EX-EMPLOYEE/DIRECTOR v ASTRAZENECA

Presentation on Seroquel

An ex-employee of AstraZeneca referred to Case AUTH/2297/1/10; in that case, he drew attention to a BBC Radio 4 programme in which he had stated that as a former medical adviser for Seroquel, he had been pressurised to approve promotional claims for the medicine which stated that weight gain was not a problem.

The complainant now referred to five presentations on the AstraZeneca website (www.astrazeneca.com) which he alleged made similar false claims to those at issue in Case AUTH/2297/1/10.

Alleged breaches of undertaking were taken up with the Director acting as the complainant as the PMCPA was responsible for ensuring compliance with undertakings.

The detailed response from AstraZeneca is given below.

The Panel noted that an undertaking was an important document. It included an assurance that all possible steps would be taken to avoid similar breaches of the Code in future. It was very important for the reputation of the industry that companies complied with undertakings.

The Panel noted that whilst the complainant referred to Case AUTH/2297/1/10 that case was considered and published alongside two closely similar cases, Cases AUTH/2294/1/10 and AUTH/2296/1/10. The rulings in these cases were interlinked and AstraZeneca had provided one undertaking in relation to all three. The Panel examined the previous rulings relating to claims about weight.

The Panel noted that AstraZeneca had provided the requisite undertaking and assurance for the previous cases in March 2010. The advertisement at issue then was last used in May 2004. Undertakings required the company concerned to cease use of the material in question and any similar material and give an assurance that all possible steps would be taken to avoid a similar breach of the Code in the future. In the Panel's view, if promotional material was originally at issue, an undertaking was not necessarily limited to closely similar claims solely in promotional material as inferred by AstraZeneca. Much would depend on the circumstances. The Panel noted that the presentations at issue, which AstraZeneca submitted were written for the international investor community, were available on www.astrazeneca.com. The Panel considered that in general, if an undertaking was given not to use a claim then the use of the same claim with a different audience was likely to be unacceptable under the Code, irrespective of whether it was in breach of the original undertaking.

On the information before it, the Panel saw no reason why material published on AstraZeneca's corporate website would not be subject to the UK Code.

It appeared from AstraZeneca UK's submission that the company had not examined the material now at issue when the undertaking was given in March 2010. The fact that AstraZeneca archived such presentations on its website for an indefinite period did not mean that if such material was in breach of the Code, it was somehow acceptable to keep it on the website. The Panel did not consider that either the need to change archiving policy for such presentations or the difficulty of finding the material on the website were relevant as to whether there had been a breach of undertaking.

The Panel noted that none of the presentations included the claim previously at issue 'The only atypical with placebo level EPS (including akathisia) and placebo level prolactin concentration and a favourable weight profile across the full dose range'.

The Panel then considered whether the claims in the presentations were sufficiently similar to the claim previously ruled in breach of the Code. The Panel considered that most of the claims relating to weight gain in the five presentations were sufficiently different from the claim previously at issue for them not to be caught by the undertaking. No breach of the Code was ruled.

However the Panel noted one slide headed 'Seroquel – strong differential advantage across the indications' included the claims 'placebo-like EPS', 'placebo-like prolactin levels', 'low incidence of sexual dysfunction' and 'weight-neutral in the long-term' which appeared beneath the subheading 'Unique tolerability profile' and above the claim 'Improvement without impairment'. The Panel considered that this slide related solely to the features of Seroquel and in effect claimed that it was the only atypical that was weight-neutral in the long-term. The Panel considered that this claim was sufficiently similar to a claim that only Seroquel had a favourable weight profile compared with other atypicals for it to be covered by the undertaking in the previous case. A breach of undertaking was ruled. The Panel ruled that high standards had not been maintained.

The Panel considered that failing to comply with the undertaking brought discredit upon, and reduced confidence in, the pharmaceutical industry. A breach of Clause 2 was ruled. The rulings were appealed by AstraZeneca.

The Appeal Board decided that the presentation came within the scope of the Code as it was information about, *inter alia*, a prescription only medicine Seroquel, which appeared on AstraZeneca's website. In that regard the age of the data was irrelevant. A potential investor in the company might look on AstraZeneca's website for information and find the presentation at issue.

The Appeal Board was concerned that AstraZeneca had not looked at archived material on its website in relation to the undertaking given in the previous cases. The Appeal Board noted AstraZeneca's submission that this was historical material. The Appeal Board further noted that the material was still in the public domain. There was no indication on the material itself that it was historical. The impression was that the material could still be current. The Appeal Board noted that an undertaking required that the promotional activity or use of the material in question and any similar material, if not already discontinued or no longer in use, would cease forthwith and that all possible steps would be taken to avoid a similar breach of the Code in the future. Details of certain actions taken by the company to implement the undertaking had to be provided, including the date on which the material was finally used or appeared and/or the last date on which the activity took place.

The Appeal Board noted AstraZeneca's submission that the presentation was clearly archived, no longer in use and not used proactively.

The Appeal Board noted that the slide was headed 'Seroquel – Strong differential advantage across the indications'. The Appeal Board noted that the first bullet point underneath the heading stated 'Broad-based efficacy' beneath which three sub-bullets stated 'as effective as other atypicals', 'efficacy in one week' and 'effective in the long-term'. The Appeal Board considered that together these three points contributed to the broad-based efficacy claim; each individual point on its own was not a claim for broad-based efficacy and would not be read as such. In the Appeal Board's view the lower half of the slide would be interpreted in the same way so that 'placebo-like EPS', 'placebo-like prolactin levels', 'low incidence of sexual dysfunction' and the claim at issue, 'weight-neutral in the long-term', would be seen to collectively contribute to Seroquel's 'Unique tolerability profile'. The Appeal Board did not consider that each point on its own would be read as a unique feature of Seroquel.

