CASE AUTH/2724/7/14

TILLOTTS v FERRING

Pentasa cost comparison chart

Tillotts complained about a cost comparison bar chart for Pentasa (mesalazine) entitled 'Pentasa is less expensive than many other brands of 5-ASA'; the chart was a 'Comparison based on annual drug cost of commonly prescribed oral mesalazine preparations at their licensed dosage(s) for the maintenance of remission of mild to moderate UC [ulcerative colitis]'. The other mesalazine products featured in the chart were, *inter alia*, Octasa marketed by Tillotts.

Tillotts alleged that the bar chart implied that Pentasa was the cheapest oral mesalazine for the maintenance treatment of mild to moderate ulcerative colitis (UC). The chart cited daily Pentasa doses of 1.5g and 2g/day, whereas the summary of product characteristics (SPC) stated 'Maintenance treatment: Individual dosage. Recommended dosage, 2g mesalazine once daily'. Tillotts alleged that the 1.5g/day dose was inconsistent with the marketing authorization and that the chart was misleading, unfair and misrepresented the cost of Pentasa. The inappropriate use of the 1.5g/day dose for Pentasa was reinforced by the fact that the daily doses of the comparator products were precisely those stated in the relevant SPCs.

The detailed response from Ferring is given below.

The Panel noted that the bar chart compared the annual medicine acquisition cost of 'commonly prescribed oral mesalazine preparations at their licenced dosage(s) for the maintenance of remission of mild to moderate UC'. The doses cited for Pentasa were 1.5g/day and 2g/day at an annual cost of £336.62 and £448.83 respectively. The Pentasa SPC stated that for the maintenance of remission in UC, the dose of Pentasa could be individualised and that the recommended dose was 2g once daily. The Panel noted the submission that according to 2013 prescription data a small minority of Pentasa maintenance prescriptions were written for 1.5g/day. The Panel noted the reference to individual doses in the SPC and considered that whilst some patients might be maintained on 1.5g/day and some on the recommended dose of 2g/day, some patients might be prescribed more than 2g/day.

The Panel noted that the doses (and costs) shown for comparator products were the lowest and highest maintenance doses as stated in their respective SPCs.

The Panel noted its comments above and considered that the doses and costs shown for Pentasa were not wholly comparable with the doses and costs shown for the other mesalazine preparations. Supplementary information to the Code stated, *inter alia*, that valid comparisons could only be made where like was compared with like. In the Panel's view the cost comparison chart at issue had not compared like with like. The doses and costs shown for Pentasa had been derived from prescription data, clinical trials, treatment guidelines and the SPC. The apparent weight given to the use of Pentasa 1.5g/day was the same as that given to the use of the recommended dose of 2g/day which was the only maintenance dose to be specifically quantified in the Pentasa SPC. The doses and costs shown for the other medicines were derived only from the range of doses specifically quantified in their respective SPCs. The Panel thus considered that the impression given in the cost comparison of the status of the 1.5g/day dose, compared with the status of all of the other doses stated was misleading as alleged and a breach of the Code was ruled.

The Panel noted that the cost comparison chart had referred to a maintenance dose of 1.5g/day for Pentasa. Although the Pentasa SPC stated that the recommended maintenance dose was 2g/day, it also referred to 'Individual dosage'. The Panel noted that clinical guidelines referred to the use of at least 1.2g/day mesalazine for maintenance therapy in UC and clinical studies had shown the benefit of Pentasa 1.5g/day in the maintenance treatment of UC. The Panel noted that although 1.5g/day was not cited in the Pentasa SPC for maintenance therapy, given the reference to individual dosing, it was not inconsistent with the particulars listed in the SPC. No breach of the Code was ruled.

Tillotts Pharma UK Limited complained about a cost comparison bar chart for Pentasa (mesalazine (5-amino-salicylic acid (5-ASA))) which was included in an e-detail aid (ref PA/283/2014/UK) produced by Ferring Pharmaceuticals Ltd. The chart was entitled 'Pentasa is less expensive than many other brands of 5-ASA' and beneath it was explained that the chart was a 'Comparison based on annual drug cost of commonly prescribed oral mesalazine preparations at their licensed dosage(s) for the maintenance of remission of mild to moderate UC [ulcerative colitis]'. The other mesalazine products featured in the chart were Octasa (marketed by Tillotts), Asacol, Mezavant and Salofalk. The annual cost or range of the costs of various doses was given. The doses ranged from 1.2g/day (Octasa) to 3g/day (Salofalk sachets).

Pentasa was indicated for the treatment of mild to moderate UC and for the maintenance of remission of UC. Section 4.2 of the Pentasa summary of product characteristics (SPC) stated that the dose for maintenance treatment was 'Individual dosage. Recommended dosage, 2g mesalazine once daily'.

