CASE AUTH/2291/1/10

HOSPITAL CONSULTANT v FLYNN

Promotion of Actiq

A hospital consultant complained about the use of Davies *et al* (2009) in an advertisement for Actiq (oral transmucosal fentanyl citrate) emailed by Flynn Pharma. Actiq was indicated for the management of breakthrough pain (BTP) in patients already receiving maintenance opioid therapy for chronic cancer pain.

The complainant alleged that the advertisement misrepresented Davies *et al*, which gave a task group's recommendations on the management of cancer related BTP, by focusing on a sub-section of one of the recommendations and ignoring the other eleven. An uninformed reader might believe that the paper recommended Actiq for breakthrough cancer pain, which it did not.

The complainant was also concerned that Christie *et al* (1998), which was the main paper cited in the advertisement, was not an appropriate paper to compare the effects of Actiq vs normal treatment. Actiq was titrated to maximal effect but the data on the normal treatment was derived from the screening phase of the study ie the study did not compare like with like! Indeed, Christie *et al* was much more positive about the effects of Actiq than other published papers.

The detailed response from Flynn is given below.

The Panel noted the headline of the advertisement 'The Task Group of the Science Committee of the Association for Palliative Medicine of Great Britain and Ireland have called for the management of cancer related breakthrough pain to be individualised'. The advertisement listed factors relevant to the optimal management of cancer related BTP. A statement in an emboldened typeface then read 'Immediate release (IR) oral opioids are not the optimal rescue medication for most episodes of cancer related BTP'. The pharmacokinetic/pharmacodynamic profiles of oral opioids were then discussed followed by two bullet points highlighting when immediate release oral opioids might be useful. The next paragraph in the same colour and size typeface read 'Actiq (oral transmucosal fentanyl citrate) – Established evidence of efficacy'.

A highlighted box at the bottom of the page listed a number of claims for Actiq – including that it had been demonstrated to have pharmacokinetics tailored to the profile of cancer related BTP. An accompanying graph adapted from Christie *et al* compared the pain intensity difference of [Actiq] with patients' usual BTP medication. A banner 'Actiq, Give them a handle on pain' with a link to prescribing information appeared at the end of the advertisement.

The Panel noted that Davies *et al*, on the basis of a literature review, were unable to make recommendations about any individual interventions but did make recommendations about certain generic strategies. Recommendation eight was that opioids were the rescue medication of choice in the management of breakthrough cancer pain. The Panel noted that fentanyl citrate was discussed but no specific recommendations were made, as acknowledged by Flynn.

Overall, the Panel did not consider it unreasonable for the advertisement to focus on one particular area of interest in the management of BTP. In that regard the Panel did not consider that the advertisement was misleading as alleged. No breach of the Code was ruled. However the Panel considered that the design and content of the advertisement implied that Davies *et al* recommended Actiq for use in BTP and that was not so. The claim 'Actiq …. Established evidence of efficacy' was presented immediately after the data from Davies *et al* and appeared to be part of the task group's recommendations. The design of the material was such that there was insufficient differentiation between the recommendations of Davies *et al* and promotional claims for Actiq. The advertisement was misleading and not capable of substantiation in this regard as alleged and breaches of the Code were ruled.

The Panel noted that a graph adapted from Christie *et al* showed a statistically significant difference in pain intensity at 15, 30 and 60 minutes in favour of Actiq vs usual BTP medication. No further details about Christie *et al* were provided. The Panel noted that a secondary objective of Christie *et al* was to compare the efficacy produced by Actiq with that of the patients' usual BTP medication in an open label manner. Assessment of patients' BTP and usual medication occurred during the baseline phase after which the dose-response relationship of Actiq was assessed.

The Panel noted that Christie *et al* was not designed to rigorously compare the usual breakthrough medication and Actiq. The usual breakthrough medication was not titrated as part of the study. The better efficacy of Actiq could thus relate to the suboptimal dose of the usual breakthrough medication. The study authors noted that their results should be considered tentative. Further blinded studies were needed before it could be concluded that Actiq produced better efficacy than patients' usual medication. The Panel thus considered that the graph gave a misleading impression of the comparative efficacy of Actiq which was incapable of substantiation as alleged.

Breaches of the Code were ruled.

