CASE AUTH/1986/4/07

ASTRAZENECA v GLAXOSMITHKLINE

Symbicort and Seretide cost comparisons

AstraZeneca complained about cost comparisons made by GlaxoSmithKline between AstraZeneca's Symbicort (budesonide/formoterol) and GlaxoSmithKline's Seretide (salmeterol/fluticasone propionate). The items at issue were a one page leavepiece and a slide from a presentation.

The leavepiece was headed 'Cost comparison for combination therapies in asthma at beclometasone equivalent daily doses' followed by 'Seretide (salmeterol/ fluticasone propionate) can be up to £35.08 cheaper for 30 days treatment at a stable dose than Symbicort (budesonide/formoterol) combination'. This was followed by a chart comparing various combinations and doses. The comparisons were grouped according to low dose steroid use (400mcg beclometasone equivalent daily dose), medium dose steroid use (800 - 1,000mcg beclometasone equivalent daily dose), and high dose steroid use (up to 2,000mcg beclometasone equivalent daily dose). The cost per 30 days' treatment at sustained dosing was given and the final column of the chart was headed 'Cost difference with Seretide per 30 day treatment'.

Five of the comparisons showed that there were savings using Seretide compared to sustained treatment with Symbicort, ranging from 86 pence to £35.08. Seretide was £12.19 more expensive than Symbicort in one of the low dose steroid use comparisons.

AstraZeneca alleged that the cost comparison shown in the leavepiece was misleading. In AstraZeneca's view the purpose of the leavepiece was to portray Symbicort as a significantly more expensive option than Seretide. This was not correct when one considered the overall price comparability across the range of their doses and when used similarly. The misleading purpose of the leavepiece was clear from the heading 'Seretide (salmeterol/fluticasone propionate) can be up to £35.08 cheaper for 30 days treatment at a stable dose than Symbicort (budesonide/formoterol) combination'. Although the potential cost difference referred to was the comparison of 30 days of Symbicort 400/12, two puffs bd vs Seretide 500 Accuhaler, one puff bd, this was an unfair comparison on which to base such a broad statement.

Symbicort 400/12, two puffs bd was not a normally recommended dose of Symbicort. The Symbicort 400/12 summary of product characteristics (SPC) stated that the recommended dose, was one puff bd. Although some adults might require up to two puffs bd. Thus very few prescriptions were for Symbicort 400/12, two puffs bd. In the chart the times where Symbicort was shown to be significantly more expensive than Seretide related to the use allowed of two puffs bd. Such comparisons were potentially unfair. Unlike pressurised metered dose inhalers (MDIs) such as Seretide Evohaler, where the unit dose was two puffs, the usual unit dose for dry powder inhalers such as Symbicort Turbohaler and Seretide Accuhaler was one puff. The marketing authorizations for Symbicort, unlike Seretide Accuhaler, allowed flexibility of dosing so the normal dose of one puff bd could be increased to two or even four puffs bd or indeed reduced to one daily. This flexibility allowed short term increases in dosage at times of increased symptoms. The Seretide Accuhaler marketing authorization did not permit similar flexibility as the recommended dose of each product strength was one puff bd, though this might in some cases be reduced to one puff daily. Dosage increases to two or four puffs bd of Symbicort would incur additional cost for the period that the higher dose was used, however, similar dosage increases with Seretide incurred further costs because a new prescription for a higher strength of Seretide would be needed. The cost impact of these important differences was omitted from the chart.

AstraZeneca considered that the statement of a price difference of up to £35.08 and the price comparisons which were based upon dosages of two puffs bd of Symbicort seriously misrepresented the overall price differences in clinical usage and were misleading and exaggerated.

The Panel noted that, according to the SPC, the recommended dose of Symbicort 400/12 was one puff bd and some patients might require up to a maximum of two puffs bd. Both doses appeared on the leavepiece in question.

