CASE AUTH/2604/5/13

NOVO NORDISK v SANOFI

Promotion of Lyxumia

Novo Nordisk complained about a Lyxumia (lixisenatide) advertisement issued by Sanofi and published in the Health Service Journal. Lyxumia was a selective glucagon-like peptide-1 (GLP-1) receptor agonist.

The detailed response from Sanofi is given below.

Novo Nordisk alleged that the emphasis on 'only once-daily' in the claim 'Lyxumia is the only once-daily GLP-1 receptor agonist licensed for type 2 diabetes mellitus patients not optimally controlled on oral antidiabetic drugs and/or basal insulin' was misleading. It implied that Lyxumia was the only once daily GLP-1 receptor agonist available, which was not so. Novo Nordisk also stated that the claim could be read with omission of the word 'and', thereby referring to the use of Lyxumia in combination with oral antidiabetic drugs only. As its product Victoza was also a once-daily GLP-1 receptor agonist for use with oral antidiabetic drugs, it was misleading to use the word 'only' in this context.

The Panel considered that emboldening 'only once-daily' in the claim 'Lyxumia is the only once-daily GLP-1 receptor agonist licensed for type 2 diabetes mellitus patients not optimally controlled on oral antidiabetic drugs and/or basal insulin', implied that Lyxumia was the only once-daily GLP-1 receptor agonist which was not so; Victoza was also a once-daily GLP-1 receptor agonist. Lyxumia and Victoza were both licensed as adjunctive therapy – to be added to existing antidiabetic therapy to achieve improved glycaemic control. Lyxumia could also be added to an existing treatment regimen which included insulin. The Panel accepted that, in the round, this claim was true, but considered that the 'and/or' made it unclear as to what 'only' referred to. Whilst the latter two treatment scenarios were correct in that only Lyxumia could be added to existing insulin therapy, the first was not; both Victoza and Lyxumia could be given to patients not currently controlled on OAD therapy. The Panel considered that the claim was misleading and ambiguous and a breach of the Code was ruled.

Novo Nordisk further alleged that the claims 'Lyxumia leads to even greater costs savings' and 'Turn to the GLP-1 that minimises costs' implied Lyxumia could save costs vs other available treatments. Such a comparison did not take into account the difference in efficacy and safety between similar treatments and was therefore alleged to be misleading, inaccurate and unfair.

In the Panel's view the claim 'Turn to the GLP-1 that minimises costs' would be read as an indirect comparison of Lyxumia with all other GLP-1 receptor agonists. The claim 'Lyxumia leads to even greater cost savings of:' appeared in the body of the advertisement above two stab points which referred respectively to a 26% saving vs Bydureon (exenatide) 2mg once-weekly and Victoza 1.2mg once-daily and a 51% saving vs Victoza 1.8mg once-daily. Without the benefit of more information, it was not clear that the claims were only based on acquisition costs and not a cost-effectiveness analysis or similar. In that regard the Panel considered that the claims as well as the comparisons were misleading and breaches of the Code were ruled.

Novo Nordisk Limited complained about a Lyxumia (lixisenatide) advertisement (ref GBIE.LYX.13.02.11) issued by Sanofi and published in the Health Service Journal, March 2013. Sanofi stated that the advertisement at issue was first used after 5 March 2013, and was withdrawn from use on 29 April 2013 at the conclusion of certain aspects of inter-company dialogue.

Lyxumia was indicated for the treatment of adults with type 2 diabetes to achieve glycaemic control in combination with oral glucose lowering medicines and/or basal insulin when these, together with diet, did not provide adequate glycaemic control. Lixisenatide was a selective glucagon-like peptide-1 (GLP-1) receptor agonist. Novo Nordisk marketed Victoza (liraglutide) which was also a GLP-1 receptor agonist used in the treatment of type 2 diabetes.

1 Claim 'Lyxumia is the *only once-daily* GLP-1 receptor agonist licensed for type 2 diabetes mellitus patients not optimally controlled on oral antidiabetic drugs and/or basal insulin'

This claim appeared beneath the heading 'New Lyxumia 15% cost saving vs Byetta' and was referenced to the Lyxumia summary of product characteristics (SPC).

COMPLAINT

Novo Nordisk stated that the emphasis on the words 'only once-daily' drew the reader to conclude that Lyxumia was the only once daily GLP-1 receptor agonist available, which was not so.

Novo Nordisk also stated that the claim could be read in different ways and highlighted the various combinations for which Lyxumia could be used, namely:

- In combination with oral antidiabetic drugs (OADs) only;
- In combination with basal insulin only;
- In combination with basal insulin and OADs.

In inter-company dialogue Sanofi submitted that the claim accurately reflected the SPC, however, as Novo Nordisk had highlighted, the phrase 'only once-daily' did not feature in the SPC. Sanofi maintained that the claim explicitly and specifically referred to the only once-daily product licensed to be used with basal insulin. While Lyxumia was the 'only' once-daily GLP-1 receptor agonist that could be used in combination with basal insulin, the claim could also be read with omission of the word 'and', thereby referring to the use of Lyxumia in combination with OADs only. As Victoza was also a once-daily GLP-1 receptor agonist licensed to be used in combination with OADs, it was misleading to use the word 'only' within this context.

Novo Nordisk alleged that the claim was misleading in breach of Clause 7.2.

RESPONSE

Sanofi stated that Novo Nordisk alleged that the claim was in breach and that if it was read with a word omitted it would have another meaning, and was therefore misleading.