Upon appeal by Flynn the Appeal Board noted the highlighted box at the bottom of the advertisement listed a number of claims for Actiq under the heading 'Actiq has been demonstrated:'. The second claim 'To provide rapid analgesia' and the third claim 'To have a short duration of action' were both referenced to Christie *et al,* Portenoy *et al* (1999), Farrar *et al* (1998) and Coluzzi *et al* (2001). The claim 'To provide rapid analgesia' was followed by two sub-claims '0-to 15-minute *Pain Intensity score* was over 2 ½ times larger than the score for usual BTP medication' and '0-to 15-minute *Pain Relief* score was more than *2 times higher* than the score for usual BTP medication' both referenced only to Christie *et al*. Flynn submitted that these sub-claims were quotations from Christie *et al*. They were not presented as such in the advertisement at issue. The graph at issue appeared next to the claims and depicted a statistically significant difference in pain intensity at 15, 30 and 60 minutes in favour of Actiq vs usual BTP medication.

The Appeal Board noted Farrar *et al* which compared Actiq and placebo had, as expected, shown a difference in favour of Actiq. However, both Portenoy *et al* (usual breakthrough medicine vs Actiq) and Coluzzi *et al,* (morphine sulphate immediate release vs Actiq), found a similar pattern of results to Christie *et al* in that Actiq produced a greater and more rapid onset of analgesia in the first hour following administration. Portenoy *et al* and Christie *et al* were both dose titration studies not intended to rigorously compare the analgesic efficacy of Actiq with usual rescue medication. At each time point measured in Christie *et al* and Coluzzi *et al* the pain intensity difference produced by Actiq was reported to be statistically significantly greater than that produced by the active comparator.

The Appeal Board considered that despite caveats in Christie *et al,* the fact that the study was not inconsistent with the available evidence meant that the graph did not mislead as to the comparative efficacy of Actiq vs usual BTP medicine. The graph could be substantiated. The Appeal Board ruled no breaches of the Code.

A hospital consultant complained about the use of Davies *et al* (2009) in an advertisement (ref ACT1809) for Actiq (oral transmucosal fentanyl citrate) emailed by Flynn Pharma Ltd.

Actiq was indicated for the management of breakthrough pain (BTP) in patients already receiving maintenance opioid therapy for chronic cancer pain.

COMPLAINT

The complainant alleged that the advertisement misrepresented Davies *et al* by focusing on a sub-section of one of the recommendations for management and ignoring the other eleven. Indeed, an uninformed reader could be led to believe that the task group recommended Actiq for breakthrough cancer pain, which it did not.

The complainant was also concerned about the use of data from research studies to support the use of Actiq in clinical practice. Christie *et al* (1998), which was the main paper cited in the advertisement, was not an appropriate paper to compare the effects of Actiq vs normal treatment. Actiq was titrated to maximal effect, and the data on the normal treatment was derived from the screening phase of the study ie the study did not compare like with like! Indeed, Christie *et al* was much more positive about the effects of Actiq than other published papers.

When writing to Flynn the Authority asked it to respond in relation to Clauses 1.7, 7.2, 7.4 and 9.1.

RESPONSE

Flynn noted that the advertisement in question (Management of breakthrough pain (BTP)) was supported by nine references, the first of which was Davies *et al*. This was an important publication that made a significant contribution to the knowledge base in the field and Flynn was understandably keen, if not obliged, to make its promotional representations consistent with the teachings of the task group. The advertisement in question was approximately one-page of A4 supported by the addition of prescribing information. A number of points were made about the optimal management of cancer related BTP and the place of immediate release oral opioids in its management which were very clearly referenced to Davies *et al*. There was no attempt to disguise or misrepresent their origin or to imply that any statement referenced had particular or even general applicability to Actiq. The references to and quotes derived from the paper were very limited. Given that Davies *et al* was a set of guideline recommendations, there was a common interest in their widespread recognition, reference and where possible, adoption or integration into practice which Flynn supported. Only very limited use had been made of statements contained within the paper, and that these were accurately reproduced was important. The messages from Davies *et al* were clearly separate from statements relating to Actiq which appeared in separate sections of the advertisement and were separately referenced. No statement linked a reference to the task group findings to any claim about Actiq. Should there be, Flynn would share the complainant's concern as the task group's recommendations stopped short of mentioning any product in particular.