The Panel noted AstraZeneca's comment that the usual unit dose for dry powder inhalers such as Symbicort Turbohaler was a single puff. However, the SPCs for Symbicort Turbohaler 100/6 and 200/6 gave doses of 1-2 puffs twice daily and stated that some patients might require up to a maximum of 4 puffs twice daily. It noted GlaxoSmithKline's submission that the cost difference in the low dose steroid (400mcg beclometasone equivalent) band related to Symbicort 200/6 one puff bd and Symbicort 400/12 od and that Symbicort 100/6 two puffs bd had been included for completeness.

The Panel noted that Symbicort allowed flexibility of dosing and patients could increase or decrease dosing. Although the leavepiece compared stable dosing there was no mention of flexible dosing with Symbicort which in the Panel's view was relevant even if the costs were clearly based on 30 days' stable dosing.

The Panel considered that the leavepiece was clear that it compared stable doses of Symbicort and Seretide over 30 days. The leavepiece did not imply equivalent control of asthma, it related to beclometasone equivalent daily doses. In that regard the Panel considered that like had been compared with like. However, the Panel considered that the claim that Seretide, '… can be up to £35.08 cheaper for 30 days' was misleading, not a fair comparison and exaggerated the differences between the products; there were instances when Seretide was more expensive than Symbicort. The Panel considered that the claim was not a fair reflection of all the data and was exaggerated. The Panel ruled breaches of the Code.

The slide at issue was headed 'Seretide and Symbicort'. The chart compared the 30 day cost of various presentations of the products at low dose (200mcg/day fluticasone 400mcg/day budesonide), medium dose (500mcg/day fluticasone 800mcg/day budesonide) and high dose (1000mcg/day fluticasone 1600mcg/day budesonide). The slide stated that 'All Seretide options gave 100mcg/day salmeterol'. The depictions of the cost of Symbicort also included the dose of formoterol.

AstraZeneca alleged that the slide was similarly misleading to the leavepiece. It compared the cost of Seretide Accuhaler one puff twice daily with Symbicort dosed at up to eight times daily.

The Panel noted that the dose of Seretide Accuhaler was one inhalation twice daily and Seretide Evohaler was two inhalations twice daily. The Panel considered that information presented in the slide was consistent with the SPC dosing instructions for the products. There was no mention of flexible dosing with Symbicort which in the Panels view was relevant.

The Panel considered that the slide, unlike the leavepiece, did not make it clear that the cost was based on a stable dose of the products. Thus the Panel considered that the slide was misleading and an unfair comparison. Breaches of the Code were ruled.

The Panel noted that the slide was effectively a bar chart presentation of the data shown in the leavepiece. Seretide bars were in purple and Symbicort were in red, with white text along them denoting the dose of formoterol. In the medium steroid dose (500mcg/day fluticasone; 800mcg/day budesonide) band extra Symbicort data had been added to that in the leavepiece ie the use of Symbicort 100/6, 4 puffs twice daily. Although the product could be used in that way, prescribers were much more likely to prescribe Symbicort 200/6 or 400/12 for long-term therapy for reasons of patient compliance and cost. The Panel considered that the addition of this data, and thus a prominent red bar, exaggerated the cost difference between Symbicort and Seretide. Without that bar prescribers would see that for low and medium steroid dose bands, Symbicort and Seretide were similarly priced. A breach of the Code was ruled.

AstraZeneca UK Limited complained about cost comparisons made by GlaxoSmithKline UK Ltd between AstraZeneca's Symbicort (budesonide/formoterol) and GlaxoSmithKline's Seretide (salmeterol/fluticasone propionate). The items at issue were a one page leavepiece (ref SFL/LVP/06/26861/2) and a slide from a presentation (ref SFL/SLK/06/28954/1).