The Appeal Board noted that the undertaking given in Cases AUTH/2294/1/10, AUTH/2296/1/10 and AUTH/2297/1/10 related to the claim, 'The only atypical with placebo level EPS (including akathisia) and placebo level prolactin concentrations and a favourable weight profile across the full dose range'.

The Appeal Board considered that the presentation of the claim 'weight-neutral in the long-term' as one of four bullet points beneath the heading 'Unique tolerability profile' in the material at issue was such that it was not sufficiently similar to the claim previously at issue for it to be covered by the undertaking. Taking all the circumstances into account, the Appeal Board ruled no breach of the Code including Clause 2. The appeal was successful.

An ex-employee of AstraZeneca referred to his previous complaint about the promotion of Seroquel by AstraZeneca, Case AUTH/2297/1/10. In that case, he drew attention to a BBC Radio 4 programme in which he had stated that as a former medical adviser for Seroquel, he had been pressurised to approve promotional claims for the medicine which stated that weight gain was not a problem.

The report for Case AUTH/2297/1/10 had been published in conjunction with two related cases, Cases AUTH/2294/1/10 and AUTH/2296/1/10.

COMPLAINT

The complainant referred to five presentations on the AstraZeneca website (www.astrazeneca.com) which he alleged made similar false claims to those at issue in Case AUTH/2297/1/10.

When writing to AstraZeneca, the Authority asked it to respond in relation to Clauses 2, 9.1 and 25.

Alleged breaches of undertaking were taken up with the Director acting as the complainant as the PMCPA was responsible for ensuring compliance with undertakings.

RESPONSE

AstraZeneca refuted the implied allegation that it had breached Clause 25 by failing to comply with undertakings to the Authority provided upon conclusion of a previous complaint that originated amongst others from the same complainant.

The presentations in question were written for international investors interested in AstraZeneca. As such, they were presented by senior AstraZeneca executives at business review meetings and in one case a research and development (R&D) update day. Full details were provided.

Due to the global audience, the presentations originated from AstraZeneca's global commercial and R&D teams. As they were not of promotional intent, in line with the requirements of the Code, they had not been certified. The presentations would have been reviewed and agreed at a corporate level in accordance with AstraZeneca process for information that reflected forward looking statements of interest to international investors.

AstraZeneca's current policy was to archive analyst and other business related presentations on its website for an indefinite period, in the spirit of making this information available to those who were unable to participate in the live events as well as for historical reference. Their removal would need to be made in consultation with AstraZeneca's Disclosure Committee as it would reflect a more general change of archiving practice for investor related presentations.

No specific group was directed to this content.

The links provided by the complainant were to presentations on AstraZeneca's corporate website. However, AstraZeneca noted the following in relation to the accessibility of the presentations:

- searching the links themselves in Google did not deliver any results because the documents had not been tagged in line with there being no intent to make these easily accessible or widely available to non-interested parties
- it was not possible to identify the web source of these documents for similar reasons above
- in order to find the documents one would have to specifically look for them. Even with prior knowledge, to get to them from the homepage of the corporate website needed at least 4 clicks. The likelihood of finding the documents when starting from a search engine like Google was very low.

AstraZeneca submitted that it was likely that, in order to access the documents, the complainant and others with a specific interest would have spent a considerable amount of time searching the archive, making it unlikely that a casual visitor to the corporate website would inappropriately stumble upon them.

AstraZeneca did not believe that the weight change claims in these presentations fell within the scope of the previous ruling insofar as these presentations were historical, non-promotional records that were not directed at health professionals. It was also clear from the chronology of the presentations that AstraZeneca's statements in relation to weight and Seroquel evolved as a balanced and fair reflection of the evidence available at the time:

- 1999 – minimal weight gain
- 2001 – weight-neutral in the long-term
- 2004 – favourable weight profile long-term
- 2006 – less weight gain than with olanzapine.

AstraZeneca submitted that the weight related claims previously ruled in breach were fully addressed when Case AUTH/2297/1/10 was considered. The claim related to a 2004 advertisement and when the undertaking was signed in 2010, AstraZeneca was, and remained, confident that the claim at issue did not form any aspect of Seroquel marketing in the UK and had not done so for some considerable time. As such AstraZeneca stated that it would not revisit the details including the data.

In conclusion, AstraZeneca denied any breaches of Clauses 2, 9.1 and 25.

AstraZeneca was asked by the Panel to respond to the case preparation manager's request for information about what action the company took following the outcome of the previous cases to ensure that all of the claims at issue, and any similar claims, were withdrawn.

AstraZeneca stated that its response to the cases in 2010 was in the context of the claims in question being of a historical nature that had ceased to be used in any UK promotional materials.

AstraZeneca submitted that the actions taken by the UK Seroquel team following the 2010 rulings were proportionate to the nature of the material found to be in breach, in that the UK Seroquel team reviewed all of the current promotional materials for the product. As the weight related claims, or similar, had long since ceased to be used, no such materials were required to be recalled as no promotional material carried such claims.

Weight related claims ceased to be used in UK promotional materials as set out and supported by the Seroquel Current Claims Document (CCD). This was an AstraZeneca confidential document for internal use only, which captured the claims approved for use as well as any undertakings and/or other decisions not to use certain claims (pages 2 and 3 specifically took into account the ABPI and inter-company undertakings). No CCD after 2007 included weight related comparisons with other treatments and the 2008 CCD was provided to support AstraZeneca's position in this regard.

AstraZeneca restated its position that the presentations in question did not fall within the scope of the previous rulings or the Code insofar as they were corporate historical records intended for the investor community; they were non-promotional and were not directed at health professionals.

AstraZeneca denied the allegation that it had breached undertakings made in relation to Case AUTH/2294/1/10 and any breaches of Clauses 25, 9.1 or 2 or at all.

