CASE AUTH/2388/2/11

JOHNSON & JOHNSON/DIRECTOR v GLAXOSMITHKLINE CONSUMER HEALTHCARE

NiQuinin leavepiece

Johnson & Johnson complained about a leavepiece for NiQuitin 21mg Clear Patch (nicotine replacement therapy (NRT)) issued by GlaxoSmithKline Consumer Healthcare. The NiQuitin patch was to be applied for 24 hours. As the complaint involved an alleged breach of undertaking that aspect was taken up by the Director as the Authority was responsible for ensuring compliance with undertakings.

The front cover of the leavepiece referred to the technology of the NiQuitin Patch which enabled a rapid delivery of nicotine on application and then a steady stream throughout the day.

Page 2 was headed 'NiQuitin 21mg Clear Patch, delivers more nicotine than 25mg/16-hour patch' beneath which was a graph comparing the mean adjusted plasma nicotine against time for NiQuitin 21mg patch and '25mg/16 hour patch'. The claim 'NiQuitin 21mg Clear Patch delivered 57% more nicotine than the 25mg/16-hour patch: [area under the curve] AUC 0-_{00} ($p<0.0001$)' appeared on the bottom of the page. This page was referenced to data on file and to DeVeaugh-Geiss (2010).

Page 3 was headed 'It also delivers more than:' above a graph comparing the plasma nicotine concentration from once daily applications of NiQuitin 21mg patch 24 hour, Nicotinell 21mg patch 24 hour and Nicorette 15mg patch 16 hour over 72 hours from initial dosing. The graph was adapted from Fant *et al* (2000). The claim which accompanied the graph, 'NiQuitin 21mg Clear Patch delivered significantly more nicotine than either of the other patches ($p<0.05$)' was also referenced to Fant *et al*. A second claim 'With NiQuitin 21mg Clear Patch, steady state is reached after the second dose. Steady state maximum concentrations are approximately 30% higher than on day one' was referenced to the NiQuitin 21mg Clear Patch summary of product characteristics (SPC).

Page 4, the back cover, included the prescribing information and was headed 'NiQuitin 21mg Clear Patch delivers more nicotine than 25mg/16-hour patch'.

Johnson & Johnson stated that the leavepiece, which detailed direct pharmacokinetic comparisons of the NiQuitin 21mg Clear Patch with other NRT patches including Nicorette Invisi 25mg Patch (nicotine) and Nicorette 15mg Patch (nicotine), was distributed to prescribing and non-prescribing health professionals.

The primary message of the leavepiece, was that the NiQuitin 21mg patch delivered more nicotine than the Nicorette 25mg patch. This was reinforced by the comparative graph underneath the heading which showed that the NiQuitin 21mg patch had a higher AUC than the Nicorette 25mg patch. The reader was likely to be left with the impression that the NiQuitin patch had a more favourable pharmacokinetic profile or was clinically superior compared with the Nicorette patch. This was likely to influence the prescribing decision, although there was no evidence of superiority. Johnson & Johnson believed that it was inappropriate to show comparative pharmacokinetic data in isolation, in an attempt to influence a prescriber's decision, without it being supported by relevant clinical and safety data.

Johnson & Johnson queried why GlaxoSmithKline Consumer Healthcare would develop a leavepiece which presented comparative pharmacokinetic data which had not been established to translate into clinical difference, unless it was to imply clinical superiority.

In inter-company dialogue, GlaxoSmithKline Consumer Healthcare had stated that health professionals were confused about the delivery of nicotine from the Nicorette 25mg patch and the NiQuitin 21mg patch. This suggested that the leavepiece at issue was intended to address this misconception by informing health professionals of the pharmacokinetic profiles of both products to allow them to make an informed decision. However the presentation of the pharmacokinetic data must comply with the Code and previous undertakings given, and in Johnson & Johnson's opinion, GlaxoSmithKline Consumer Healthcare had not ensured this. Furthermore, it was likely that the way in which the pharmacokinetic data had been presented would confuse health professionals more as only part of the overall story had been told with the remainder being left open to interpretation by the health professional ie the fact that no differences in clinical outcomes between 24 and 16 hour patches had been demonstrated. Presenting the comparative pharmacokinetic profiles in isolation did not help health professionals make an 'informed decision'.

Johnson & Johnson noted that in Case AUTH/2298/2/10 it had similarly alleged that the presentation of single and multiple dose pharmacokinetic profiles had falsely implied clinical superiority in terms of quit rates for NiQuitin

compared with Nicorette patches.