Whilst Flynn believed these arguments addressed the question of misrepresentation in part, the complainant was concerned that the company had focussed on only one recommendation and ignored the others. Flynn noted that the material at issue was an advertisement which set out and supported a few specific claims and points about Actiq; it was

not a review of the management of BTP or indeed a review of the task group's recommendations. It was reasonable, justified and understandable that it focused on a particular issue or aspect of care rather than précis or review the full paper. This did not amount to misrepresentation either by virtue of its selective but accurate use of limited parts of the paper, or possibly in misrepresenting the views of the authors insofar as its use did not reflect the totality of their views.

Flynn noted the complainant's concern about the use of Christie *et al* as 'the main paper cited in the advertisement'. Christie *et al*, however, was one of six references cited in support of the Actiq claims, although it was the only one from which a figure was taken (Pain Intensity Difference (adapted from Christie *et al*)). Four of the cited references, including Christie *et al*, were also cited in Davies *et al* and as such were deemed 'relevant' papers by the task group. Thus, not withstanding that the advertisement was short and few claims were made, all without exception were expressly and clearly referenced and in Flynn's view complied with the requirements of Clause 7.4 that 'any information, claim or comparison must be capable of substantiation'.

The complainant was concerned about Christie *et al* as the pain intensity difference comparisons of Actiq and usual breakthrough medication (reported in the paper and referred to in the advertisement in question) were biased in favour of Actiq. The reasoning given was that the usual breakthrough medication dose data were derived from the baseline phase, but the Actiq doses were determined following a dose titration in the second phase of the study.

However, one of the eligibility criteria for patients entering the study was that they had 'stable pain, defined as persistent pain, no more than moderate on average, tolerable opioid side effects, and the use of four or fewer doses of opioid medication for breakthrough pain daily'. The key take-home message was that patients were 'stable' and pain management was under control. This inferred that whatever their previous or usual BTP medication was, it was sufficient to meet treatment goals and was near optimal.

When they entered the second phase of the study, patients would receive Actiq for the first time for BTP management and the study methodology directed that 'patients were titrated to an effective dose of [Actiq] and the performance of this dose was evaluated'. An 'effective' dose was not synonymous with a dose 'titrated to maximal effect' as the complainant suggested, and there was no evidence in the paper to indicate that study investigations expressly sought to achieve higher levels of control than in the baseline case. Dose titration was to a level that gave appropriate pain control, with acceptable side effects. Flynn noted that most patients were dosed on 200mcg (49%) and out of all patients, 64% were on either 200mcg or 400mcg, the two lowest available doses of Actiq.

Flynn did not therefore consider that Christie *et al* reported an unfair comparison and nor was it the main paper relied upon in support of the claims made.

PANEL RULING

The Panel noted that the prominent blue banner headline of the advertisement read 'The Task Group of the Science Committee of the Association for Palliative Medicine of Great Britain and Ireland have called for the management of cancer related breakthrough pain (BTP) to be individualised'. The advertisement began by listing factors relevant to the optimal management of cancer related BTP. A statement in an emboldened typeface then read 'Immediate release (IR) oral opioids are not the optimal rescue medication for most episodes of cancer related BTP'. The pharmacokinetic/ pharmacodynamic profiles of oral opioids were then discussed followed by two bullet points highlighting when immediate release oral opioids might be useful. The next paragraph in the same colour and size typeface read 'Actiq (oral transmucosal fentanyl citrate) – Established evidence of efficacy'.

A highlighted box at the bottom of the page listed a number of claims for Actiq – including that it had been demonstrated to have pharmacokinetics tailored to the profile of cancer related BTP. An accompanying graph adapted from Christie *et al* compared the pain intensity difference of transmucosal fentanyl [Actiq] with patients' usual BTP medication. A banner 'Actiq, Give them a handle on pain' with a link to prescribing information appeared at the end of the advertisement.

The Panel noted that Davies *et al*, on the basis of a literature review, were unable to make recommendations about any individual interventions but did make recommendations about certain generic strategies. Recommendation eight was that opioids were the rescue medication of choice in the management of breakthrough cancer pain. The Panel noted that fentanyl citrate was discussed but no specific recommendations were made, as acknowledged by Flynn.