PANEL RULING

The Panel noted that an undertaking was an important document. It included an assurance that all possible steps would be taken to avoid similar breaches of the Code in future. It was very important for the reputation of the industry that companies complied with undertakings.

The Panel noted that whilst the complainant referred to Case AUTH/2297/1/10 that case was considered and published alongside two closely similar cases, Cases AUTH/2294/1/10 and AUTH/2296/1/10. The rulings in these cases were interlinked and AstraZeneca had provided one undertaking in relation to all three.

The Panel examined the three previous rulings relating to claims about weight.

Case AUTH/2294/1/10

The Panel noted that the Seroquel advertisement at issue, published in the British Journal of Psychiatry, April 2004, featured the claim 'The only atypical with placebo level EPS [extra-pyramidal symptoms] (including akathisia) and placebo level prolactin concentrations and a favourable weight profile across the full dose range'. The Panel thus considered that the claim in full sought to establish Seroquel as an atypical antipsychotic which was distinctly different to the others in the class in that it was the only one to have

placebo level EPS, placebo level prolactin concentrations and a favourable weight profile across the full range.

The Panel noted that in the absence of any explanation it was left to the readers' judgement as to what was meant by a 'favourable weight profile'. The Panel noted that Allison *et al* (1999) had estimated and compared the effects of antipsychotics (both conventional and atypical) on bodyweight. The authors concluded that all of the antipsychotics examined were associated with weight gain. Among the atypical agents the mean increases in weight were 4.55kg (clozapine), 4.15kg (olanzapine), 2.92kg (sertindole), 2.1kg (risperidone) and 0.04kg (ziprasidone). The mean increase in weight with Seroquel was not calculated due to lack of data.

The Panel considered that if all of the other atypical antipsychotics were known to cause weight gain then it was not unreasonable for readers to assume that if Seroquel was 'The only atypical with … a favourable weight profile across the full dose range' then it might be an atypical with no effect on bodyweight. This was not so. Arvanitis and Rak (1997) reported that the mean increase in weight was 2.2kg (n=1085). Allison *et al* had reported that the mean increase in weight for risperidone was 2.1kg and 2.92kg for sertindole. Across the dose range for Seroquel, 75/150/300/600/750mg daily, the mean increase in weight was 0.9/2.9/2.0/2.6/2.3kg respectively. Jones and Huizar (2003) reported a mean increase in weight of 1.8kg with Seroquel therapy. Brecher *et al* (2000) reported on the long-term weight changes in 427 patients over 18 months. Weight change differed over time from -1.53kg after weeks 40-52 (n=41) to +1.94kg after weeks 53-78.

The Panel noted that the relevant Seroquel SPC (October 2003) listed weight gain as a common (≥1% - <10%) adverse event which occurred predominantly during the early weeks of therapy.

Overall the Panel considered that the advertisement was misleading with regard to the effect on bodyweight that would be expected to be observed with Seroquel therapy compared with the other atypical medicines. Although the advertisement did not state 'no weight gain' as alleged it sought to differentiate Seroquel from other medicines in the class in that it was the only one with a 'favourable weight profile across the full dose range'. Given that the other medicines caused weight gain, the advertisement could be read as implying that Seroquel did not. This was not so. Similarly, the advertisement could be read as implying that Seroquel had a clear advantage regarding its 'favourable weight profile …' and this was not supported by the data submitted by AstraZeneca. The claim 'The only atypical with … a favourable weight profile…' was thus misleading and could not be substantiated. A breach of Clauses 7.2 and 7.4 was ruled. The Panel considered that the claim did not reflect the evidence regarding the side-effect of weight gain. A breach of Clause 7.9 of the Code was ruled.

Case AUTH/2296/1/10

The complainant referred to an online news item which referred to the advertisement at issue in Case AUTH/2294/1/10.

The Panel considered that its rulings in Case AUTH/2294/1/10 of breaches of Clauses 7.2, 7.4 and 7.9 applied here also. The Panel further considered that, given the data, high standards had not been maintained. A breach of Clause 9.1 was ruled.

Misleading prescribers about a potential side-effect of therapy could prejudice patient safety and this was referred to in the supplementary information to Clause 2 as an example of an activity likely to be in breach of that clause. On balance, however, the Panel considered that the circumstances were not such as to warrant a ruling of a breach of Clause 2 of the Code which was a sign of particular censure and reserved for such use. No breach of Clause 2 was ruled.

Case AUTH/2297/1/10

This case concerned, *inter alia*, the same advertisement at issue in Case AUTH/2294/1/10.

The Panel considered that its rulings above in Cases AUTH/2294/1/10 and AUTH/2296/1/10 applied here also.

The complainant in this case appealed the Panel's ruling of no breach of Clause 2.

The Appeal Board noted that between 1997 and 2004 there was increasing evidence that weight gain was an issue with Seroquel. Spielmans and Parry reported that in July 2008 an internal analysis of quetiapine studies in schizophrenia conducted from 1993-1999, concluded that 'the incidence rate in adult patients with weight gain ≥7% in all trials was 18.2%'. In the 2004 SPC weight gain was listed as a common (≥1% - <10%) adverse event; in the 2009 SPC it was listed as a very common (>10%) event. There was also data to show that in terms of the amount of weight gained, Seroquel was no different to some other atypical antipsychotics. The Appeal Board was concerned that the claim 'The only atypical with placebo level EPS [extra-pyramidal symptoms] (including akathisia) and placebo level prolactin concentrations and a favourable weight profile across the full dose range' had favoured Seroquel in terms of its weight gain profile vs other atypical antipsychotics yet the evidence had not supported this.