1 Leavepiece SFL/LVP/06/26861/2

The leavepiece was headed 'Cost comparison for combination therapies in asthma at beclometasone equivalent daily doses' followed by 'Seretide (salmeterol/ fluticasone propionate) can be up to £35.08 cheaper for 30 days treatment at a stable dose than Symbicort (budesonide/formoterol) combination'. This was followed by a chart comparing various combinations and doses. The comparisons were grouped according to low dose steroid use (400mcg beclometasone equivalent daily dose), medium dose steroid use (800-1,000mcg beclometasone equivalent daily dose), and high dose steroid use (up to 2,000mcg beclometasone equivalent daily dose). The cost per 30 days' treatment at sustained dosing was given and the final column of the chart was headed 'Cost difference with Seretide per 30 day treatment'.

Five of the comparisons showed that there were savings using Seretide compared to sustained treatment with Symbicort. The savings made ranged from 86 pence to £35.08. Seretide was £12.19 more expensive than Symbicort in one of the low dose steroid use comparisons.

GlaxoSmithKline stated that the leavepiece had been used proactively and reactively by both primary care and secondary care representatives where there was a discussion on cost of Seretide. The leavepiece had also been mailed to health professionals in specific primary care trusts (PCT) regions where there had been pressure to switch to Symbicort from Seretide as a result of the perception that Symbicort was cheaper than Seretide.

COMPLAINT

AstraZeneca alleged that the leavepiece was misleading with respect to the relative cost of treatment with Symbicort compared to Seretide. In AstraZeneca's view the purpose of the leavepiece was to portray Symbicort as a significantly more expensive option than Seretide. This was not correct when one considered the overall price comparability of Symbicort with Seretide across the range of their doses and when used similarly. The misleading purpose of the leavepiece was clear from the heading 'Seretide (salmeterol/fluticasone propionate) can be up to £35.08 cheaper for 30 days treatment at a stable dose than Symbicort (budesonide/formoterol) combination'. Although the potential cost difference referred to was the comparison of 30 days of Symbicort 400/12, two

puffs bd vs Seretide 500 Accuhaler, one puff bd, this was an unfair comparison on which to base such a broad statement of price difference because:

a) Symbicort 400/12, two puffs bd was not a normally recommended dose of Symbicort. The recommended dose of Symbicort 400/12 as stated in its summary of product characteristics (SPC) was one puff bd. For adult asthmatics there was an additional statement that some patients might require up to a maximum of two puffs bd.

b) Consistent with this dosing recommendation only 2.2-3.6% of Symbicort prescriptions were for Symbicort 400/12, two puffs bd. A breakdown of prescribed doses was provided.

c) In the chart the occurrences where Symbicort was shown to be significantly more expensive than Seretide related to dosing regimens of two puffs bd. Such comparisons were potentially unfair. Unlike pressurised metered dose inhalers (MDIs) such as Seretide Evohaler, where the unit dose was two puffs, the usual unit dose for dry powder inhalers such as Symbicort Turbohaler and Seretide Accuhaler was one puff.

   The marketing authorizations for Symbicort, unlike Seretide Accuhaler, allowed flexibility of dosing so the normal dose of one puff bd could be increased to two or even four puffs bd or indeed reduced to one daily. This flexibility could be very useful in clinical practice and was utilised in patients' personal asthma action plans where short term increases in dosage might be recommended at times of increased symptoms. The Seretide Accuhaler marketing authorization did not permit similar flexibility as the recommended dose of each product strength was one puff bd, though this might in some cases be reduced to one puff daily.

   Dosage increases to two or four puffs bd of Symbicort would obviously incur additional cost for the period that the higher dose was maintained, however, similar dosage increases with Seretide incurred further costs because a new prescription for a higher strength of Seretide needed to be issued. The cost impact of these important differences between the products was omitted from the chart.

AstraZeneca considered that the statement of price difference of up to £35.08 and the price comparisons which were based upon dosages of two puffs bd of Symbicort seriously misrepresented the overall price differences between Symbicort and Seretide in clinical usage and were misleading, exaggerated and in breach of Clauses 7.2, 7.3 and 7.10 of the Code.

