison in the advertisement. The heading in the detail aid ('20% less expensive than other fixed combinations') was different to the heading in the advertisement. However taking all the circumstances into account the Panel did not consider that the cost comparison in the detail aid was incomplete, unfair or misleading as alleged. No breach was ruled.

AstraZeneca UK Limited complained about a cost comparison chart used by Trinity-Chiesi Pharmaceuticals Ltd to promote Fostair, its combined corticosteroid (beclometasone 100mcg) and long-acting ß-agonist (formoterol 6mcg) inhaler for asthma. The chart compared the cost of Fostair, two puffs twice daily, with Seretide (GlaxoSmithKline's combination inhaler) two puffs twice a day, and AstraZeneca's combined corticosteroid/long-acting ß-agonist inhaler Symbicort. Symbicort was available in three strengths but only one (budesonide 200mcg plus salmeterol 6mcg (Symbicort 200/6)) was included in the chart – also at a dose of two puffs twice daily. For each inhaler the chart gave the NHS price for 30 days, the NHS price per patient per year, the annual NHS inhaler cost saving per patient with Fostair and the percentage annual inhaler cost saving per patient with Fostair. It was stated that there was a 23% annual saving if Fostair (two puffs bd) was used instead of Symbicort 200/6 (two puffs bd), and a 20% annual saving compared with Seretide. The chart had appeared in an advertisement in Pulse in June 2008 (ref TRF0S20080298) and a detail aid (ref TRF0S20080198) which had been prepared in April 2008.

The cost comparison in Pulse was headed 'Fostair is less expensive than comparable doses of Symbicort or Seretide' referenced to Papi *et al* (2007a/b). Papi *et al* (2007a) had compared Fostair with Symbicort 200/6. The claim was also referenced to MIMS May 2008. The cost comparison in the detail aid was headed '20% less expensive than other fixed combinations' and referenced to MIMS, March 2008.

This case was considered under the 2008 Constitution and Procedure. The clauses cited by AstraZeneca, 7.2 and 7.3 were the same in the 2008 Code as in the 2006 Code.

COMPLAINT

AstraZeneca alleged that the cost comparison chart which compared acquisition costs for Fostair, Seretide and Symbicort was incomplete, unfair and misleading in breach of Clauses 7.2 and 7.3 of the Code. Following inter-company dialogue AstraZeneca had been reassured by Trinity-Chiesi that the chart would be amended and no longer used in its current format. However, AstraZeneca had evidence that Trinity-Chiesi had continued to use the offending chart despite this agreement and this now justified complaining to the Authority.

Both the advertisement and the detail aid contained the cost comparison chart that AstraZeneca had discussed with Trinity-Chiesi previously. The table showed the 30-day and one-year NHS acquisition costs for Fostair 100/6, Seretide 125/25 and Symbicort 200/6, all taken as two inhalations twice daily. The table showed that Fostair was 23% cheaper than Symbicort in the doses chosen over a year. AstraZeneca considered that the chart was incomplete and misleading as it only showed one presentation and one dosing regimen for Symbicort, which happened to be more expensive than the Fostair comparator dose. Readers would be unaware that Symbicort was available in different presentations (eg 100/6 and 400/12) or that there were other dosing regimens including using Symbicort as maintenance and reliever therapy (Symbicort SMART) and that some of these regimens or presentations were cheaper than Fostair.

The cost comparison chart was included in a document entitled 'Information for drugs and therapeutics committees' (ref TRFOS20070581) which was discussed in recent inter-company dialogue; AstraZeneca believed agreement was reached that the chart was incomplete and would be amended. In a letter dated 14 May, Trinity-Chiesi accepted AstraZeneca's rationale that the chart, if taken in isolation, might be considered incomplete and the company agreed to change it to show that the doses used were those taken from the randomised comparative studies and the chart was therefore able to stand in isolation of the document.

Having admitted that the chart was incomplete, AstraZeneca assumed that Trinity-Chiesi would comply with the spirit of the Code and withdraw not only the drugs and therapeutics document, but also all other potentially misleading materials promptly whilst it revised the chart.