Johnson & Johnson believed that the material now at issue was not consistent with the ruling in Case AUTH/2298/2/10 in which the Panel considered that 'the leaflet was misleading as alleged on this point; it implied the differences in pharmacokinetic profiles led to differences in quit rates and this had not been proven'.

The detailed submission from GlaxoSmithKline Consumer Healthcare is given below.

The Panel noted that there was no mention of clinical outcome data in the leavepiece in question. In the Panel's view the leavepiece was sufficiently different to the mailing at issue in Case AUTH/2298/2/10 which had included pharmacokinetic data and clinical data regarding short- and long-term quit rates such that there appeared to be a consequential link between the two. Thus the Panel considered that GlaxoSmithKline Consumer Healthcare had not failed to comply with its undertaking in Case AUTH/2298/2/10 and no breach of the Code was ruled.

The Panel noted GlaxoSmithKline Consumer Healthcare's concern that since the launch of the Nicorette Invisi 25mg Patch, health professionals believed that the 25mg patch would deliver higher plasma nicotine levels than the NiQuitin 21mg Patch. In the Panel's view it was not unreasonable for GlaxoSmithKline Consumer Healthcare to inform them that this was not so.
The Panel noted that the clear message from the leavepiece was that the NiQuitin 21mg patch delivered more nicotine than the Nicorette 25mg patch. Market research had shown that the majority of prescribers preferred the 25mg patch because of its strength and/or thought that it delivered more nicotine than the NiQuitin 21mg patch. The graph and the claims in the leavepiece sought to reverse that thinking. Although the leavepiece did not refer to any clinical data, it also did not state that the pharmacokinetic differences highlighted and quantified had not been shown to result in any difference in clinical outcome ie quit rate. In the Panel's view, prescribers might now regard the NiQuitin 21mg patch as 'stronger' than the 25mg patch and thus assume that it was clinically more effective. There was no evidence that this was so. This was similarly the case for the graph on page 3 of the leavepiece which compared the pharmacokinetic data for NiQuitin 21mg with that for two other NRT patches. The Cochrane Review on Nicotine Replacement Therapy for Smoking Cessation (2008) stated that indirect comparison failed to detect evidence of a difference in effect between the 16 hour and 24 hour patches. The Panel considered that the leavepiece gave a misleading impression as to the relative clinical efficacy of NiQuitin 21mg clear patch vs the 25mg patch as alleged and a breach of the Code was ruled.

Johnson & Johnson Limited complained about a four page leavepiece (ref NCQ/SYN/KG/0610/02) for NiQuitin 21mg Clear Patch (nicotine replacement therapy (NRT)) issued by GlaxoSmithKline Consumer Healthcare. The NiQuitin patch was to be applied for 24 hours. Inter-company dialogue had failed to resolve all of the issues. As the complaint involved an alleged breach of undertaking that aspect was taken up by the Director as the Authority was responsible for ensuring compliance with undertakings.

Page 1 of the leavepiece, the front cover, provided details of the technology behind the design of the NiQuitin 21mg Clear Patch which enabled it to provide nicotine in two stages; first a rapid delivery on application and then a steady stream of nicotine throughout the day.

Page 2 was headed 'NiQuitin 21mg Clear Patch, delivers more nicotine than 25mg/16-hour patch' beneath which was a graph comparing the mean adjusted plasma nicotine against time for NiQuitin 21mg patch and '25mg/16 hour patch'. The claim 'NiQuitin 21mg Clear Patch delivered 57% more nicotine than the 25mg/16-hour patch: AUC [area under the curve] 0-00 ($p<0.0001$)' appeared on the bottom of the page. This page was referenced to data on file and to DeVeaugh-Geiss (2010).

Page 3 was headed 'It also delivers more than:' followed by a graph comparing the plasma nicotine concentration from once daily applications of NiQuitin 21mg patch 24 hour, Nicotinell 21mg patch 24 hour and Nicorette 15mg patch 16 hour over 72 hours from initial dosing. The graph was adapted from Fant *et al* (2000). The claim which accompanied the graph, 'NiQuitin 21mg Clear Patch delivered significantly more nicotine than either of the other patches ($p<0.05$)' was also referenced to Fant *et al*. A second claim 'With NiQuitin 21mg Clear Patch, steady state is reached after the second dose. Steady state maximum concentrations are approximately 30% higher than on day one' was referenced to the NiQuitin 21mg Clear Patch summary of product characteristics (SPC).