AstraZeneca stated that it had restricted its comments on the two items to specific aspects of the comparisons as presented. However the company noted that comparisons of this type between products that contained different inhaled steroids were complex because of the lack of consensus on equipotent doses of the different treatments. For example the British Thoracic Society/Scottish Intercollegiate Guidelines Network (BTS/SIGN) asthma guidelines suggested a 2:1 ratio in the equipotent doses of budesonide to fluticasone, but they noted that there might be variations with different delivery devices. Specifically with respect to the Turbohaler they stated 'There is limited evidence from two open studies of less than ideal design that budesonide via the Turbohaler is more clinically effective'. The more recent Global Initiative for Asthma (GINA, 2006) guideline advised a ratio of 8:5 in equipotent doses. The lack of consensus on equipotent doses added further complexity to the understanding of such these data and therefore it was not possible to make accurate direct comparisons between Symbicort and Seretide.

RESPONSE

GlaxoSmithKline noted AstraZeneca's statement that Symbicort 400/12 was not a normally recommended dose of Symbicort but further noted that it was clear from the SPC that two puffs bd was a recommended dose and it was therefore appropriate to include information regarding this dose.

The recommendations for stepwise management of asthma in adults published in the BTS Guideline on the Management of Asthma stated that:

> 'If control remains inadequate on 800mcg daily (adults) of an inhaled steroid plus a long-acting β2-agonist, consider the following interventions:
> - increasing inhaled steroids to 2000mcg/day (adults)…'

In such cases, the most appropriate formulation of Symbicort for delivering this dose would be Symbicort 400/12, two puffs bd.

Given that this dose of Symbicort was recommended in the SPC, and would be the most appropriate formulation for delivering high dose steroid (up to 2000mcg) it was entirely appropriate that this dose was included in the chart.

The IMS prescribing data showed that this dose was used in clinical practice, therefore it was appropriate to tell prescribers that in a stable dosing regimen required to deliver high dose steroid, Symbicort 400/12, two puffs bd was considerably more expensive [£76] than the equivalent beclometasone dose of Seretide, both via an Evohaler [£62.29] or in particular via an alternative dry powder device, the Accuhaler [£40.92].

GlaxoSmithKline stated that the actual frequency of prescribing of the doses referred to in the chart was irrelevant unless a claim of population or median dose was being made. Since no such claim was being made it was appropriate for GlaxoSmithKline to include this information in order to give a complete picture of the cost differences apparent throughout the range of doses and devices available with Seretide and Symbicort for use with all asthma patients receiving low, medium and high doses of steroid medication. This allowed prescribers to use this simple and factual

information based on doses used in clinical practice.

GlaxoSmithKline noted that AstraZeneca had claimed that in both the low dose and high dose bands, the occurrences where Symbicort was shown to be significantly more expensive than Seretide related to dosing regimens of two puffs bd. AstraZeneca claimed that such comparison was potentially unfair as unlike pressurised MDIs such as Seretide Evohaler where the unit dose was two puffs, the usual unit dose for dry powder inhalers such as Symbicort Turbohaler was one puff.

GlaxoSmithKline stated that unfortunately AstraZeneca's statements were factually incorrect on a number of counts:

Firstly, with regard to the low dose steroid (400mcg beclometasone equivalent) band, whilst a dosage regimen of two puffs bd had been included for Symbicort 100/6, the cost difference which was highlighted against the Seretide 50 Evohaler of a saving of at least 86 pence was a comparison of the cost of this device (£18.14) with the cost of either the Symbicort 200/6, one puff bd or Symbicort 400/12, one puff od (both £19), not the cost of Symbicort 100/6, two puffs bd (£33). Furthermore, the cost comparison of Seretide 100 Accuhaler with Symbicort, which highlighted that Seretide might be up to £12.19 more expensive, was a comparison with Symbicort 200/6, one puff bd and Symbicort 400/12, one puff od. It was interesting to note that if the comparison had been made with the two puffs Symbicort option which AstraZeneca had claimed had been done, this would actually have shown that Seretide 100 Accuhaler was £1.81 cheaper than Symbicort 100/6, two puffs.