The detail aid now at issue was produced in April 2008 and contained the disputed chart during the period where inter-company discussions about it were ongoing. It was clear that the detail aid was not withdrawn as agreed as it was given to a GP by a sales representative in mid-June 2008. The advertisement was not published until 25 June 2008 which gave Trinity-Chiesi ample time to change the chart before final copy was required. However it seemed that Trinity-Chiesi failed to do so and the chart was reproduced unaltered. AstraZeneca felt strongly that this illustrated, at best, systematic failure of internal recall procedures and processes within Trinity-Chiesi to update material, or at worst, a blatant disregard for the process of inter-company dialogue and failure to adhere to agreed undertakings.

RESPONSE

Trinity-Chiesi stated that the comparable dosages

used in the chart came from two published head-to-head studies, one which compared Fostair two puffs bd with Seretide 125/25 two puffs bd (Papi *et al* 2007b) and the other Fostair (n=109) two puffs bd with Symbicort 200/6 (n=110) two puffs bd (Papi *et al* 2007a). Both studies had similar design; phase III, multinational, multicentre, double-blinded, randomised, two-arm parallel groups and controlled trial lasting 12 weeks in moderate-to-severe asthmatics. The non-inferiority primary end-point of both studies was morning peak expiratory flow in the last two weeks of treatment and it showed no difference between the treatments for both studies. There were also no differences in the results for the secondary end-points measured in Papi *et al* (2007a) (Fostair vs Symbicort). Papi *et al* (2007a) was published in the official journal of the European Respiratory Society. Trinity-Chiesi believed that the comparable dosages used in the chart were scientifically and clinically validated and therefore complied with Clauses 7.2 and 7.3.

Furthermore, following inter-company dialogue in May 2008, Trinity-Chiesi agreed to amend the chart, as evident in the advertisement, by adding superscripts of the references of the two head-to-head studies in the heading above the table as follows: 'Fostair is less expensive than comparable doses of Symbicort or Seretide', referenced to Papi *et al* (2007a/b).

Trinity-Chiesi noted AstraZeneca's assertion that the chart should have included other available strengths of Symbicort (100/6 and 400/12) or other dosing regimens like Symbicort SMART. Trinity-Chiesi did not undertake to do this firstly because it was not incumbent for a company to include strengths or dosing regimen of competitors' products in its promotional materials without valid reasons to do so; secondly to have included these other strengths and dosing regimen of Symbicort could have misled the reader into thinking that Fostair had similar strengths and dosing regimen, which it did not. This was possible as both Fostair and Symbicort contained formoterol with a corticosteroid and finally Trinity-Chiesi mentioned only the doses of Fostair 100/6 and Symbicort 200/6 as used in Papi *et al* (2007a).

Trinity-Chiesi noted that the detail aid obtained by AstraZeneca was prepared in April 2008, ie before inter-company dialogue was concluded. Given that dialogue was only offered for closure by AstraZeneca on 27 May (by email), it was only reasonable that AstraZeneca allowed Trinity-Chiesi sufficient time to amend and re-print the detail aid. The April detail aid was re-issued by 12 June and the cost comparison chart was amended to be similar to that used in the advertisement. Given AstraZeneca's allegation that the April detail aid was used in mid-June, it would be helpful if it would give more details about exactly when and where the item was used. Trinity-Chiesi could investigate the matter and take the necessary action if one of its representatives had been proved to use the April detail aid after 12 June.

Trinity-Chiesi submitted that the cost comparison chart was fair, complete and was not misleading, and therefore did not breach Clauses 7.2 and 7.3.

