CASE AUTH/1834/5/06

PFIZER CONSUMER HEALTHCARE v NOVARTIS CONSUMER HEALTH

Nicotinell journal advertisement

Pfizer Consumer Healthcare complained about a journal advertisement for Nicotinell (nicotine transdermal patches) issued by Novartis Consumer Health. Nicotinell released nicotine over 24 hours. Pfizer Consumer Healthcare supplied Nicorette transdermal patches which released nicotine over 16 hours.

Pfizer Consumer Healthcare alleged that the claims 'When cravings peak in the afternoon… and the evening… …Nicotinell: a 24-hour patch with a profile to match', 'Recommend a patch to match their craving profile…' and 'A recent study showed that 93% of your patients' lapses occurred during the afternoon and evening. Nicotinell's patch delivers peak plasma concentrations during the afternoon with consistent nicotine delivery whatever the time of day' were misleading with regard to the efficacy profile of Nicotinell.

The advertisement emphasised the importance of controlling afternoon and evening cravings when the majority of relapses occurred.

The claims, in conjunction with the graph which showed plasma nicotine concentration vs hours from initial dose, implied that Nicotinell had a profile that was specifically suited to cover the afternoon and evening periods, and that this was clinically beneficial. However, this was not the case. Nicotinell delivered nicotine at a steady rate over 24 hours, and there was no data to suggest that it provided greatest craving relief in the afternoon and evening. It was therefore misleading to imply that Nicotinell was particularly suitable for controlling afternoon and evening cravings.

The Panel considered that the advertisement implied that the pharmacokinetic profile of Nicotinell was such that plasma nicotine levels peaked in the afternoon and evening and so coincided with craving peaks in smokers trying to quit. Fant *et al* showed that at steady state T_{max} for Nicotinell was 8 hours which, if the patch had been applied in the morning, would mean that plasma levels peaked somewhere between 2pm and 4pm according to the time of application. Between 10 and 24 hours post dose plasma nicotine levels fell although at around 13 hours post dose, and again at about 20 hours there were slight rises in otherwise declining levels. The Panel considered that the advertisement implied two completely separated peaks in nicotine plasma levels which was not so. Fant *et al* concluded by stating that further study was required to determine the clinical advantages of the profile of nicotine delivery. No data had been submitted to show that the pharmacokinetic profile of Nicotinell had a positive impact on afternoon or evening cravings. The Panel considered that the advertisement was misleading as alleged. A breach of the Code was ruled.

Pfizer Consumer Healthcare also alleged that the claim 'Combined with an intensive behavioural support programme Nicotinell's patch can increase quit rates by up to four times compared to unaided levels' represented an unbalanced view of smoking cessation using nicotine replacement therapy (NRT); a Cochrane Review concluded that all commercially available forms of NRT increased quit rates by 1.5 to 2 fold.

Furthermore, the 20% quit success figure quoted by West and Shiffman was an estimated figure for the optimal treatment available (the best combination of NRT/bupropion plus behavioural support), whereas

patch-specific data from Cochrane gave a quit success rate of 13.6% (OR 1.86) for nicotine patches plus low intensity support and 15.6% (OR 1.79) for nicotine patches plus high intensity support.

The 'four times' claim was based upon the Cochrane Review of all forms of NRT/bupropion plus behavioural support for smoking cessation, and not specifically nicotine patches, Nicotinell or otherwise. Furthermore, the 'four times' quit rate was only achieved with intensive behavioural support which was received by relatively few NRT patients.

The Panel considered that the claim implied that a study had compared Nicotinell plus intensive behavioural support with no aid which was not so. The Panel considered that the claim was misleading in that regard. A breach of the Code was ruled.

Pfizer Consumer Healthcare alleged that the graph, from Fant *et al*, had been inaccurately reproduced, with the values for plasma nicotine levels being exaggerated.

The Panel noted that the graph in the advertisement showed the pharmacokinetic profile of Nicotinell from 0 to 72 hours. In the first 24 hours C_{max} was shown as approximately 17.5ng/ml; Fant *et al* had reported a C_{max} of 17.6ng/ml. The graph in the advertisement showed higher C_{max} values on days 2 and 3 of just less than 20ng/ml; Fant *et al* had reported a C_{max} of 19.5ng/ml during that time. The Panel thus did not consider that the graph was inaccurate as alleged. No breach of the Code was ruled.