Secondly, with regard to the high dose steroid (2000mcg beclometasone equivalent) band, it was impossible for GlaxoSmithKine to use anything but Symbicort 400/12, two puffs bd as the comparator. This dosage regimen of Symbicort 400/12 was included in the SPC, as a licensed dose, it was therefore an altogether appropriate dosage regimen for the delivery of a high dose steroid, required in some patients. Since Symbicort 400/12 Turbohaler was the highest dose presentation, there was no formulation of Symbicort that would deliver 2000mcg in a single puff dosing regimen. Consequently it was impossible for clinicians to use any Symbicort formulation for the delivery of 2000mcg in a single puff regimen, and as a result it was entirely logical for GlaxoSmithKline to include the two puffs dosing regimen in the table for the delivery of high dose steroid as this was how it would be delivered in practice.

Sections 4.2 of the Symbicort 100/6 and 200/6 SPCs gave the recommended doses as follows: 'Adults (18 years and older): 1-2 inhalations twice daily. Some patients may require up to a maximum of 4 inhalations twice daily' and 'Adolescents (12-17 years): 1-2 inhalations twice daily.'

It was clear therefore that the recommended doses of Symbicort were either one or two puffs twice daily, and the SPC made no recommendations or suggestions that one dosing regimen had any preference over another. AstraZeneca's suggestion that the usual unit dose for dry powder inhalers such as Symbicort Turbohaler was one puff was not supported by the SPC.

AstraZeneca also highlighted that the marketing authorizations for Symbicort and Seretide were different, and that the SPC for Symbicort allowed flexibility of dosing, with short term dose increases at times of increased symptoms, which was not permitted with Seretide. The purpose of the leavepiece was to compare the price of two competitor medicines based on the dose equivalents of beclometasone. As such the clinician could plainly see the dose equivalency. The suggestion that flexible use of Symbicort when control was lost altered the comparative acquisition cost of Seretide was not relevant. To include such data would require a comparative claim of the relative frequency of exacerbations from a head-to-head study to make such a comparison clinically relevant. This was not GlaxoSmithKline's intention and it made no claim in the leavepiece in that regard. As previously stated the intention of the leavepiece was a simple statement of the acquisition cost of two competitor products at relevant comparator doses. No statement of relative efficacy or frequency of exacerbations and thus dose escalation was made.

For the above reasons it was not relevant to compare costs when a flexible treatment approach was advocated without reference to clinical trial data. GlaxoSmithKline had compared the costs of treatment on the basis of a monthly stable treatment regimen which was factual and not misleading.

It was very useful for clinicians and prescribing advisors who often compared treatment options on the basis of a standard 30 days' treatment cost. Furthermore, whilst the use of Symbicort in a flexible dosing approach was an option, the SPC also recommended a stable dosing regimen reinforcing the fact that this information was consistent with the Symbicort SPC and clinical use.

Therefore it was entirely appropriate for GlaxoSmithKline to compare the costs of a stable dosing regimen of Seretide and Symbicort in order to guide treatment decisions. So as to limit the use of these cost comparisons to only this situation GlaxoSmithKline had made it quite clear in the leavepiece, both in the headline statement and the table, that the cost comparisons were for a stable dosing regimen:

- the headline statement clearly stated that Seretide could be up to £35.08 cheaper for 30 days treatment at a stable dose than Symbicort;
- the column heading in the table indicated cost/30 days treatment at sustained dosing.