Trinity-Chiesi stated that it had fulfilled its side of the inter-company agreement by amending the chart and the detail aid. Trinity-Chiesi wrote to AstraZeneca on 14 May with its undertakings but did not receive an acknowledgement until 27 May when it considered the complaint closed. Hence, it was reasonable for Trinity-Chiesi to use the April version of the detail aid until it instituted a change by 12 June. With regard to the chart itself, in a letter to AstraZeneca of 14 May Trinity-Chiesi undertook to change the chart to show that the doses cited were taken from the randomised comparative studies and the chart was therefore able to stand alone. As explained above, Trinity-Chiesi did not undertake to include information about other strengths of Symbicort (100/6 and 400/12) or other dosing regimens like Symbicort SMART. Trinity-Chiesi only mentioned the respective doses of Fostair and Symbicort 200/6 as used in Papi *et al* (2007a).

Trinity-Chiesi took inter-company undertakings seriously and in this instance it maintained that it fulfilled all its undertakings to AstraZeneca. Trinity-Chiesi believed that the amended cost comparison chart was fair, not misleading, and not in breach of Clauses 7.2 and 7.3.

PANEL RULING

The Panel noted that the advertisement in Pulse had appeared as a double page spread. The left-hand page detailed the results of Papi *et al* (2007a) and showed that at a dose of two puffs twice daily Fostair and Symbicort (200/6), over a twelve week treatment period, resulted in comparable morning peak expiratory flows. The published paper concluded that the two products produced equivalent benefits in lung function and clinical symptoms and led to a significant decrease in the use of rescue medicines. No significant differences were observed in terms of rates of asthma exacerbations and/or the need for additional prevention therapy. The cost comparison chart appeared on the right-hand page under the heading 'Fostair is less expensive than comparable doses of Symbicort or Seretide' which was referenced to Papi *et al* (2007a/b) and to MIMS, May 2008. The strengths and doses cited in the chart were the same as those used in Papi *et al* (2007a).

The Panel considered that in the context of an advertisement which had discussed the results of Papi *et al* (2007a), it was not unreasonable to use a cost comparison chart based on those results. In that regard the Panel did not consider it was necessary to include other strengths or dosage regimens for Symbicort. The Panel noted AstraZeneca's submission with regard to Symbicort SMART (Symbicort as maintenance and reliever therapy). The Symbicort (200/6) summary of

product characteristics (SPC) stated that SMART treatment should be especially considered for, *inter alia*, asthmatics with exacerbations in the past requiring medical intervention. One of the exclusion criteria in Papi *et al* (2007a) was three or more courses of oral corticosteroids or hospitalisation due to asthma in the previous 6 months. The Panel did not consider that, given the context in which it appeared, the chart was incomplete, unfair or misleading as alleged; it was clear that the figures cited were based on the strengths, dosages and clinical results of Papi *et al* (2007a). The Panel ruled no breach of Clauses 7.2 and 7.3.

With regard to the detail aid the Panel noted that the cost comparison chart appeared on page 9; pages 6, 7 and 8 had detailed the results of the Papi *et al* studies. The Panel noted its comments regarding the cost comparison in the advertisement. The heading in the detail aid ('20% less expensive than other fixed combinations') was different to the heading in the advertisement. However taking all the circumstances into account the Panel did not consider that the cost comparison in the detail aid was incomplete, unfair or misleading as alleged. No breach of Clauses 7.2 and 7.3 was ruled.

During its consideration of this case the Panel noted that the annual cost savings cited in the chart were based on patients taking a constant dose of Symbicort (200/6) and Fostair two puffs twice a day. This was the maximum dose for Symbicort (200/6) when used as maintenance therapy and the maximum dose for Fostair. The Symbicort (200/6) SPC stated for maintenance therapy 'In usual practice when control of symptoms is achieved with the twice daily regimen, titration to the lowest effective dose could include Symbicort given once daily …'. The Fostair SPC stated 'The dose should be titrated to the lowest dose at which effective control of symptoms is maintained. When control of symptoms is maintained with the lowest recommended dose, then the next step could include a test dose of inhaled corticosteroid alone'. The Panel thus queried the validity of extrapolating three month clinical data, using the maximum dose of each product, to one year financial data. The cost comparison chart implied that patients would take two puffs twice daily continuously and this would not necessarily be so. The Panel requested that Trinity-Chiesi be advised of its concerns in this regard.

Complaint received **28 July 2008**

Case completed **5 September 2008**