Page 4, the back cover, included the prescribing information and was headed 'NiQuitin 21mg Clear Patch delivers more nicotine than 25mg/16-hour patch'.

COMPLAINT

Johnson & Johnson stated that the leavepiece, which detailed direct pharmacokinetic comparisons of the NiQuitin 21mg Clear Patch with other NRT patches including Nicorette Invisi 25mg Patch (nicotine) and Nicorette 15mg Patch (nicotine), was distributed to prescribing and non-prescribing health professionals.

The primary message of the leavepiece, as stated in the heading on page two, was that the NiQuitin 21mg patch delivered more nicotine than the Nicorette 25mg patch. However, Johnson &

Johnson believed that the overall impression was that NiQuitin had a 'superior' pharmacokinetic profile, and/or that the pharmacokinetic profile of the NiQuitin patch conferred a clinical advantage over the Nicorette patch. This was reinforced by the comparative graph underneath the heading which showed that the NiQuitin 21mg patch had a higher AUC than the Nicorette 25mg patch. Although the reader was likely to be left with the impression that the NiQuitin patch had a more favourable pharmacokinetic profile or was clinically superior compared with the Nicorette patch, there was no evidence to support this.

Johnson & Johnson believed that prescribers would consider that the comparative pharmacokinetic profiles were meaningful, and that because the data showed that the NiQuitin 21mg patch delivered more nicotine, it was therefore also clinically superior. This was likely to influence the prescribing decision, although there was no evidence of superiority. Johnson & Johnson believed that it was inappropriate to show comparative pharmacokinetic data in isolation, in an attempt to influence a prescriber's decision, without it being supported by relevant clinical and safety data. On balance, Johnson & Johnson believed GlaxoSmithKline Consumer Healthcare asked prescribers to decide purely on relative pharmacokinetic profiles of the patches, where this had not been shown to be directly relevant.

Although the leavepiece included pharmacokinetic data, there was no information relating to the clinical implications of this and also GlaxoSmithKline Consumer Healthcare had made no attempt to interpret the data in order to provide a health professional with a reason to prescribe this product. Johnson & Johnson queried why GlaxoSmithKline Consumer Healthcare would develop a leavepiece which presented comparative pharmacokinetic data which had not been established to translate into clinical difference, unless it was to imply clinical superiority.

In Johnson & Johnson's opinion, the overall impression of this leavepiece was similar to that of the NiQuitin leavepiece at issue in Case AUTH/2298/2/10. In that case Johnson & Johnson alleged that the presentation of the data implied clinical superiority in terms of smoking cessation outcomes for NiQuitin vs Nicorette patches. The use of the graphs showing higher plasma levels in terms of single and multiple dose pharmacokinetic profiles compared with other NRT patches implied superiority in terms of clinical efficacy.

In relation to the leavepiece now at issue GlaxoSmithKline Consumer Healthcare had informed Johnson & Johnson that health professionals were confused about the delivery of nicotine from the Nicorette 25mg patch and the NiQuitin 21mg patch. GlaxoSmithKline Consumer Healthcare's response suggested that the leavepiece was intended to address this misconception by informing health professionals of the pharmacokinetic profiles of both products to allow them to make an informed decision. However, even if GlaxoSmithKline Consumer Healthcare believed this was true, the presentation of the pharmacokinetic data in this leavepiece must comply with the Code and previous undertakings given, and in Johnson & Johnson's opinion, GlaxoSmithKline Consumer Healthcare had not ensured this. Furthermore, it was likely that presentation of the pharmacokinetic data in this way would further serve to increase confusion amongst health professionals as this only provided part of the overall story and left the remainder open to interpretation by the health professional ie the fact that no differences in clinical outcomes between 24 and 16 hour patches had been demonstrated. Presenting the comparative pharmacokinetic profiles in isolation did not help health professionals make an 'informed decision' as GlaxoSmithKline Consumer Healthcare had suggested.

GlaxoSmithKline Consumer Healthcare had referred to the Panel's ruling in Case AUTH/2298/2/10 in which the Panel acknowledged the value of using pharmacokinetic data and stated that '… whilst pharmacokinetic data was useful such data must not be presented in a way that implied consequential clinical benefits unless a direct link between the two had been established'.