The Appeal Board was concerned about the lack of information provided by AstraZeneca about the generation of the advertisement at issue. It was also extremely concerned about email trails which implied that the company was keen not to disclose certain data. However, the Appeal Board noted that it was limited to making its decision based on activity in the UK and in that regard the advertisement at issue was the only one that had been specifically identified. The Appeal Board noted the Panel's ruling of breaches of the Code which had been accepted by AstraZeneca. The Appeal Board did not consider that the circumstances warranted a ruling of a breach of Clause 2 and so it upheld the Panel's ruling of no breach of that clause. The appeal was thus unsuccessful.

Case AUTH/2538/10/12

Turning to the present case, Case AUTH/2538/10/12, the Panel noted that AstraZeneca had provided the requisite undertaking and assurance for the previous

cases on 12 March 2010. The advertisement at issue in those cases was last used in May 2004. An undertaking required a company to cease use of the material in question and any similar material and give an assurance that all possible steps would be taken to avoid a similar breach of the Code in the future. In the Panel's view, if the material originally at issue was a claim in promotional material, an undertaking was not necessarily limited to closely similar claims solely in promotional material as inferred by AstraZeneca. Much would depend on the circumstances. The Panel noted that the presentations at issue were available on www.astrazeneca.com. AstraZeneca submitted that the presentations were written for the international investor community. The Panel considered that in general, if an undertaking was given not to use a claim then the use of the same claim with a different audience was likely to be unacceptable under the Code, irrespective of whether it was in breach of the original undertaking.

Firstly, the Panel had to consider whether the material came within the scope of the Code as it was placed on the corporate (astrazeneca.com) website. The Panel noted that there was no submission from the company specifically on this point, however, AstraZeneca was a UK company and thus its activities and materials, those of any UK based affiliate and other activities taking place in the UK organised by an overseas affiliate all had to comply with the Code. The Panel noted that AstraZeneca's corporate headquarters were based in the UK. On the information before it, the Panel saw no reason why material published on the corporate website would not be subject to the UK Code.

It appeared from AstraZeneca UK's submission that the company had not examined the material now at issue when the company had given its undertaking in March 2010. The fact that AstraZeneca archived such analyst and business related presentations on its website for an indefinite period did not mean that if such material was in breach of the Code, it was somehow acceptable to keep it on the website. The Panel did not consider that the need to change archiving policy for such presentations was relevant as to whether or not there had been a breach of undertaking. Similarly, the Panel did not accept AstraZeneca's submission that the difficulty of finding the material on the website was relevant as to whether or not there had been a breach of undertaking.

The Panel examined each presentation separately and each of the slide sets referring to weight. None of the slides included the claim previously at issue 'The only atypical with placebo level EPS (including akathisia) and placebo level prolactin concentration and a favourable weight profile across the full dose range'.

The Panel considered whether the claims in the presentations were sufficiently similar to the claim previously ruled in breach of the Code.

1 Seroquel Presentation 2004

This presentation included two slides headed 'The ideal schizophrenia treatment' and 'The ideal bipolar mania treatment'. Each compared Seroquel, risperidone, olanzapine and aripiprazole for certain features including 'Favourable weight profile long-term'. On each slide there was a cross for olanzapine for this feature and ticks for the other three products indicating that olanzapine was the only one of these medicines which did not have a favourable weight profile long-term.

The Panel did not consider that either of these two slides in effect claimed that Seroquel was the only medicine with a favourable weight profile. The slides were not sufficiently similar for them to be covered by the previous undertaking. No breach of Clause 25 was ruled and consequently no breach of Clauses 9.1 and 2. These rulings were not appealed.

During the consideration of this aspect of the case the Panel was concerned that the title of the slides implied that Seroquel was the ideal treatment and queried whether this was consistent with the requirements of Clause 7.10. The Panel requested that AstraZeneca be advised of its concerns.

2 Seroquel Presentation 2006

This presentation included two slides headed 'Seroquel physician perceptions: Schizophrenia' and 'Seroquel physician perception: Bipolar' which stated under the bullet point 'Superior tolerability' three further bullet points, 'Low rate of EPS (inc.akathisia)', 'Low rate of prolactin induction' and 'Less weight gain than with olanzapine'. The slide concluded that Seroquel had an overall favourable benefit/risk profile.

Again, the Panel did not consider that the claim 'Less weight gain than with olanzapine' in effect claimed that Seroquel was the only medicine with a favourable weight profile. The claim was not sufficiently similar for it to be covered by the previous undertaking. No breach of Clause 25 was ruled and consequently no breach of Clauses 9.1 and 2. These rulings were not appealed.

3 AstraZeneca Presentation 1999

This presentation included a slide headed 'Seroquel – minimal weight gain' beneath which appeared data showing weight gain for Seroquel, presented as a bar chart, and for olanzapine, presented as a graph.

The Panel did not consider that the claim 'Seroquel – minimal weight gain' in effect claimed that Seroquel was the only medicine with a favourable weight profile. The claim was not sufficiently similar for it to be covered by the previous undertaking. No breach of Clause 25 was ruled and consequently no breach of Clauses 9.1 and 2. These rulings were not appealed.

4 Development Portfolio Review Presentation 2002

This presentation included two slides, one headed 'Seroquel Improvement without impairment' which compared a number of features for risperidone, olanzapine, ziprasidone, aripiprazole and Seroquel including 'Weight-neutral long-term'. There was a tick for Seroquel, ziprasidone and aripiprazole and a cross for olanzapine and risperidone.

The Panel did not consider that the claim that Seroquel, ziprasidone and aripiprazole were 'Weight-neutral long-term' was sufficiently similar to the previous claim that Seroquel was the only medicine with a favourable weight profile for it to be covered by the previous undertaking. No breach of Clause 25 was ruled and consequently no breach of Clauses 9.1 and 2. These rulings were not appealed.