COMPLAINT

Tillotts explained that the material in question was a slide which presented a chart of annual costs for various oral mesalazine preparations used for the maintenance treatment of UC. The bar chart was

headed 'Pentasa is less expensive than many other brands of 5-ASA' and included annual costs of a range of mesalazine products, including Octasa 400mg and 800mg tablets. Tillotts alleged that the bar chart implied that Pentasa was the cheapest oral mesalazine for the maintenance treatment of mild to moderate UC.

Tillotts alleged that one of the daily doses of Pentasa used for comparison purposes was not supported in the posology section (Section 4.2) of the Pentasa SPC. The chart cited daily doses of 1.5g and 2g per day for Pentasa, whereas the SPC stated 'Maintenance treatment: Individual dosage. Recommended dosage, 2g mesalazine once daily'. Tillotts alleged that the chart was deliberately misleading and that it was not appropriate to base cost comparisons on doses which were not specifically stated in the SPC. Tillotts alleged that the chart misrepresented the cost of Pentasa and presented an unfair comparison.

The inappropriate use of the 1.5g/day dose for Pentasa was reinforced by the fact that the daily doses of the comparator products cited in the chart were precisely those stated in the relevant SPCs. In the case of Octasa 400mg and 800mg, maintenance treatment was possible within a range of recommended doses ie 1.2g to 2.4g per day. The bar chart in question made that clear and provided a range of annual medicine costs at the minimum and maximum doses. However, the range of doses depicted for Pentasa was inconsistent with the product's SPC.

The only dose at which Pentasa and Octasa might be directly compared was 2g/day, due to the differences in available tablet strengths. At such a dose, Pentasa was more expensive than Octasa (£448.83 vs £395.42 respectively), rendering false the claim that Pentasa was less expensive. During inter-company dialogue, Ferring contended that 1.5g/day was a commonly used dose and stated in written correspondence that 1.5g/day was the 'minimum daily dose' for Pentasa.

Tillotts alleged a breach of Clause 3.2 in that a dose cited for Pentasa was not supported by the Pentasa SPC and was thus inconsistent with the marketing authorization, and a breach of Clause 7.2 in that the comparison was misleading and unfair.

RESPONSE

Ferring submitted that the bar chart was an accurate, balanced and fair comparison of the acquisition costs of various mesalazine formulations available for the maintenance of remission in UC; it was not designed to imply that Pentasa was the cheapest choice. The chart was clear and showed that Salofalk was the cheapest brand in terms of annual medicine costs of commonly prescribed oral mesalazine preparations for the maintenance of remission of mild to moderate UC.

Ferring denied that the calculations used to derive the comparative annual cost of the various mesalazine products were misleading. The chart demonstrated the dosage range costs for various brands of mesalazine and took into account the respective SPCs, the available drug formulations (Monthly Index of Medical Specialities (MIMS), June-August 2014) and the British Society of Gastroenterology (Mowat *et al* 2011) and European Crohn's and Colitis Organisation recommendations (Dignass *et al* 2012).

Due to the different quantitative composition of the products, a 'direct dose-by-dose comparison' could not be made. The doses and respective annual costs shown in the chart were based on the information provided in MIMS, June-August 2014 and Ferring provided details of the calculations used.

Ferring denied that the chart was inconsistent with the Pentasa SPC. The Pentasa SPCs for 500mg tablet, 1g tablet, 1g sachet and 2g sachet all stated: 'for maintenance treatment: Individual dosage. Recommended dosage, 2g mesalazine once daily'.

Although 2g per day was the recommended dose, other individualised doses could be used within the product licence, as stated in the SPC. The 1.5g/day dose was commonly used based on the following:

a) The 1.5g dose was consistent with the British Society of Gastroenterology guidelines (Mowat at al) recommending oral mesalazine 1.2-2.4g daily for maintenance of remission in UC.
b) The European Crohn´s and Colitis Organisation guidelines stated that the minimum effective dose of oral 5-aminosalicylic acid was 1.2g per day for maintenance of remission in UC (Dignass *et al*).
c) The 1.5g dose has been shown to be an effective dose in clinical trials (Fockens *et al* 1995, Mulder *et al* 1988 and Munakata *et al* 1995).
d) UK patients were currently prescribed the 1.5g/day maintenance dose of Pentasa (Ferring Data on File). Prescription data showed that, in 2013, 18,873 prescriptions were issued where the 1.5g/day dose of Pentasa 500mg tablets was prescribed as either 1 tablet 3 times a day, or 3 tablets once a day. This represented 7.1% of all 500mg Pentasa tablet prescriptions or 6.1% of all Pentasa tablets prescribed (1g and 500mg). In addition, an analysis of co-prescribed medicines showed that in 2013 there were 1,025 co-prescribed prescriptions for Pentasa (711 prescriptions for 500mg Pentasa tablet where a 1g Pentasa tablet was co-prescribed and 314 prescriptions for 1g Pentasa tablet where a 500mg Pentasa tablet was co-prescribed).