Overall the Panel did not consider it unreasonable for the advertisement to focus on one particular area of interest in the management of BTP. In that regard the Panel did not consider that the advertisement was misleading as alleged. No breach of Clause 7.2 was ruled. However the Panel considered that the design and content of the advertisement implied that Davies *et al* recommended Actiq for use in BTP and that was not so. The claim 'Actiq …. Established evidence of efficacy' was presented immediately after the data from Davies *et al* and appeared to be part of the task group's recommendations. The design of the material was such that there was insufficient

differentiation between the recommendations of Davies *et al* and promotional claims for Actiq. The advertisement was misleading and not capable of substantiation in this regard as alleged and a breach of Clauses 7.2 and 7.4 was ruled. This ruling was not appealed.

The Panel noted that a graph adapted from Christie *et al* showed a statistically significant difference in pain intensity at 15, 30 and 60 minutes in favour of Actiq vs usual BTP medication. No further details about Christie *et al* were provided. The Panel noted that a secondary objective of Christie *et al* was to compare the efficacy produced by Actiq with that of the patients' usual breakthrough pain medication in an open label manner. Assessment of patients' BTP and usual medication occurred during the baseline phase after which the dose-response relationship of Actiq was assessed.

The Panel noted that Christie *et al* stated that the study was not designed to rigorously compare the usual breakthrough medication and Actiq. The usual breakthrough medication was not titrated as part of the study. The better efficacy of Actiq could thus relate to the suboptimal dose of the usual breakthrough medication. The study authors noted that their results should be considered tentative. Further blinded studies were needed before it could be concluded that Actiq produced better efficacy than patients' usual medication. The Panel thus considered that the graph gave a misleading impression of the comparative efficacy of Actiq which was incapable of substantiation as alleged. A breach of Clauses 7.2 and 7.4 was ruled. This ruling was appealed.

APPEAL BY FLYNN

Flynn noted that in reaching its determination the Panel had drawn on and specifically quoted, albeit in the narrowest of terms, only from Christie *et al* notwithstanding that Christie *et al* was one of a number of supporting references. From the discussion section of that paper, the Panel had quoted: 'This study was not designed to compare rigorously the usual breakthrough pain medication and Actiq' and 'The better efficiency of Actiq **could** relate to suboptimal dose selection for the usual breakthrough medicine'(emphasis added) and finally that 'These results should be considered tentative. Further blinded studies will be needed before it can be concluded that Actiq produces better efficacy than patients' usual medication'.

Flynn submitted that the test or case at issue was the extent to which the data and material derived from Christie *et al*, did or did not give a misleading impression (Clause 7.2), and secondly, the extent to which the promotional claims were, or were not capable of substantiation (Clause 7.4).

Flynn noted that in the advertisement, immediately above the boxed data and graph at issue was the claim 'Actiq (oral transmucosal fentanyl citrate) - Established evidence of efficacy'. Within the box itself in the left hand panel, was the bold heading 'Actiq has been demonstrated:' below which four bullet points set out various claims. The graph adapted from Christie *et al* appeared in the right-hand panel of the boxed information and Christie *et al* was referenced to support the first two of the four claims made.

Flynn submitted that the question to consider was what was the established evidence of efficacy relied upon and referenced to demonstrate or support the claims made? Was it unfair, insufficient and overly narrow to only consider Christie *et al* as supporting evidence? Eight references, including six which provided clinical data and/or commentary, were clearly cited, using superscripted annotations against each claim. Flynn did not rely solely or even in large part on just the evidence of Christie *et al* in the substantiation of any claim(s).

Flynn noted that the first of the four claims made was that (Actiq has been demonstrated:) 'To have pharmacokinetics tailored to the profile of cancer related BTP'. The claim was referenced to Portenoy and Hagen (1990) and Streisand *et al* (1991). Portenoy and Hagen stated that an onset of pain within 3 minutes was described in 43% of pains, the median duration of pains was 30 minutes (range 1-240 mins) and further that, 41% of pains were characterised by both rapid onset and brief duration. Streisand *et al* discussed the absorption and bioavailability of oral transmucosal fentanyl citrate and, *inter alia*, reported that peak plasma concentrations of fentanyl were statistically significantly higher and occurred sooner (P=0.003). Thus on balance, Flynn submitted that the references to the claim supported it. Particularly, Portenoy and Hagen and Streisand *et al* highlighted the relevance of events within the first 30 minutes of onset of an episode of BTP. Although the Panel rulings and complaint had not alleged or ruled a breach in regard to the claim, it was pertinent to highlight the point as the claims themselves, to have proper meaning, were related, notwithstanding that they each stood independently. They were grouped together and the design was such that they would be read and considered together, notwithstanding that each was capable of substantiation. It was noted that the first claim did not rely on Christie *et al*.