A second slide headed 'Seroquel – strong differential advantage across the indications' included the claims 'placebo-like EPS', 'placebo-like prolactin levels', 'low incidence of sexual dysfunction' and 'weight-neutral in the long-term' which appeared beneath the subheading 'Unique tolerability profile' and above the claim 'Improvement without impairment'.

The Panel considered that this slide related solely to the features of Seroquel and in effect claimed that it had an advantage in that it was the only atypical that was weight-neutral in the long-term. This appeared to be inconsistent with the first slide referred to above. The Panel queried which of these claims was accurate. However, it only considered whether there had been a breach of undertaking. The Panel considered that to claim that Seroquel was the only atypical that was weight-neutral was sufficiently similar to a claim that only Seroquel had a favourable weight profile compared with other atypicals for it to be covered by the undertaking in the previous case. A breach of Clause 25 was ruled. The Panel considered that high standards had not been maintained and ruled a breach of Clause 9.1. These rulings were appealed by AstraZeneca.

Failing to comply with an undertaking and assurance was cited as an example of an activity likely to be in breach of Clause 2. The Panel considered that failing to comply with the undertaking brought discredit upon, and reduced confidence in, the pharmaceutical industry. A breach of Clause 2 was ruled. This ruling was appealed by AstraZeneca.

5 AstraZeneca Portfolio Presentation 2001

This presentation included a slide headed 'Seroquel substainable benefits in $7 billion market' which again compared certain features of Seroquel, olanzapine, risperidone and ziprasidone including 'weight neutral in the long term' which was listed as a positive feature for Seroquel and ziprasidone.

The Panel did not consider that this slide in effect claimed that Seroquel was the only one of these medicines with a favourable weight profile. The slide was not sufficiently similar for it to be covered by the previous undertaking. No breach of Clause 25 was ruled and consequently no breach of Clauses 9.1 and 2. These rulings were not appealed.

During its consideration of this case, the Panel was concerned that AstraZeneca UK had apparently interpreted the undertaking so narrowly. Further, the Panel considered that the local company, in this instance AstraZeneca UK, needed to ensure that relevant rulings, including those relating to the acceptability of clinical claims, were disseminated so that corporate claims and activities used in the UK could be reviewed if appropriate.

APPEAL FROM ASTRAZENECA

AstraZeneca submitted that the undertaking at issue related to the following claim for Seroquel: 'The only atypical with placebo level EPS (including akathisia) and placebo level prolactin concentrations and a favourable weight profile across the full dosage range'. In the previous cases (Journalist, Member of the public and Ex-employee v AstraZeneca - Cases AUTH/2294/1/10, AUTH/2296/1/10 and AUTH/2297/1/10), the Panel ruled that the claim misleadingly implied that Seroquel was the only atypical with a favourable weight profile. Accordingly, it was not disputed that, as a consequence of its undertaking, AstraZeneca was not entitled to claim or imply that Seroquel was the only atypical with a favourable weight profile.

In the present case, Case AUTH/2538/10/12, the Panel analysed five slide presentations in order to assess whether AstraZeneca had implied that Seroquel was the only atypical with a favourable weight profile (the Panel acknowledged that the identical claim was not used). These slide presentations were held in the archived material for investors on AstraZeneca's website (www.astrazeneca.com). In just one of the five presentations, entitled 'Development Portfolio Review' the Panel considered that the weight claim was 'similar' to the prohibited claim. Specifically, the Panel concluded that the presentation effectively stated that Seroquel was the only atypical that was weight-neutral in the long-term, and that it therefore fell within the scope of the undertaking (the term 'weight-neutral' was, in the Panel's estimation, equivalent to 'favourable weight profile').

AstraZeneca strongly contested the Panel's interpretation of the claim at issue. Specifically, the Panel had misconstrued the claim: AstraZeneca had not presented Seroquel as the only atypical that was weight-neutral; Seroquel was presented as unique as regards the totality of its advantages. For this reason, AstraZeneca refuted the ruling of breach of Clause 25. However, even if the Appeal Board disagreed with AstraZeneca's interpretation and upheld the ruling of a breach of Clause 25, it submitted that all the circumstances of the case could not support a ruling of a breach of Clause 9.1, let alone a ruling of a breach of Clause 2. Before setting out AstraZeneca's grounds for appeal in relation to each of the clauses at stake, it was important to recall these circumstances, namely: the context of the present complaint, and the nature of the material at issue.

AstraZeneca submitted that the 2002 presentation was aimed at an international investor audience, and was developed as an integral part of the annual business review process. As such it did not focus solely on Seroquel but covered other areas of interest to investors. Along with other analyst and business related presentations, this presentation was maintained on AstraZeneca's corporate website as a historical record. These presentations were not promotional in

either intent or effect: they had short-term relevance for the international investor audience from the business review perspective, but beyond that they were not actively disseminated and were of interest only to someone actively seeking historical information. In fact, the presentation in question was of interest only to a vexatious complainant who had a particular agenda and who knew what he was looking for. This was supported by the fact that the presentation was:

- historic material from 2002
- not proactively distributed
- not tagged and therefore very difficult to find via an internet search engine without prior specific knowldege of the presentation contents
- held in a website archive
- difficult to find within the website itself (at least four clicks were needed to get to this content from the homepage).

AstraZeneca submitted that in the circumstances, the Panel's ruling was disproportionate and unfounded. Even if the weight claim in the presentation fell within the scope of the undertaking (which AstraZeneca strongly refuted), the alleged breach was not such as to bring discredit upon or reduce confidence in the industry; such a conclusion was not consistent with what the Code tried to achieve. AstraZeneca noted that this was not the 'typical' breach of undertaking case where a particular claim was ruled in breach of the Code was used again in the future (in some cases due to the company's error, in other cases due to the action of agents/publishers). Rather, this complaint arose as a consequence of a vexatious ex-employee who wanted to find fault with the company; the Code should not be the forum for such conduct.