In summary, GlaxoSmithKline did not agree that the leavepiece had been designed to deliberately mislead and that it seriously misrepresented the overall price differences. Symbicort was available in a range of formulations which were licensed to give a range of steroid doses by using either one or two puffs, and up

to four puffs, twice daily or even once daily. GlaxoSmithKline had been entirely transparent with the cost comparisons by including the full range of Symbicort Turbohaler devices, and the full range of dosing regimens, which were available to enable the administration of low, medium or high dose steroids; GlaxoSmithKline had clearly grouped the products according to these patient populations. Furthermore, GlaxoSmithKline had clearly stated where Seretide was both cheaper *and* more expensive than Symbicort, so in this regard the comparison was balanced, presented all the relevant information, and made no exaggerated claims. The headline clearly stated that Seretide *could* be cheaper than Symbicort, but did not make the claim that Seretide was *always* cheaper than Symbicort, and consequently this claim was not exaggerated or misleading. Furthermore the heading was balanced by the fact that all the relevant information about the cost of the products across the entire dose range was contained in a clear and obvious manner in the chart directly below it, in the same font and typeface.

PANEL RULING

The Panel noted that, according to the SPC, the recommended dose of Symbicort 400/12 was one puff bd and some patients might require up to a maximum of two puffs bd. Both doses appeared on the leavepiece in question.

The Panel noted AstraZeneca's comment that the usual unit dose for dry powder inhalers such as Symbicort Turbohaler was a single puff. However, the SPCs for Symbicort Turbohaler 100/6 and 200/6 gave doses of 1-2 puffs twice daily and stated that some patients might require up to a maximum of 4 puffs twice daily. It noted GlaxoSmithKline's submission that the cost difference in the low dose steroid (400mcg beclometasone equivalent) band related to Symbicort 200/6 one puff bd and Symbicort 400/12 od and that Symbicort 100/6 two puffs bd had been included for completeness.

The Panel noted that Symbicort allowed flexibility of dosing and patients could increase or decrease dosing. Although the leavepiece compared stable dosing there was no mention of flexible dosing with Symbicort which in the Panel's view was relevant even if the costs were clearly based on 30 day's stable dosing. With regard to AstraZeneca's comments about the lack of consensus on equipotent doses, the Panel noted that the Seretide SPCs stated that 100mcg of fluticasone propionate was approximately equivalent to 200mcg of beclomethasone dipropionate (CFC containing) or budesonide.

The Panel considered that the leavepiece was clear that it compared stable doses of Symbicort and Seretide over 30 days. The leavepiece did not imply equivalent control of asthma, it related to beclometasone equivalent daily doses. In that regard the Panel considered that like had been compared with like. However, the Panel considered that the claim that Seretide, '… can be up to £35.08 cheaper for 30 days' was misleading, not a fair comparison and exaggerated the differences between the products; there were instances when Seretide was more expensive that Symbicort. The Panel considered that the claim was not a fair reflection of all the data and was exaggerated. The Panel ruled breaches of Clauses 7.2, 7.3 and 7.10.

2 Presentation slide SFL/SLK/06/28954/1

The slide at issue was headed 'Seretide and Symbicort'. The chart compared the 30 day cost of various presentations of the products at low dose (200mcg/day fluticasone 400mcg/day budesonide), medium dose (500mcg/day fluticasone 800mcg/day budesonide) and high dose (1000mcg/day fluticasone 1600mcg/day budesonide). The slide stated that 'All Seretide options gave 100mcg/day salmeterol'. The depictions of the cost of Symbicort also included the dose of formoterol.

COMPLAINT

AstraZeneca stated that the slide emerged recently and since the concerns were very similar to the first item, AstraZeneca considered it appropriate to include it in this complaint even though it had not been discussed specifically with GlaxoSmithKline.

AstraZeneca alleged that the slide was similarly misleading to the leavepiece because:

a) It compared the cost of Seretide Accuhaler one puff twice daily with Symbicort dosed at up to eight times daily. For example: in the 'medium dose' band Seretide 250 one puff bd was compared with the cost of Symbicort 100/6 four puffs bd. Although this dosage of Symbicort was within the terms of the marketing authorization, it was misleading to represent it as a comparator when higher strength Symbicort presentations were available which were more appropriate other than for very short-term use.

b) As described above, increasing the number of puffs of Symbicort as a measure to restore or maintain asthma control at times of symptoms could be clinically useful and would incur additional cost for the period of higher dosing. However the chart ignored the cost of similar measures with Seretide where a new prescription was required.

c) Through additional labelling of the Symbicort bars, the chart showed the different daily doses of formoterol associated with the Symbicort regimens. The purpose of this was not made clear. However, alongside the chart it was stated that 'All Seretide options give 100mcg/day of salmeterol'. Such presentation was open to interpretation that the variable dosage of formoterol had some disadvantage. This was potentially misleading.