Pfizer Consumer Healthcare complained about a journal advertisement (ref Nico001-01/06) for Nicotinell (nicotine transdermal patches) issued by Novartis Consumer Health UK Ltd. Nicotinell released nicotine over 24 hours. Pfizer Consumer Healthcare supplied Nicorette transdermal patches which released nicotine over 16 hours.

Pfizer Consumer Healthcare stated that in its opinion both the content and overall impression of the advertisement were misleading and in breach of the Code.

1 Efficacy profile

COMPLAINT

Pfizer Consumer Healthcare believed that the following claims misled as to the nature of the efficacy profile of the Nicotinell patch:

i) 'When cravings peak in the afternoon… and the evening… …Nicotinell: a 24-hour patch with a profile to match.'

ii) 'Recommend a patch to match their craving profile – it needn't be hell with Nicotinell.'

iii) 'A recent study showed that 93% of your patients' lapses occurred during the afternoon and evening [Ussher and West 2003]. Nicotinell's patch delivers peak plasma concentrations during the afternoon with consistent nicotine delivery whatever the time of day.'

The advertisement emphasised the importance of controlling afternoon and evening cravings. This was clearly an important time for quitters; Ussher and West demonstrated that this was the time when the majority of relapses occurred.

The claims listed above, in conjunction with the graph [adapted from Fant *et al* 2000] which showed plasma nicotine concentration vs hours from initial dose, strongly implied that Nicotinell had a profile that was specifically suited to cover the afternoon and evening periods, and that this pharmacokinetic profile implied a clinical benefit. However, this was not the case. Unlike 16 hour patches which released nicotine in the daytime only, Nicotinell delivered nicotine at a steady rate over 24 hours, and there was no data to suggest that it provided greatest craving relief in the afternoon and evening. It was therefore misleading to imply that Nicotinell was particularly suitable for controlling afternoon and evening cravings.

Pfizer Consumer Healthcare considered that this particular issue was similar to a previous case, Case AUTH/1563/3/04, where Pharmacia (subsequently Pfizer Consumer Healthcare) had a complaint upheld against it with regard to a similar claim which linked plasma nicotine levels to craving control.

RESPONSE

Novartis Consumer Health stated that in its view the Fant *et al* pharmacokinetic study could not be correlated to clinical efficacy. As the authors had noted, further clinical studies were needed to demonstrate whether the different pharmacokinetic profiles related into clinical differences.

The creative expectations of the advertisement were to use the 24-hour pharmacokinetic profile of Nicotinell and create an image of 24 hour cover. The graphical representation began on the left hand side of the page and travelled over the cake and cocktail, through the graph finally encompassing the Nicotinell TTS 30 box. The Nicotinell box clearly showed the 24-hour patch program and the graph represented the consistent nicotine levels over 24 hours and extrapolated over a 3 day period. The graph was a smaller part of the overall advertisement and while close examination of it showed the peak nicotine levels in the afternoon and evening, this was not easily discernable at first glance. The reader had to look very carefully to realise the peak at these times. The important message was that Nicotinell was a 24-hour patch and could provide cover for the whole 24 hours. Consequently the patch could offer cover to those who failed in the afternoon and evening. The findings of Ussher and West were not unexpected. Afternoon and evening was a time when it would be expected that a smoker's determination to stop was reduced.

Furthermore, to avoid any comparative advertising and complaint from competitors, the pharmacokinetic profiles of the Niquitin and Nicorette patches were removed.

With respect to the individual claims, claim (i), the rhyme of patch and match in the claim 'Nicotinell: a 24-hour patch with a profile to match' could be justified as it was a 24-hour patch which could cover the cravings over the whole 24-hour period, no matter when they occurred.

On reflection, combining the patch to match in the claim 'When cravings peak in the afternoon … and the evening … … Nicotinell: a 24-hour patch with a profile to match' could be less challengeable if 'with a profile to match' was deleted, to read 'When cravings peak in the afternoon … and the evening … … Nicotinell: a 24-hour patch'.