Flynn noted the second and third claims, which it considered together since both included Christie *et al* as one of a number of supporting references, the advertisement read (Actiq has been demonstrated:) 'To provide rapid analgesia' and 'To have a short duration of action'. Each of these claims was referenced to Christie *et al*, Portenoy *et al* (1999), Farrar *et al* (1998) and Coluzzi *et al* (2001). Collectively, these references constituted the supporting evidence relied upon. Portenoy *et al* and Coluzzi *et al* post-dated Christie *et al* and thus contributed to the knowledge base that Christie *et al* had alluded to in its comment that 'Further blinded studies will be needed before it can be concluded that transmucosal fentanyl produces better efficacy

than patients' usual medication. Flynn stressed that it did not rely on Christie *et al* alone.

Flynn submitted that the claims were supported by all of the cited references and were accurate, balanced, fair and unambiguous and based on an up-to-date evaluation of all the evidence. Christie *et al* did not stand alone or apart in terms of its learning points – indeed the broad findings of Christie *et al* were consistent with, and sat within the range of findings of the four papers as the subsequent arguments would illustrate. Christie *et al*, irrespective of design features and details of the study itself, was representative of the literature evidence. Further, to the extent that its findings were consistent with the later studies, Christie *et al* could be relied upon and regarded as representative of the balanced literature on the subject.

Christie *et al* reported a study of oral transmucosal fentanyl citrate for the treatment of BTP in cancer patients using transdermal fentanyl citrate for persistent pain. Sixty-two patients were randomised and Christie *et al* reported the findings in 47 who completed the study per protocol. The paper reported that eligible patients had stable pain and that they experienced four or fewer episodes of BTP daily. The management of their BTP was evaluated initially over a two day period in the baseline phase of the study, in which the pain was managed with their usual BTP medication. Following the baseline phase, patients were introduced to and titrated to an appropriate dose of Actiq in the Actiq phase of the study, and the management of BTP was further assessed over a second two day period. Two widely used measures of analgesia, Pain Intensity Difference (PID) and Pain Relief (PR), were evaluated at time points of 15, 30, 45 and 60 minutes. The graph of PID data derived from Christie *et al* formed the right-hand part of the boxed information and accurately reflected that data as reported by Christie *et al*. Flynn noted that a footnote made it clear the graph was adapted from Christie *et al*.

Flynn submitted that the complaint, and presumably an influencing factor on the Panel in reaching its conclusions, was that it was unreasonable to compare the pain measures from the baseline phase (on usual background medication) to those in the Actiq phase, where patients were titrated to an effective dose. The complainant was concerned that the usual baseline medication dose might be suboptimal and/or that the data were flattered by the titration of Actiq to an optimal dose, such that the product benefits (in terms of PID and PR measures) were misleadingly and unduly exaggerated. On the evidence of Christie *et al* and the other three supporting references Flynn rejected these concerns.

Flynn submitted that in Christie *et al* 19/47 (40%) patients completing the study used only the lowest dose of Actiq (200mcg) and 30/47 (64%) used either 200mcg or 400mcg (the next highest strength available from a range of six product strengths in the dose range 200mcg – 1600mcg). Further, patients entering the study had stable pain and could thus be regarded as relatively well-managed and by interference then, receiving BTP medication that was generally appropriate and effective. In other words, their dose of usual breakthrough medication was generally considered adequate.

Flynn submitted that it was important to consider whether the design of Christie *et al* was biased in favour of Actiq, to the extent that it presented an unduly or misleading favourable effect of Actiq. Portenoy *et al* (n = 48 vs n = 47 in Christie *et al*) reported a controlled dose titration study of Actiq in breakthrough pain in cancer patients. Key observations pertinent to the product claims at issue, reported in that study were:

- Pain intensity scores of approximately 6 (0-10 scale) were recorded before Actiq dose
- 60 minutes post-dose, average pain intensity scores were 1.5
- The pain intensity reduction with Actiq in 15 minutes was 56% of the total pain intensity decline
- The pain intensity reduction with usual medication (rescue) in 15 minutes was 32% of the total.