As Pentasa was not available in a tablet strength that could be administered as 1.2g, which was the minimum dose recommended by the British Society of Gastroenterology and the European Crohn's and Colitis Organisation for maintenance treatment of ulcerative colitis, Ferring submitted that it was justifiable to use the 1.5g/day dose as the low prescribed dose for cost demonstration.

Ferring submitted that as stated above, the aim of the cost comparison bar chart was to demonstrate the range of annual medicine acquisition costs of commonly prescribed mesalazine formulations available for the maintenance treatment of remission in UC.

Ferring denied a breach of Clause 3.2 as the cited dose of 1.5g Pentasa was consistent with its marketing authorization as noted above. Ferring also denied a breach of Clause 7.2 as the material was not misleading and represented an accurate, balanced, fair, objective and unambiguous comparison of the acquisition costs of commonly prescribed mesalazine formulations available for maintenance of remission in UC as explained above.

PANEL RULING

The Panel noted that the bar chart compared the annual medicine acquisition cost of 'commonly prescribed oral mesalazine preparations at their licenced dosage(s) for the maintenance of remission of mild to moderate UC'. The doses cited for Pentasa were 1.5g/day and 2g/day at an annual cost of £336.62 and £448.83 respectively. The Pentasa SPC stated that for the maintenance of remission in UC, the dose of Pentasa could be individualised and that the recommended dose was 2g once daily. The Panel noted the submission that according to 2013 prescription data some patients were prescribed 1.5g/day Pentasa which was assumed to be for maintenance treatment given that the dose for acute treatment was likely to be larger (the SPC referred to an individual dosage of up to 4g mesalazine per day). It appeared from the data submitted by Ferring that only a small minority of Pentasa prescriptions were written for 1.5g/day (either as 3 x 500mg or 1 x 500mg + 1 x 1g). The Panel noted the reference to individual doses in the SPC and considered that whilst some patients might be maintained on 1.5g/day and some on the recommended dose of 2g/day, some patients might be prescribed more than 2g/day.

The Panel noted that the doses (and costs) shown in the chart for the other mesalazine preparations were the lowest and highest maintenance doses as stated in their respective SPCs. Thus the dose stated in the Octasa MR tablets 400mg SPC for maintenance therapy was three to six tablets a day in divided doses and so the two doses shown in the bar chart were three tablets a day (1.2g, £237.25) and six tablets a day (2.4g/day, £474.50). Comparable data was given for Octasa MR 800mg tablets, Asacol 400mg and 800mg tablets, Mezavant XL tablets, Salofalk 500mg tablets and Salofalk 3g sachets. The Panel thus noted that no maintenance dose other than that specifically quantified in the SPC was shown for any of the mesalazine preparations apart from Pentasa.

The Panel noted its comments above and considered that the doses and costs shown for Pentasa were not wholly comparable with the doses and costs shown for the other mesalazine preparations. The supplementary information to Clause 7.2, price comparisons, stated that as with any other comparison, price comparisons must be accurate and fair and must not mislead. Valid comparisons could only be made where like was compared with like. In the Panel's view the cost comparison chart at issue had not compared like with like. The doses and costs shown for Pentasa had been derived from prescription data, clinical trials, treatment guidelines and the SPC. The apparent weight given to the use of Pentasa 1.5g/day was the same as that given to the use of the recommended dose of 2g/day which was the only maintenance dose to be specifically quantified in the Pentasa SPC. The doses and costs shown for the other medicines had been derived only from the range of doses specifically quantified in the respective SPCs. The Panel thus considered that the impression given in the cost comparison of the status of the 1.5g/day dose, compared with the status of all of the other doses stated was misleading as alleged and a breach of Clause 7.2 was ruled.

The Panel noted that the cost comparison chart had referred to a maintenance dose of 1.5g/day for Pentasa. Although the Pentasa SPC stated that the recommended maintenance dose was 2g/day, it also referred to 'Individual dosage'. The Panel noted that clinical guidelines (Mowat *et al* and Dignass *et al*) referred to the use of at least 1.2g/day mesalazine for maintenance therapy in UC and clinical studies (Fockens *et al* and Mulder *et al*) had shown the benefit of Pentasa 1.5g/day in the maintenance treatment of UC. The Panel noted that although 1.5g/day was not cited in the Pentasa SPC for maintenance therapy, given the reference to individual dosing, it was not inconsistent with the particulars listed in the SPC. No breach of Clause 3.2 was ruled.

Complaint received **30 July 2014**

Case completed **9 September 2014**