Bearing in mind the above, claim (ii) could also be made less challengeable by using 'cover' rather then 'match' so the statement read 'Recommend a patch to cover their craving profile – it needn't be hell with Nicotinell'.

Finally in claim (iii) there was an inconsistency between 'delivers peak plasma concentrations' and 'consistent nicotine delivery'. This statement would be clearer by deleting 'delivers peak plasma concentrations' to read: 'A recent study showed that 93% of your patients' lapses occurred during the afternoon and evening. Nicotinell's patch delivers consistent nicotine delivery, whatever the time of the day'.

In the previous case, Case AUTH/1563/3/04, the claim used by the complainant was that '…. Nicorette 16-hour patch also provided maximum craving control when patients are most vulnerable'. The Nicotinell advertisement was different in that it highlighted when the relapse was highest and that Nicotinell offered support by having high nicotine blood levels in the afternoon and evening but also provided consistent nicotine delivery, whatever the time of the day.

As far as Novartis was concerned, this advertisement was not intended to mislead. It was no longer in print and there was no intention to use it again in its original form.

PANEL RULING

The Panel considered that the advertisement implied that the pharmacokinetic profile of Nicotinell patches was such that plasma nicotine levels peaked in the afternoon and evening and so coincided with peaks in cravings for smokers trying to quit. Fant *et al* showed that at steady state T_{max} for Nicotinell was 8 hours which, if the patch had been applied in the morning, would mean that plasma levels peaked somewhere between 2pm and 4pm according to the time of application. Between 10 and 24 hours post dose plasma nicotine levels fell although not consistently; at around 13 hours post dose, and again at about 20 hours there were slight rises in otherwise declining levels. The Panel considered that the advertisement implied two completely separate peaks in nicotine plasma levels which was not so. Fant *et al* concluded by stating that further study was required to determine the clinical advantages of the profile of nicotine delivery. No data had been submitted to show that the pharmacokinetic profile of Nicotinell had a positive impact on cravings in the afternoon or evening. The Panel considered that the advertisement was misleading as alleged. A breach of Clause 7.2 was ruled.

2 Smoking cessation data

COMPLAINT

Pfizer Consumer Healthcare alleged that the claim 'Combined with an intensive behavioural support programme Nicotinell's patch can increase quit rates by up to four times compared to unaided levels' represented an unbalanced view of smoking cessation using nicotine replacement therapy (NRT); the Cochrane Review of NRT for smoking cessation recognised the heterogeneity of NRT and concluded that all commercially available forms of NRT increased quit rates by 1.5 to 2 fold, regardless of setting. The above 'four times' claim thus misled the reader.

Furthermore, the 20% quit success figure quoted by West and Shiffman (reference used to support claim iii) was an estimated figure for the optimal treatment available (the best combination of NRT/bupropion plus behavioural support), whereas patch-specific data from Cochrane gave a quit success rate of 13.6% (OR 1.86) for nicotine patches plus low intensity support and 15.6% (OR 1.79) for nicotine patches plus high intensity support.

Furthermore, the 'four times' claim gave the misleading impression that it was based upon Nicotinell clinical trial(s) – ie '… Nicotinell's patch can increase quit rates …', when in fact the claim was based upon the Cochrane Review of all forms of NRT/bupropion plus behavioural support for smoking cessation, and not specifically nicotine patches, Nicotinell or otherwise.

The claim was further misleading as the 'four times' quit rate was only achieved with intensive behavioural support (eg group therapy to include coping skills, training and social support, approximately five sessions of behavioural support of about one hour over approximately one month, and follow up) which was received by relatively few patients who used NRT.

Pfizer Consumer Healthcare considered that this particular issue had distinct similarities to a previous case (Case AUTH/1402/12/02) where Pharmacia (subsequently Pfizer Consumer Healthcare) had a complaint upheld against it with regard to making the similar claim 'Up to 4 times the success of placebo at 1 year'.

RESPONSE

Novartis Consumer Health stated that this claim was based on the effect of intensive behavioural support which could increase quit rates by up to four times.