GlaxoSmithKline Consumer Healthcare had believed that pharmacokinetic data was useful on this occasion to address the misconception about delivery of nicotine. However, Johnson & Johnson believed that GlaxoSmithKline Consumer Healthcare's presentation of the data was not consistent with the ruling in Case AUTH/2298/2/10 in which the Panel also considered that 'the leaflet was misleading as alleged on this point; it implied the differences in pharmacokinetic profiles led to differences in quit rates and this had not been proven'.

The average prescriber would consider that the comparative pharmacokinetic profiles actually showed a different meaning to that which GlaxoSmithKline Consumer Healthcare attempted to demonstrate. The data presented showed that the NiQuitin 21mg patch delivered more nicotine, and so implied that the NiQuitin patches were pharmacokinetically or clinically superior. However, it had not been established that a 24-hour patch which delivered more nicotine than a 16-hour patch, conferred any clinical benefit whatsoever. It was yet to be established as to whether the break in nicotine dosing overnight provided by a 16-hour patch had any impact on overall efficacy. It was conceivable that the relative difference between the minimal nicotine levels in the morning and higher levels throughout the day, provided by a 16-hour patch, could have a bearing on efficacy. The Cochrane Review on Nicotine Replacement Therapy for Smoking Cessation (2008) stated that 'Indirect comparison failed to detect evidence of a difference in effect between 16-hour and 24-hour patch, with

similar point estimates and overlapping confidence intervals in the two subgroups[1]'.

In summary, Johnson & Johnson believed that the comparative pharmacokinetic data presented in the leavepiece over-emphasised the importance of pharmacokinetic data in this context and implied a meaningful advantage for the NiQuitin 21mg patch over and above the Nicorette 25mg patch, which could not be supported. The impression for prescribers would be that the product would also produce better clinical outcomes, which had not been proven. Johnson & Johnson therefore alleged a breach of Clause 7.2.

Although Johnson & Johnson acknowledged that GlaxoSmithKline Consumer Healthcare had amended the data presented following the outcomes and conclusion of Case AUTH/2298/2/10, the same comparative data was presented in the leavepiece at issue and the graphs remained similar. No clinical data was presented within the leavepiece to demonstrate that nicotine plasma levels or differences in pharmacokinetic profiles had a direct bearing on clinical efficacy.

A breach of the Code was ruled in Case AUTH/2298/2/10 and the Panel provided clarity that pharmacokinetic data must not be presented such as to imply consequential clinical benefits unless a direct link between the two had been established. The material at issue was ruled in breach of the undertaking given in Case AUTH/1253/11/01.

The leavepiece now in question was produced as a direct replacement for that found in breach in Case AUTH/2298/2/10 and Johnson & Johnson understood that, following inter-company correspondence in that case, GlaxoSmithKline Consumer Healthcare reviewed its standard operating procedures for the approval of promotional materials. As the leavepiece now in question gave the same overall impression, Johnson & Johnson believed this also represented a further breach of undertaking and therefore alleged a breach of Clause 25. As previously stated, Johnson & Johnson believed this constituted a second breach of the original undertaking made by GlaxoSmithKline Consumer Healthcare in relation to Case AUTH/1253/11/01.

When writing to GlaxoSmithKline Consumer Healthcare, the Authority asked it to respond to Clause 2 in relation to the alleged breach of undertaking in addition to Clause 25 as cited by Johnson & Johnson.

RESPONSE

GlaxoSmithKline Consumer Healthcare stated that traditionally, the starting dose for NRT patches had been either 21mg (worn for 24 hours) or 15mg (worn for 16 hours). Johnson & Johnson introduced its 25mg patch in 2009. Unsurprisingly, health professionals believed that the 25mg patch would deliver more nicotine to the bloodstream than a 21mg patch. This misconception was confirmed by anecdotal feedback from the representatives, and by market research conducted by GlaxoSmithKline Consumer Healthcare. The market research carried out on 12 and 13 January 2011 showed that when asked 'Which of the following patches delivers more nicotine?' 71% of GPs and 78% of practice nurses chose Nicorette 25mg over NiQuitin or Nicotinell 21mg patches. Sixty per cent of respondents who used a 25mg patch for patients who smoked more than 20 cigarettes a day, cited strength as the reason why they prescribed the product and 28% that it delivered more nicotine. From the representative feedback and the market research it was clear that the majority of health professionals believed the Nicorette 25mg patch delivered more nicotine than the NiQuitin 21mg patch and a substantial proportion prescribed it for this reason. However, as the results of the head-to-head study showed, NiQuitin 21mg delivered the most nicotine, not Nicorette 25mg. Thus it was important that health professionals knew about the data so they could make informed and rational treatment decisions. If they wanted to prescribe the patch that delivered the most nicotine, then they should prescribe NiQuitin 21mg rather than Nicorette 25mg.