AstraZeneca alleged that this chart was misleading in breach of Clauses 7.2, 7.3 and 7.10.

AstraZeneca reiterated its comments from point 1 above that comparisons of this type between products

that contained different inhaled steroids were complex because of the lack of consensus on equipotent doses of the different treatments. For example the BTS/SIGN asthma guidelines suggested a 2:1 ratio in the equipotent doses of budesonide to fluticasone, but they noted that there might be variations with different delivery devices. Specifically with respect to the Turbohaler they stated 'There is limited evidence from two open studies of less than ideal design that budesonide via the Turbohaler is more clinically effective'. The more recent GINA 2006 guideline advised a ratio of 8:5 in equipotent doses. The lack of consensus on equipotent doses added further complexity to the understanding of such these data and therefore it was not possible to make accurate direct comparisons between Symbicort and Seretide

RESPONSE

GlaxoSmithKline stated that it was disappointed to see that this complaint included the slide referred to above as this was not previously subject to intercompany dialogue. Although there was a similarity to the complaint above, new complaints were made in that a different dose comparison was referred to at point a and 'additional labelling' at point c. GlaxoSmithKline had serious misgivings concerning the progression of this element of the complaint because of the lack of intercompany dialogue as required by Paragraph 5.2 of the Constitution and Procedure.

For completeness, AstraZeneca's concerns were addressed below, but GlaxoSmithKline asked that the Authority clarify the appropriateness of accepting this complaint.

Although AstraZeneca acknowledged that dosing Symbicort up to eight times daily was within the SPC, it suggested that it was misleading to include it as a comparator when higher strength formulations were available which were more appropriate. GlaxoSmithKline disagreed with this assertion since it was clear that the higher strength formulations were included in the bar chart. AstraZeneca's complaint also made assumptions regarding the formulations that prescribers would use for the delivery of steroid doses, and that prescribers would eliminate certain presentations from their options despite these options being possible through the licences of the products. GlaxoSmithKline considered that it was more appropriate to provide complete information for prescribers concerning the full range of formulations and devices that were available to deliver required doses of steroid. For example, since Symbicort 100/6 was licensed for use at four puffs bd this option had appropriately been included for the delivery of medium doses steroid (800mcg daily) alongside all other formulations of Symbicort that were licensed to deliver this dose. As this presentation was available to clinicians it was likely that it was used in clinical practice to deliver medium dose steroid and it was appropriate to make prescribers aware of the cost of this treatment option, and likewise any other treatment option.

AstraZeneca stated that comparisons between products that contained different inhaled steroids were complex due to the lack of consensus on equipotent doses of the different treatments. AstraZeneca quoted evidence from the BTS/SIGN asthma guidelines which suggested a 2:1 ratio of equipotent doses of budesonide to fluticasone in addition to the GINA 2006 guideline which advised a ratio of 8:5 as equipotent.

GlaxoSmithKline considered this point somewhat superfluous as, in accordance with the Code, all promotion of a medicine must follow its SPC. The SPC for Seretide (and Flixotide) stated quite clearly that:

'Prescribers should be aware that, in patients with asthma, fluticasone propionate is as effective as other inhaled steroids at approximately half the microgram daily dose. For example, 100mcg of fluticasone propionate is approximately equivalent to 200mcg of beclometasone dipropionate (CFC-containing) or budesonide.'