Flynn submitted that in other words, nearly half of the total reduction in pain intensity following dosing with Actiq, was realised in the first 15 minutes. Secondly, the reduction in pain intensity in 15 minutes following Actiq was 1.75 times that of the usual rescue medication (56/32). This compared favourably with the observation reported by Christie *et al* although one must caution against making direct comparison of efficacy endpoints from studies conducted by different investigators, at different times in different patient populations. The take-home message of both studies was simply that significant advantages in terms of pain intensity were realised in the 0-15 minute period with Actiq.

Flynn noted that Farrar *et al* concluded that '[Actiq] produced significantly larger changes in pain intensity and better pain relief than placebo at all time points'. Farrar *et al* studied PID at 15, 30, 45 and 60 minutes in a per protocol population of 86 patients. PID15 and PID30 scores for Actiq were both 159% greater than placebo at the same time points.

Coluzzi *et al* reported a randomised trial comparing Actiq and morphine sulphate immediate release (MSIR) and obtained data in 75 evaluable patients. The PID15 score was the primary efficacy variable. The authors concluded that '[Actiq] yielded outcomes (PI, PID and PR) at all time points that were significantly better then MSIR.' and that '[Actiq] was more effective that MSIR in treating breakthrough cancer pain'.

Finally Flynn noted that Davies *et al* identified Christie *et al*, Portenoy *et al*, Portenoy and Hagen and Coluzzi *et al* but not Farrar *et al* as 'relevant' papers. That was, three of the four references cited

by Flynn to substantiate claims were identified by Davies *et al* and used in some part to inform and shape its findings. Indeed the same three references were specifically referred to collectively in Section 3.8 of Davies *et al* as 'controlled trials'. There was no comment as to methodological weaknesses or differences in these studies.

In conclusion, Flynn submitted that breaches of Clause 7.2 and 7.4 should be overruled. The arguments above made it clear that the findings of Christie *et al* were consistent with the broader literature on which Flynn also relied and referenced in supporting the claim that Actiq provided rapid analgesia in the 0-15 minute period. Christie *et al* was only one of a number of studies that was recognised and widely cited and Flynn was justified in using it.

COMMENTS FROM THE COMPLAINANT

There were no further comments from the complainant.

APPEAL BOARD RULING

The Appeal Board noted that the advertisement at issue was emailed to pain specialists that had previously consented to being sent promotional material by email.

The Appeal Board noted the highlighted box at the bottom of the advertisement listed a number of claims for Actiq under the heading 'Actiq has been demonstrated:'. The second claim 'To provide rapid analgesia' and the third claim 'To have a short duration of action' were both referenced to Christie *et al*, Portenoy *et al*, Farrar *et al* and Coluzzi *et al*. The claim 'To provide rapid analgesia' was followed by two sub-claims '0-to 15-minute **Pain Intensity score** was over **2 ½ times larger** than the score for usual BTP medication' and '0-to 15-minute **Pain Relief score** was more than **2 times higher** than the score for usual BTP medication' both referenced only to Christie *et al*. Flynn submitted that these sub-claims were quotations from Christie *et al*. They were not presented as direct quotations in the advertisement at issue. The graph at issue appeared next to the claims and depicted a statistically significant difference in pain intensity at 15, 30 and 60 minutes in favour of Actiq vs usual breakthrough pain medication. The graph was referenced as being adapted from Christie *et al*.

The Appeal Board noted Farrar *et al* which compared Actiq and placebo had, as expected, shown a difference in favour of Actiq. However, both Portenoy *et al*, that compared usual breakthrough medicine against Actiq, and Coluzzi *et al*, that compared morphine sulphate immediate release with Actiq, found a similar pattern of results to Christie *et al* in that Actiq produced a greater and more rapid onset of analgesia in the first hour following administration. Portenoy *et al* and Christie *et al* were both dose titration studies not intended to rigorously compare the analgesic efficacy of Actiq with usual rescue medication. At each time point measured in Christie *et al* and Coluzzi *et al* the pain intensity difference produced by Actiq was reported to be statistically significantly greater than that produced by the active comparator.

The Appeal Board considered that despite the authors' concerns with regard to Christie *et al*, the fact that the study was not inconsistent with the available evidence meant that the graph did not mislead as to the comparative efficacy of Actiq vs usual breakthrough pain medicine. The graph could be substantiated. The Appeal Board ruled no breach of Clauses 7.2 and 7.4 of the Code. The appeal on this point was successful.

Complaint received	**4 January 2010**
Case completed	**21 April 2010**