

CASE AUTH/2056/10/07

LILLY v NOVO NORDISK

Levemir journal advertisement

Lilly alleged that the artwork in a Novo Nordisk advertisement for Levemir (insulin detemir) in *Diabetes Update*, Autumn 2007, was misleading and ambiguous in that the picture of five overweight adult bodies in a swimming pool in conjunction with the strapline 'Levemir is Changing Figures', implied that Levemir was associated with weight loss.

Weight gain was a recognised side-effect of insulin therapy and while Levemir caused less weight gain compared with other insulins (Levemir summary of product characteristics (SPC)) there was no evidence to substantiate weight loss. The SPC stated that in type 2 diabetes, Levemir treated patients had been shown to gain 0.7-3.7kg, depending on the dosing regime. Lilly agreed that the artwork represented typical patients with type 2 diabetes but the proximity of the 'changing figures' strapline meant that the emphasis became that of weight loss.

The Panel noted that the advertisement featured an underwater photograph of five overweight women treading water in a swimming pool. Only their bodies from the neck down could be seen. Beneath the photograph was the prominent claim 'Levemir is changing figures'. In the Panel's view the implication was that Levemir would change the women's figures for the better ie they would lose weight. Although boxed text contained the claim 'Less weight gain than NPH and insulin glargine' this did not negate the otherwise misleading impression given by the photograph and claim. The Panel considered that the advertisement was misleading as alleged. Breaches of the Code were ruled which were upheld on appeal by Novo Nordisk with the Appeal Board further considering that the prominent claim 'Levemir is changing figures' was a play on words and, in conjunction with the photograph, implied that Levemir would change the women's figures for the better ie they would lose weight and their shape would change. 'Figures' was much more likely to be thought of in terms of ladies' figures rather than clinical values such as HbA1c etc as submitted by Novo Nordisk.

Eli Lilly and Company Limited complained about an advertisement (ref UK/LM/0707/0052) for Levemir (insulin detemir) placed by Novo Nordisk Limited in *Diabetes Update*, Autumn 2007. Lilly supplied a number of insulins.

COMPLAINT

Lilly alleged that the artwork (five overweight adult bodies in a swimming pool) in conjunction with the strapline 'Levemir is Changing Figures' was misleading; it implied that Levemir was associated with weight loss.

Weight gain was a recognised side-effect of insulin therapy and while Levemir had been proven to cause less weight gain compared with other insulins (Levemir summary of product characteristics (SPC)) there was no evidence to substantiate weight loss in the SPC or the references cited. In addition, the SPC clearly showed that in studies of patients with type 2 diabetes, Levemir caused a weight gain ranging from 0.7-3.7kg, depending on the dosing regime.

Novo Nordisk argued that the artwork used represented typical patients with type 2 diabetes; and while Lilly agreed this was true, the proximity of the artwork to the 'changing figures' strapline meant that the emphasis to the reader became that of weight loss with this treatment.

Lilly alleged that the advertisement was ambiguous and in breach of Clauses 7.2 and 7.8 of the Code.

RESPONSE

Novo Nordisk stated that Lilly had failed to realise that the tagline clearly referred to the key findings from two randomized clinical trials conducted by Novo Nordisk (Philis-Tsimikas *et al*, 2006, and Rosenstock *et al*, 2006) in which the numerical values for the following figures were consistently and significantly changed:

- **Effective once-daily HbA1c control**
(HbA1c improvement with Levemir is -1.48%, Philis-Tsimikas *et al*)
- **Less weight gain compared to NPH and insulin glargine**
(weight gain with Levemir 0.7kg, Philis-Tsimikas *et al*)
(weight gain with Levemir 3kg, Rosenstock *et al*)
- **A low risk of nocturnal hypoglycaemia compared with NPH**
(53% risk reduction (24-hour rate) compared to NPH, Philis-Tsimikas *et al*)
(65% risk reduction (nocturnal) compared to NPH, Philis-Tsimikas *et al*)

These claims about the complex, multifactorial management of diabetes could be substantiated by the above mentioned studies. The weight benefit of Levemir as compared to other basal insulins had also been recognized by the European Medicines Evaluation Agency (EMA) and Levemir had this statement in its SPC 'Studies in patients with type 2 diabetes treated with basal insulin in combination with oral antidiabetic drugs demonstrates that glycaemic control (HbA1c) with Levemir is comparable to NPH insulin and insulin glargine and associated with less weight gain'. Novo Nordisk had

never claimed that Levemir would result in weight loss in patients with type 2 diabetes.

Novo Nordisk believed that its letter to Lilly of 24 September provided adequate response to this issue and asked that that letter form part of its substantive response.

Novo Nordisk agreed that the picture was of overweight women. However, almost 80% of patients with type 2 diabetes were overweight and of these more than one third were obese (Ridderstrale *et al*, 2006). Thus this picture represented typical patients with type 2 diabetes. Since the licensed indication of Levemir was the treatment of diabetes mellitus, Novo Nordisk could hardly see any other option than using a picture of typical type 2 diabetic patients when advertising the product in this type of diabetes. Using a picture of patients with normal weight when the advertisement was about type 2 diabetes would be rather atypical. The picture itself did not imply weight loss, but highlighted the complex treatment approach type 2 diabetics needed.

Novo Nordisk submitted that using photographs of obese people when promoting a medicine for the treatment of type 2 diabetes was acceptable under the Code and specifically Clause 7.8. Novo Nordisk therefore believed this artwork was not in breach of Clause 7.8.