AstraZeneca noted the Panel was concerned in relation to the company's interpretation of the undertaking given in Cases AUTH/2294/1/10, AUTH/2296/1/10 and AUTH/2297/1/10. AstraZeneca emphasised that it took all regulatory matters seriously and that the actions it took when it provided the undertaking were thorough and proportionate in the circumstances.

AstraZeneca refuted the Panel's ruling of a breach of Clause 25 and submitted that the Panel had misconstrued the weight claim in the presentation. When properly construed, AstraZeneca submitted that the claim did not fall within the scope of the undertaking.

AstraZeneca submitted that it was important first to summarise the content of the two slides within the Seroquel section of the presentation which referred to weight. The two slides should be considered in the context of each other and the flow of the entire presentation (an individual slide was clearly not intended to be presented or viewed in isolation).

The Panel considered two slides, both of which contained statements about Seroquel with regard to weight. The first slide (slide 13) headed 'Seroquel Improvement without Impairment' compared several features for risperidone, olanzapine, ziprasidone, aripiprazole and Seroquel and, through the use of ticks and crosses, explained that Seroquel, ziprasidone and aripiprazole were weight-neutral long-term (whereas the others were not). As slide 13 did not claim or imply that Seroquel was the only medicine with a favourable weight profile, the Panel concluded that this claim did not fall within the scope of the undertaking and therefore ruled no breach. AstraZeneca agreed with this analysis. However, the Panel objected to slide 18 which was headed 'Seroquel – Strong differential advantage across the indications' and contained the following bullet and sub-bullets:

- 'Unique tolerability profile
  - placebo-like EPS
  - placebo-like prolactin levels
  - low incidence of sexual dysfunction
  - weight-neutral in the long-term.'

According to the Panel, 'this slide related solely to the features of Seroquel and in effect claimed that it had an advantage in that it was the only atypical that was weight-neutral in the long-term'. The Panel thus interpreted the word 'unique' as relating to each of the four qualities individually, and it concluded that the claim that Seroquel was unique in being weight-neutral was sufficiently similar to the claim that only Seroquel had a favourable weight profile such that it fell within the scope of the undertaking. Based on its interpretation, the Panel noted that it considered the claim to be inconsistent with the claim made in slide 13 that Seroquel was one of three, out of five products, which were weight-neutral in the long-term.

AstraZeneca submitted that the Panel's interpretation of slide 18 was not justified when considered in the proper context of the presentation as a whole; nor was it justified on the basis of the intended or manifest meaning of slide 18 when considered in isolation. When properly interpreted, it might be seen that the claim in slide 18 did not fall within the scope of the undertaking, and further that there was no inconsistency between slides 13 and 18.

AstraZeneca submitted that, when read in the context of slide 13 and the presentation as a whole, slide 18 could not be interpreted as claiming that Seroquel was the only atypical that was weight-neutral in the long-term. Indeed, slide 13 set the scene by comparing Seroquel with other atypical antipsychotics against specific criteria one of which was 'weight-neutral long-term'. Therefore, as the Panel acknowledged, slide 13 made it clear that Seroquel was one of three atypical antipsychotics that were 'weight-neutral long-term'. AstraZeneca submitted that it was within this context that slide 18 detailed the qualities of Seroquel. The intended and manifest meaning of the slide was to present a unique overall tolerability profile made up of four factors; there was no suggestion that Seroquel was unique in respect of each or any single characteristic assessed separately. This was consistent with slide 13 which presented Seroquel as having a unique profile overall – as it was the only product with ticks in each category. Indeed, it was inconceivable that readers would interpret slide 18 to mean that Seroquel was unique in being weight-neutral in the long-term; rather, the slide would be interpreted in the context of slide 13, which showed that Seroquel was one of three atypical antipsychotics having this particular characteristic.

AstraZeneca submitted that this was also supported by the wording at the bottom of slide 18 – 'Improvement without Impairment' – which directly echoed the title of slide 13, 'Seroquel Improvement without Impairment'. Accordingly, the two slides were not inconsistent with one another as the Panel claimed; AstraZeneca submitted that they were fully consistent as the first presented an overview of Seroquel's benefits as against its competitors, and the second focused on the specific benefits of Seroquel. The slides therefore followed a logical and coherent order and were intended to be read in their entirety. Finally, on this point, the presentation in question could only be downloaded as a PDF, and not as a PowerPoint file, so the two slides could not be separated from one another. This underscored AstraZeneca's position that the slide ruled in breach could not and should not be considered independently and out of context of the whole presentation.

AstraZeneca submitted that even when considered in isolation, slide 18 did not make any claim that each individual element of the profile was unique. Rather, it was the combination of the four factors listed which together constituted a 'Unique tolerability profile'. This meaning was also achieved visually through the structure of the statement, namely the use of a main bullet ('Unique tolerability profile') followed by sub-bullets detailing the four factors of that profile as noted above. There was no suggestion that any factor, taken in isolation, would result in a 'unique' tolerability profile.

Accordingly, contrary to the Panel's ruling, AstraZeneca submitted that the content of slide 18 could not be construed as a claim that Seroquel was the only atypical that was weight-neutral in the long-term; the uniqueness of Seroquel related to the totality of its advantages.

On the basis of the above, AstraZeneca submitted that it had not breached its undertaking by retaining the presentation on its website, and that there was therefore no breach of Clause 25.

AstraZeneca submitted that the Panel's ruling of a breach of Clauses 9.1 and 2 were based on the ruling of a breach of Clause 25, which AstraZeneca refuted. As such, for the reasons stated above, the ruling of breaches of Clauses 2 and 9.1 automatically fell away.

However, even if the Appeal Board did not agree with AstraZeneca regarding the meaning of slide 18 and ruled a breach of Clause 25, AstraZeneca submitted that it had not, in any event, failed to maintain high standards (Clause 9.1) or brought discredit upon and reduced confidence in the pharmaceutical industry (Clause 2).