That NiQuitin 21mg delivered more nicotine than Nicorette 25mg might seem counter-intuitive based on the product labelling. However, Johnson & Johnson and GlaxoSmithKline Consumer Healthcare used different technologies of patch manufacture and based their labelled strength on different methods of calculation. GlaxoSmithKline Consumer Healthcare labelled its patch according to the amount of nicotine actually delivered to the bloodstream, whereas Johnson & Johnson labelled its patch according to the 'average amount of nicotine released over 16 hours'.

In July 2008 GlaxoSmithKline Consumer Healthcare contacted the Medicines and Healthcare products Regulatory Agency (MHRA) regarding the difference in nomenclature of the transdermal patches, specifically that different companies used different methodologies to calculate their labelled dose. The MHRA acknowledged the inconsistent approach and whilst companies were not required to align, it hoped that the industry would be able to reach a harmonised position. However, no progress had been made in this regard. The inconsistency had not impacted prescribers until the introduction of the 25mg patch and the consequential assumption that it was the strongest/highest strength/delivered most nicotine. GlaxoSmithKline Consumer Healthcare was keen to ensure that prescribers made informed prescribing decisions based on robust evidence and therefore it needed to address the misconception that the Nicorette 25mg patch delivered more nicotine than the NiQuitin 21mg patch.

GlaxoSmithKline Consumer Healthcare regarded undertakings to the PMCPA extremely seriously and was concerned that the leavepiece should be

fundamentally different from the material found in breach in Cases AUTH/2298/2/10 and AUTH/1253/11/01, and comply with previous advice by removing any reference to comparative clinical benefits. The leavepiece simply presented the pharmacokinetic data and made no clinical benefit claims. It informed health professionals that NiQuitin 21mg delivered more nicotine than Nicorette 25mg, Nicorette 15mg and Nicotinell 21mg, and graphically displayed the nicotine levels in two separate head-to-head studies. In the previous cases pharmacokinetic data had been presented in the same item as data which discussed quit rates and the Panel noted that, although pharmacokinetic data was useful, it must not imply consequential clinical benefits unless a direct link between the two had been established. In the most recent case (Case AUTH 2298/2/10) GlaxoSmithKline Consumer Healthcare believed that it had separated the quit rate data from the pharmacokinetic data by putting it on separate pages, but the Panel considered by highlighting the NiQuitin quit rates this implied an advantage for NiQuitin, especially as there was also a claim that no other patch had been found to be more effective. Consequently, in producing the leavepiece now at issue GlaxoSmithKline Consumer Healthcare took the undertakings seriously and removed all reference to clinical outcomes to ensure compliance.

Johnson & Johnson agreed that the primary message of the leavepiece was that the NiQuitin 21mg patch delivered more nicotine than the Nicorette 25mg patch, but believed that the overall impression was that NiQuitin 21mg had a superior pharmacokinetic profile and/or the pharmacokinetic profile offered a clinical advantage over the Nicorette 25mg patch. On the contrary, the leavepiece was clear and unambiguous in its message – the NiQuitin 21mg patch delivered more nicotine than the Nicorette 25mg patch and it also delivered more than the Nicotinell 21mg and Nicorette 15mg patches. The pharmacokinetic claims were factual and highlighted only one pharmacokinetic parameter – that of dose delivered – as there was a clear need to educate health professionals in this regard. There were no claims of pharmacokinetic superiority or implications of clinical superiority.

It was important that health professionals saw the data as generated in these two head-to-head studies so that they could have an informed opinion and base their treatment decisions on evidence rather than assumption. Each of the pharmacokinetic profiles displayed in the graphs were different, and one was not necessarily superior over the others as there were many different elements that made up a pharmacokinetic profile. One person's superior pharmacokinetic profile was another's inferior. Aspects of one profile might be considered more beneficial to some health professionals than others. For years Nicorette had promoted the benefits of not delivering nicotine overnight and this could be seen in the substantial decline in overnight nicotine levels for the 25mg patch plotted clearly in the graph on page 2 and also for the 15mg patch in the graph on page 3. Conversely, the 24-hour patches both maintained significant overnight nicotine levels. For health professionals who preferred patches that did not maintain overnight nicotine levels, then the NiQuitin 21mg patch pharmacokinetic profile was clearly not superior.