Novartis Consumer Health noted that the Cochrane Collaboration was a meta analysis of clinical studies to determine the effectiveness of NRT in achieving long-term smoking cessation. Only studies with 6 or 12 months follow up were included in the analysis. Under the limitations of the trial selection, some assessment was made regarding the intensity of behavioural support but this was not relevant in this case.

The reference supporting the four times claim was West and Shiffman. The results were initially published as West *et al* (2000). This reference was

different to the Cochrane Collaboration in that it concentrated on the effect of different levels of behavioural support in smoking cessation. Here West *et al* quoted brief opportunistic advice given by a physician to smokers attending a GP surgery or an outpatient clinic as having an effective result of 2% (with 95% confidence limits between 1% to 3%). Intensive behavioural support plus NRT or bupropion in moderate to heavy smokers seeking help from a smokers clinic gave an effective result of 13 – 19%. Taking the upper confidence limits of 3% effect with opportunistic advice and lower confidence limits of 13% with intensive behavioural support showed an increase quit rate of up to 4 times for nicotine replacement therapy.

What was confusing was that Pfizer Consumer Healthcare acknowledged the validity of the four times claim. It acknowledged that the four times claim was supportable with intensive behavioural support but then went on to object to the level of support needed. West *et al*, suggested that that intensive smoking cessation treatment was effective and like all smoking cessation interventions was extremely cost effective in producing population health gain. With respect to the definition of intensive behavioural support, Pfizer Consumer Healthcare had referred to the National Electronic Library for Health. However this reference was not taken from West *et al* but from Raw *et al* (1998). Raw *et al* recommended that intensive smoking cessation support should, where possible, be conducted in groups, include coping skills training and social support, and should offer around five sessions and follow up, together with nicotine replacement therapy. This was achievable in a smoking cessation clinic.

With regard to the noted similarity between this claim and the claim at issue in Case AUTH/1402/12/02, Novartis Consumer Healthcare stated that the claim now at issue was quite different; the previous claim was based on 'up to four times the success of placebo at 1 year' and referenced to Tonnesen *et al* (1991).

In conclusion the claim was generic and applied to any NRT and could be used by Pfizer Consumer Healthcare.

PANEL RULING

The Panel disagreed with the submission that the claim 'Combined with an intensive behavioural support programme Nicotinell's patch can increase quit rates by up to four times compared with unaided level' was a generic claim. The inclusion of the product name made it specific to Nicotinell. The claim implied that a study had compared Nicotinell plus intensive behavioural support with no aid which was not so. The Panel considered that the claim was misleading in that regard. A breach of Clause 7.2 was ruled.

3 Graph from Fant *et al*

COMPLAINT

Pfizer Consumer Healthcare stated that the graph had been inaccurately reproduced, with the values for plasma nicotine levels being exaggerated – eg maximum plasma nicotine levels achieved with Nicotinell 30 in the advertisement were approximately 20ng/ml, whereas the original publication had maximum values of approximately 18ng/ml.

RESPONSE

Novartis Consumer Health stated that with reference to the graphical representation it was unclear as to what Pfizer Consumer Healthcare was referring. Table 1 of Fant *et al* referred to 0 to 24 hour pharmacokinetic profiles of Nicotinell. In this instant C_{max} (ng/ml) was 17.6 and T_{max} of 10 hours.

Table 2 Pharmacokinetic profiles from 48 to 72 hours (modelled on steady state) gave C_{max} 19.5ng/ml and T_{max} of 8 hours.

These were the figures reflected on the graph. It was not clear as to how Pfizer Consumer Healthcare could claim the values were exaggerated.

PANEL RULING

The Panel noted that the graph in the advertisement showed the pharmacokinetic profile of Nicotinell from 0 to 72 hours. In the first 24 hours C_{max} was shown as approximately 17.5ng/ml; Fant *et al* had reported a C_{max} of 17.6ng/ml. The graph in the advertisement showed higher C_{max} values on days 2 and 3 of just less than 20ng/ml; Fant *et al* had reported a C_{max} of 19.5ng/ml during that time. The Panel thus did not consider that the graph was inaccurate as alleged. No breach of Clause 7.8 was ruled.

Complaint received	**4 May 2006**
Case completed	**23 June 2006**