AstraZeneca submitted that if the Appeal Board did not rule a breach of Clause 25 it had nevertheless maintained high standards.

The circumstances discussed in detail below in relation to the Clause 2 ruling (namely, the impact that the alleged breach of undertaking would have, and how obvious the alleged breach was) were equally relevant to AstraZeneca's appeal of a breach of Clause 9.1.

AstraZeneca submitted that it maintained high standards and acted in a proportionate manner.

With regard to Clause 2, AstraZeneca submitted that the Panel had not provided any reasons for its conclusion that it had brought discredit upon and reduced confidence in the pharmaceutical industry. Whilst the supplementary information to Clause 2 included 'inadequate action leading to a breach of undertaking' as an activity 'likely' to be ruled in breach of Clause 2, an assessment must still be made on the facts of the particular case as to whether such ruling was warranted because, as the supplementary information also stated: 'A ruling of a breach of this clause is a sign of particular censure and is *reserved for such circumstances*' (emphasis added). However, the Panel's ruling appeared to have been made arbitrarily as it was based purely on the fact that failure to comply with an undertaking was cited in the Code as an activity likely to be in breach of Clause 2.

Even if the Appeal Board did not overturn the ruling of a breach of Clause 25, AstraZeneca submitted that a Clause 2 ruling was not warranted in this case; such a ruling would be entirely inappropriate and disproportionate. Whether or not the steps taken by a company to prevent a breach of an undertaking were adequate depended on all the circumstances, including the impact that any breach of undertaking would have, and how obvious the breach was. The circumstances relevant to the Appeal Board's assessment of the severity of the breach were set out below. As regards the impact that the alleged breach of undertaking would have, there were two main considerations: the historic nature of the material, and the non-promotional nature of the material. These were addressed separately below, followed by a consideration of how 'obvious' the alleged breach was.

With regard to the historic nature of the material AstraZeneca acknowledged that an undertaking related not only to the future dissemination of material, but also to material already disseminated and maintained by the company (which might include material on its website). However, in terms of material already disseminated before an undertaking was given, AstraZeneca submitted that there was a clear distinction to be drawn between material which remained in active circulation, and material which was of purely historic interest. This distinction lay in the severity of the breach; by its very nature, material of purely historic interest could not cause the same impact as material which was in active circulation. The presentation was of purely historic interest. In fact, it was of interest only to a vexatious complainant who had a particular agenda and who knew what he was looking for. This was supported by the fact that the presentation was:

- historic material from 2002
- not proactively distributed
- not tagged and therefore very difficult to find via an internet search engine without prior specific knowldege of the presentation contents
- held in a website archive
- difficult to find within the website itself (at least four clicks were needed to get to this content from the homepage).

AstraZeneca submitted that the presentation would no longer interest the investor community as investors would not look back to 2002 in order to make investment decisions. In these circumstances, AstraZeneca questioned in whose eyes the industry was discredited by the maintenance of the presentation on the company's corporate website.

AstraZeneca noted that whilst an undertaking was not limited to promotional material, the non-promotional nature of the presentation was of relevance to the assessment of whether it brought discredit upon and reduced confidence in the industry. This was because promotional material persuaded its audience to make a particular decision (namely, under Clause 1.2, to administer, consume, prescribe, purchase, recommend, sell, supply or use a particular medicine). Accordingly, promotional material necessarily had a different impact from non-promotional material. The potentially greater damage caused by promotional material was recognised in the wording of Clause 2 itself: 'Activities or materials *associated with promotion* must never be such as to bring discredit upon, or reduce confidence in, the pharmaceutical industry.' (emphasis added)

AstraZeneca submitted that whilst non-promotional material could be damaging (for example, if it misled), this was only a risk in so far as the material was actually relied upon. As explained above, the presentation would no longer be relied upon as a source of information due to its obviously historic nature (the presentations were ordered by date on the website).

AstraZeneca further submitted that whether or not a breach of undertaking was obvious or flagrant was relevant to the assessment of the adequacy of the action taken.

AstraZeneca submitted that in the present case, even if the Appeal Board disagreed with the company's interpretation of slide 18 (and upheld the ruling of a breach of Clause 25), the point was clearly open to interpretation. Accordingly, by not removing the presentation from its website, AstraZeneca could not be accused of inadequate action. In other words, the alleged breach was not so flagrant that a breach of Clause 2 was warranted.

AstraZeneca noted the ambiguity of the Code in relation to websites, in particular whether they fell within the scope of the Code or not. A review of Clauses 1.8, 24.1 and 24.2 indicated that material placed on a website outside the UK would only fall within the scope of the Code if:

- it was directed to a UK audience
- it was placed there by a UK company or an affiliate of a UK company or at the authority or instigation of a UK company and
- it specifically referred to the availability to the availability or use of the medicine in the UK.

AstraZeneca noted that in Case AUTH/2046/9/07, a global press release placed on a corporate website was held to fall outside the scope of the Code because it did not refer to the use or availability of the product within the UK.

AstraZeneca submitted that in the present case, the website (astrazeneca.com) was operated by AstraZeneca. It was therefore a UK website, and the Panel considered that material published thereon fell within the scope of the Code. This was notwithstanding that the presentation was not addressed to a specifically UK audience and did not specifically refer to the availability or use of the medicine in the UK. In these circumstances, it appeared illogical that materials that did not satisfy all three criteria above would, according to the Panel, fall within the scope of the Code if they were placed on the internet from within the UK, but not if they were placed on the internet outside the UK, as the impact would be the same. Specifically, it seemed perverse that the presentation fell within the scope of the Code, whilst similar business presentations by non-UK companies of interest to investors (including those based in the UK) would not fall within the scope of the Code if they did not meet all three criteria above.