The leavepiece was specifically designed to disabuse health professionals of the understandable misconception that the Nicorette 25mg patch delivered more than the NiQuitin 21mg patch. A standard treatment course of the Nicorette 25mg patch cost 20% more than a standard treatment course of the NiQuitin 21mg patch, but many health professionals prescribed or recommended the Nicorette 25mg patch because they assumed that they got more nicotine for their money; the pharmacokinetic data demonstrated that this was not so.

GlaxoSmithKline Consumer Healthcare refuted the allegation that the comparative pharmacokinetic data over-emphasised the importance of pharmacokinetic data and implied a meaningful advantage for NiQuitin 21mg over Nicorette 25mg. The leavepiece was used to correct the widespread misconception that the Nicorette 25mg patch delivered more nicotine than the NiQuitin 21mg patch. It was accurate, factual, unambiguous and not misleading. It made no claims for clinical outcomes and did not claim or imply superiority of pharmacokinetic profile. It was simply a presentation of the direct head-to-head pharmacokinetic data. GlaxoSmithKline Consumer Healthcare did not believe it had breached Clause 7.2.

GlaxoSmithKline Consumer Healthcare was confident it had not breached any undertakings previously given. This leavepiece was fundamentally different from previous items found in breach which discussed both pharmacokinetic data and clinical outcome data. The leavepiece discussed pharmacokinetic data only and no direct or indirect reference was made to relative clinical benefits. Thus GlaxoSmithKline Consumer Healthcare refuted the alleged breach of Clause 25 and as such also refuted the allegation of a breach of Clause 2.

PANEL RULING

The Panel noted that there was no mention of clinical outcome data in the leavepiece in question. In the Panel's view the leavepiece was sufficiently different to the mailing at issue in Case AUTH/2298/2/10 which had included pharmacokinetic data and clinical data regarding short- and long-term quit rates such that there appeared to be a consequential link between the two. Thus the Panel considered that GlaxoSmithKline Consumer Healthcare had not failed to comply with its undertaking in Case AUTH/2298/2/10 and no breach of Clause 25 was ruled.

The Panel also ruled no breach of Clause 2 in this regard.

The Panel noted GlaxoSmithKline Consumer Healthcare's concern that since the launch of the Nicorette Invisi 25mg Patch, health professionals believed that the 25mg patch would deliver higher plasma nicotine levels than the NiQuitin 21mg Patch. In the Panel's view it was not unreasonable for GlaxoSmithKline Consumer Healthcare to inform them that this was not so. Page 2 of the leavepiece was headed 'NiQuitin 21mg Clear Patch delivers more nicotine than 25mg/16 hour patch' and the graph below depicted a greater AUC for NiQuitin than the 25mg patch. A claim below the graph quantified the additional nicotine delivered by the NiQuitin patch vs the 25mg patch (57%, $p<0.0001$).

The Panel noted GlaxoSmithKline Consumer Healthcare's submission that its patch was labelled according to the amount of nicotine delivered to the bloodstream whereas the Nicorette patch was labelled according to 'the average amount' of nicotine released over 16 hours. This was not clear in the material at issue.

The Panel noted that the clear message from the leavepiece was that the NiQuitin 21mg patch delivered more nicotine than the Nicorette 25mg patch. Market research had shown that 60% (n=40) of prescribers preferred the 25mg patch because of its strength and out of 151 prescribers, 74% (n=111) thought that it delivered more nicotine than the NiQuitin 21mg patch. The graph and the claims in the leavepiece sought to reverse that thinking. Although the leavepiece did not refer to any clinical data, it also did not state that the pharmacokinetic differences highlighted and quantified had not been shown to result in any difference in clinical outcome ie quit rate. In the Panel's view, prescribers might now regard the NiQuitin 21mg patch as 'stronger' than the 25mg patch and thus assume that it was clinically more effective. There was no evidence that this was so. This was similarly the case for the graph on page 3 of the leavepiece which compared the pharmacokinetic data for NiQuitin 21mg with that for the Nicotinell 21mg/24 hour patch and the Nicorette 15mg/16 hour patch. The Cochrane Review on Nicotine Replacement Therapy for Smoking Cessation stated that indirect comparison failed to detect evidence of a difference in effect between the 16 hour and 24 hour patches. The Panel considered that the leavepiece gave a misleading impression as to the relative clinical efficacy of NiQuitin 21mg clear patch vs the 25mg patch as alleged and a breach of Clause 7.2 was ruled.

Complaint received **16 February 2011**

Case completed **19 April 2011**