Consequently, in order to comply with the requirements of the Code, GlaxoSmithKline must consider that fluticasone and fluticasone-containing products were equivalent to double the dose of budesonide and beclometasone. As such the cost comparisons at issue did precisely this, and would be required to do so until such time as the SPCs changed.

The purpose of the slide was not to take account of flexible treatment options in the management of asthma, but to provide information on a commonly used metric - 30 days' treatment cost. The fact that these cost comparison referred to 30 days' treatment at stable dose was highlighted and made clear in the presentation.

AstraZeneca raised concerns regarding additional labelling of the Symbicort bars which showed the dose of formoterol which was delivered with each treatment option, and alleged that the statement alongside the chart which read 'All Seretide options give 100mcg/day salmeterol' was open to interpretation that formoterol had some disadvantage, and could be potentially misleading. However, the statements were provided in order that the cost comparison bar chart was completely transparent in showing that at higher doses of Symbicort the patient received increasing doses of long acting beta agonist (LABA), but that all presentations of Seretide delivered the same dose of LABA. GlaxoSmithKline considered that prescribers would be aware that the characteristics of formoterol and salmeterol were different. As such the intent was to be transparent that if Symbicort flexible dosing was used, patients would be receiving more LABA product with the higher doses of Symbicort, whereas with Seretide there was no increase in dose of LABA. There was absolutely no information shown on the slide or any other part of the presentation that would lead prescribers to believe that variable dosing of formoterol incurred any disadvantage as the doses presented were completely in line with the SPC for Symbicort.

The cost comparison chart had been used in both

primary and secondary care. The presentation had only been used to respond to questions about the costs of Seretide and Symbicort. Representatives were briefed via a teleconference regarding the reactive use of the material, and further guidance on its use was contained within the notes attached to each slide in the presentation.

PANEL RULING

Although it noted GlaxoSmithKline's comments about the lack of intercompany discussion about the slide, the Panel nonetheless considered that most of the allegations about the slide and the leavepiece were very similar. The Panel noted that AstraZeneca had raised additional points in relation to the slide. The Panel noted that Paragraph 5.2 of the Constitution and Procedure stated that complaints from pharmaceutical companies would only be accepted if the Director was satisfied that intercompany dialogue at a senior level had been offered in an attempt to resolve the matter. The Director noted that there had been no intercompany activity about AstraZeneca's comments regarding the information about the different daily doses of formoterol (point 2c above). Thus this aspect was not considered. The Director considered that there had been intercompany dialogue on AstraZeneca's comment about the comparison of one inhalation of Seretide with four inhalations of Symbicort in point 1 above so points 2a and 2b were considered.

The Panel noted that the dose of Seretide Accuhaler was one inhalation twice daily and Seretide Evohaler was two inhalations twice daily.

The Panel considered that information presented in the slide was consistent with the SPC dosing instructions for the products. There was no mention of flexible dosing with Symbicort which in the Panel's view was relevant.

The Panel considered that the slide was different to the leavepiece in that the slide did not make it clear that the cost was based on a stable dose of the products. Thus the Panel considered that the slide was misleading and an unfair comparison. Breaches of Clauses 7.2 and 7.3 were ruled.

The Panel noted that the slide was effectively a bar chart presentation of the data shown in the leavepiece. Seretide bars were in purple and Symbicort were in red, with white text along them denoting the dose of formoterol. In the medium steroid dose (500mcg/day fluticasone; 800mcg/day budesonide) band extra Symbicort data had been added to that in the leavepiece ie the use of Symbicort 100/6, 4 puffs twice daily. Although the product could be used in that way, prescribers were much more likely to prescribe Symbicort 200/6 or 400/12 for long-term therapy for reasons for patient compliance and cost. The Panel considered that the addition of this data, and thus a prominent red bar, exaggerated the cost difference between Symbicort and Seretide. Without that bar prescribers would see that for low and medium steroid dose bands, Symbicort and Seretide were similarly priced. A breach of Clause 7.10 was ruled.

Complaint received 5 April 2007

Case completed 11 June 2007