In conclusion, AstraZeneca disagreed with the Panel's conclusion that the presentation breached the undertaking, and so it refuted the Panel's ruling of breach of Clause 25. However, in so far as the Appeal Board concluded that there was a breach of the undertaking, AstraZeneca strongly refuted the Panel's ruling of a breach of Clauses 9.1 and 2. Taking into account all the circumstances of the case, AstraZeneca submitted that it had acted appropriately, maintained high standards and had not brought discredit upon or reduced confidence in the industry. In particular, a ruling of breach of Clause 2 would give credence to a vexatious complaint at the cost of AstraZeneca's reputation; a common sense approach showed that the Panel's ruling was disproportionate.

COMMENTS FROM THE COMPLAINANT

The complainant alleged that, to date, AstraZeneca had admitted no wrongdoing whatsoever regarding Seroquel and its promotion in the US. The complainant provided links to two articles from 'The New York Times', one from 2010 entitled 'For $520 million, AstraZeneca Settles Case Over Marketing of a Drug', and another from 2011 entitled 'AstraZeneca Settles Most Seroquel Suits'; both articles discussed Seroquel.

The complainant alleged that from its launch, AstraZeneca knew that Seroquel caused significant weight gain. This was both time and dose related. When the complainant worked at AstraZeneca UK he was unwilling to sign off any advertising claims that said otherwise. He was told by his marketing colleagues this was 'a career limiting step'.

The complainant alleged that AstraZeneca knew that the claim 'weight-neutral' was never true. The complainant provided three links to US blog articles from 2011 discussing Seroquel, an AstraZeneca email from 1997 discussing Seroquel entitled 'weight gain', and a copy of a paper entitled 'From Evidence-based Medicine to Marketing-based Medicine: Evidence from Internal Industry Documents' (Spielmans and Parry 2010).

The complainant alleged that the issues he raised were both pertinent and current as demonstrated in a link he provided to an article in the Bermudan publication 'The

Royal Gazette online' from 2013 entitled 'Ace and XL sued by pharmaceutical giant' concerning an ongoing court case between AstraZeneca and two insurance companies regarding Seroquel.

The complainant submitted that he had repeatedly requested a meeting with AstraZeneca's chief medical officer to discuss his concerns, but his requests had been rebuffed.

The complainant stated that a vexatious litigant was defined as 'the bringer of an action that is brought without sufficient grounds for winning, purely to cause annoyance'. This could not be the case here as the Panel had found in his favour and AstraZeneca had appealed the decision. Consequently the complainant referred AstraZeneca to the reply given in Arkell vs Pressdram (1971).

APPEAL BOARD RULING

The Appeal Board noted that the presentation at issue appeared in the 'Investors' section of the AstraZeneca corporate website under 'Presentations and Webcasts' in a folder labelled 2002. The Appeal Board considered that, contrary to AstraZeneca's submission at the hearing, such information did not have the same status as a company's annual report or other announcements made to inform shareholders, the Stock Exchange and the like.

The Appeal Board decided that the presentation came within the scope of the Code as it was information about, *inter alia*, a prescription only medicine Seroquel, which appeared on AstraZeneca's website. In that regard the Appeal Board considered that it was irrelevant how old the data was. A potential investor in the company might look on AstraZeneca's website for information and find the presentation at issue.

The Appeal Board was concerned that AstraZeneca had not looked at archived material on its website in relation to the undertaking and assurance given in the previous cases. The Appeal Board noted AstraZeneca's submission that this was historical material. The Appeal Board further noted that the material was still in the public domain. There was no indication on the material itself that it was historical. The impression was that the material could still be current. The Appeal Board noted that an undertaking required that the promotional activity or use of the material in question and any similar material, if not already discontinued or no longer in use, would cease forthwith and that all possible steps would be taken to avoid a similar breach of the Code in the future. Details of certain actions taken by the company to implement the undertaking had to be provided, including the date on which the material was finally used or appeared and/or the last date on which the activity took place.

The Appeal Board noted AstraZeneca's submission that the presentation was clearly archived, no longer in use and not used proactively.

The Appeal Board noted that slide 18 was headed 'Seroquel – Strong differential advantage across the indications'. The Appeal Board noted that the first bullet point underneath the heading stated 'Broad-based efficacy' beneath which three sub-bullets stated 'as effective as other atypicals', 'efficacy in one week' and 'effective in the long-term'. The Appeal Board considered that together these three points contributed to the broad-based efficacy claim; each individual point on its own was not a claim for broad-based efficacy and would not be read as such. In the Appeal Board's view the lower half of the slide would be interpreted in the same way so that 'placebo-like EPS', 'placebo-like prolactin levels', 'low incidence of sexual dysfunction' and the claim at issue, 'weight-neutral in the long-term', would be seen to collectively contribute to Seroquel's 'Unique tolerability profile'. The Appeal Board did not consider that each point on its own would be read as a unique feature of Seroquel.

The Appeal Board noted that the undertaking given in Cases AUTH/2294/1/10, AUTH/2296/1/10 and AUTH/2297/1/10 related to the claim, 'The only atypical with placebo level EPS (including akathisia) and placebo level prolactin concentrations and a favourable weight profile across the full dose range'.

The Appeal Board considered that the presentation of the claim 'weight-neutral in the long-term' as one of four bullet points beneath the heading 'Unique tolerability profile' in the material at issue was such that it was not sufficiently similar to the claim at issue in Cases AUTH/2294/11/10, AUTH/2296/1/10 and AUTH/2297/1/10 for it to be covered by the undertaking given in those cases. Taking all the circumstances into account, the Appeal Board ruled no breach of Clause 25 and consequently no breaches of Clauses 2 and 9.1. The appeal was successful.

Complaint received **30 October 2012**

Case completed **13 February 2013**