PANEL RULING

The Panel noted that the advertisement featured an underwater photograph of five overweight women treading water in a swimming pool. Only their bodies from the neck down could be seen. Beneath the photograph was the prominent claim 'Levemir is changing figures'. In the Panel's view the implication was that Levemir would change the women's figures for the better ie they would lose weight. Although boxed text contained the claim 'Less weight gain than NPH and insulin glargine' this did not negate the otherwise misleading impression given by the photograph and claim. The Panel considered that the advertisement was misleading as alleged. Breaches of Clauses 7.2 and 7.8 of the Code were ruled.

APPEAL BY NOVO NORDISK

Novo Nordisk submitted that there were two claims equally close to the artwork. The first one 'Now approved: Once-daily Levemir + [oral antidiabetic] OADs therapy' clearly set the scene. The advertisement was about the benefits of the most popular form of insulin initiation in type 2 diabetes ie basal insulin plus OAD(s). There was no reason to believe that anyone treating type 2 diabetics would not know that insulin initiation was traditionally associated with weight gain (Yki-Jarvinen *et al* 1997). The only reason to introduce insulin to OAD therapy in type 2 diabetes was to improve glycaemic control, as measured by HbA1C. It was clear that the primary figure that Levemir was changing did not relate to weight but to the improvement/reduction in HbA1C figure. This aspect was adequately clarified in the

boxed text where the three claims were referenced by the results of Philis-Tsimikas *et al*, Rosenstock *et al*, 2006 and the Levemir SPC. The claim 'Levemir is changing figures' was also referenced to Philis-Tsimikas *et al* in which the results showed an improvement in: the level of HbA1C (-1.48% reduction from baseline), the risk of hypoglycaemia when compared to NPH insulin (53% risk reduction of 24-hour events and 65% risk reduction of nocturnal events) and the magnitude of treatment associated weight gain compared to NPH insulin (0.9kg (56%) less weight gain after insulin initiation).

Novo Nordisk submitted that inevitably the treatment of diabetes required a complex multifactorial management of several clinical parameters (primarily glycaemic control) in order to prevent/delay late complications (eg diabetic eye and kidney disease). This complex, stepwise approach was widely recognized, followed and applied at all stages of this progressive metabolic disorder. Physicians were well aware of the importance of addressing glycaemic control along side reducing the risk of hypoglycaemic events and weight gain together. Therefore it was clear to the reader that 'changing figures' in relation to the use of insulin directly impacted and could only relate to HbA1C, hypoglycaemia and weight gain.

On the basis of the above Novo Nordisk submitted that the claim did not mislead by implying that use of Levemir would result in weight loss; as such the claim was not in breach of Clause 7.2.

Novo Nordisk noted the Panel also ruled a breach of Clause 7.8 as the artwork was considered to be misleading as showing five overweight women and implying that the use of Levemir would result in weight loss. As defined clearly by the heading, the advertisement was about an insulin treatment for type 2 diabetes. Nobody could argue that a typical patient with type 2 diabetes was overweight/obese, as accepted by Lilly. Therefore to use an image that did not reflect the characteristics of a type 2 diabetic would be inappropriate. In the circumstances, there appeared no other option than to use an image that portrayed the typical characteristics of this disease. For these reasons, Novo Nordisk submitted that this artwork was not in breach of Clause 7.8.

COMMENTS FROM LILLY

Lilly noted, Novo Nordisk's submission that the context of the advertisement was set out in two claims equally close to the artwork. However, it failed to comment that 'Levemir is changing figures' was at least twice the size and thus of far greater prominence than the other claim. It was clearly positioned in the centre of the advertisement for maximum effect.

Lilly noted that weight gain was a recognised side effect of insulin therapy. Despite this, the impression given by the claim and artwork was that Levemir was associated with weight loss. While Levemir caused less weight gain compared with other insulins (Levemir SPC) there was no evidence to substantiate weight loss in the SPC or references given. The

Levemir SPC clearly stated that in studies of patients with type 2 diabetes, Levemir caused a weight gain ranging from 0.7-3.7kg, depending on the dosing regime.

Lilly noted that in Novo Nordisk's response, it commented on the 'weight benefit' associated with Levemir relative to insulin glargine. However, Lilly alleged that any weight gain could only be seen as a disadvantage in a condition such as type 2 diabetes where, as accepted by Novo Nordisk, 80% of the patients were overweight and of these more than one third obese (Ridderstrale *et al*). Lilly reiterated that the common interpretation of 'weight benefit', particularly in patients with diabetes, would be of weight loss.

Regarding the choice of artwork, Lilly considered that there were many alternatives to describe a typical type 2 diabetic other than overweight swimmers.

Lilly alleged that both the picture and claim were chosen with the precise purpose of introducing ambiguity and implying that Levemir had 'benefits', specifically weight loss, which could not be substantiated.

APPEAL BOARD RULING

The Appeal Board noted that the advertisement featured an underwater photograph of five overweight women treading water in a swimming pool. Only their bodies from the neck down could be seen. Beneath the photograph was the prominent claim 'Levemir is changing figures'. In the Appeal Board's view the claim was a play on words and, in conjunction with the photograph, implied that Levemir would change the women's figures for the better ie they would lose weight and their shape would change. 'Figures' was much more likely to be thought of in terms of ladies figures rather than clinical values such as HbA1c etc. Although boxed text contained the claim 'Less weight gain than NPH and insulin glargine' this did not negate the otherwise misleading impression given. The Appeal Board considered that the advertisement was ambiguous and upheld the Panel's ruling of breaches of Clauses 7.2 and 7.8 of the Code. The appeal was unsuccessful.

Complaint received	10 October 2007
Case completed	7 January 2008