GLP-1 receptor agonists were used in the treatment of type 2 diabetes and activated the endogenous GLP-1 receptor. Once activated, this receptor acted on multiple pathways serving to reduce circulating glucose concentrations and improve the hyperglycaemia that was characteristic of diabetes.

There were four GLP-1 receptor agonists licensed for use in the UK. Lyxumia and Victoza were the only two indicated to be used once-daily; the other two, Byetta (exenatide) and Bydureon (exenatide LAR) were indicated twice daily or once weekly, respectively.

The Lyxumia SPC stated that it was indicated:

> '... for the treatment of adults with type 2 diabetes mellitus to achieve glycaemic control in combination with oral glucose-lowering medicinal products and /or basal insulin...'

The Victoza SPC stated that the product was indicated:

> '... for treatment of adults with type 2 diabetes mellitus to achieve glycaemic control:
> In combination with:
> – Metformin or a sulphonylurea ...
> – Metformin and a sulphonylurea or metformin and a thiazolidinedione ...'

Sanofi submitted that it was self-evident that the two indications were fundamentally different. It was clear to the reader that Lyxumia had an indication to be used in combination with basal insulin and that this indication did not exist for Victoza. On this basis, Sanofi submitted that it was neither misleading nor inappropriate to reference this fact within materials – it was a genuine point of differentiation between the two medicines. Lyxumia was the only GLP-1 receptor agonist indicated for use in combination with 'oral antidiabetic drugs and/or basal insulin'. The claim was therefore an accurate and truthful representation of the uniqueness of the indication for Lyxumia. The phrase 'only once-daily' was emboldened to emphasise a genuine difference not to claim that Lyxumia was the only once-daily GLP-1 receptor agonist as alleged. If that were implied, all these words would be emboldened. Regardless, the sentence needed to be considered in its entirety and this was an accurate representation of a unique indication for the product.

In summary, Lyxumia was the only GLP-1 receptor agonist available that was indicated for use once-daily with oral antidiabetic agents and/or basal insulin, the claim was an accurate representation of the uniqueness of Lyxumia's indication, and was not misleading.

Novo Nordisk invited the claim to be read with a word omitted. The claim however was to be read as written, and Sanofi had responded to the claim as written. Novo Nordisk presented a fallacious argument – it was completely illogical to suggest that the indication for Victoza (in combination with oral agents) was the same as that for Lyxumia because it matched one of the three ways in which the latter was indicated. To ignore the fact that Lyxumia was also indicated for use in combination with basal insulin, or in combination with oral agents plus basal insulin, could not be negated by this approach. The indication for Lyxumia, when considered in total (as reflected in the advertisement), was unquestionably different from that of Victoza. Sanofi submitted it was not misleading to position Lyxumia as unique in that respect.

PANEL RULING

The Panel noted the claim at issue 'Lyxumia is the **only once-daily** GLP-1 receptor agonist licensed for type 2 diabetes mellitus patients not optimally controlled on oral antidiabetic drugs and/or basal insulin'. The Panel considered that by emboldening 'only once-daily' there was an implication that Lyxumia was the only once-daily GLP-1 receptor agonist which was not so; Victoza was also a once-daily GLP-1 receptor agonist. Lyxumia and Victoza were both licensed as adjunctive therapy – to be added to existing antidiabetic therapy to achieve improved glycaemic control. Both medicines could be added to existing OAD therapy but only Lyxumia could also be added to an existing treatment regimen which included insulin. The Panel considered that the use of 'and/or' in the claim did not make this distinction between the two medicines entirely clear. The claim meant that Lyxumia was the only once-daily GLP-1 receptor agonist that was licensed for use in patients not optimally controlled on OADs, not optimally controlled on OADs and basal insulin and not optimally controlled on basal insulin alone. The Panel accepted that, in the round, this claim was true, but considered that the 'and/or' made it unclear as to what 'only' referred to. Whilst the latter two treatment scenarios were correct in that only Lyxumia could be added to existing insulin therapy, the first was not; both Victoza and Lyxumia could given to patients not currently controlled on OAD therapy. The Panel considered that the claim

was misleading and ambiguous. A breach of Clause 7.2 was ruled.

2 Claims 'Lyxumia leads to *even greater costs savings* of:' and 'Turn to the GLP-1 that minimises costs'

COMPLAINT

Novo Nordisk alleged that both of these claims implied Lyxumia could save costs vs other available treatments within the same class. While these claims were correct when the pack price of Lyxumia was compared to the pack price of other similar treatments, this comparison did not take into account the differences in efficacy and safety between similar treatments. While the advertisement included comparative efficacy and safety data between Lyxumia and twice daily exenatide to support a cost saving claim, Sanofi failed to include comparative data vs Victoza when making the same cost saving claim. Kapitza *et al*, (2013) demonstrated that Victoza provided 60% better reduction in HbA_{1c} levels and 50% better weight reduction vs Lyxumia over a 4 week period. True cost savings which were meaningful to health professionals and payers could not be based on pack price alone, but instead must take into account comparative efficacy and safety data in order for long-term cost savings to be realised.

As stated within the supplementary information to Clause 7.2, 'price comparisons, as with any comparison, must be accurate, fair and must not mislead. Valid comparisons can only be made where like is compared with like'.

In inter-company dialogue Sanofi acknowledged that cost saving comparisons might invite conclusions beyond acquisition cost and committed to amend such claims. Novo Nordisk considered this matter closed. Two days later, on 1 May 2013, Sanofi issued a press release (ref GBIE.LYX.13.03.12, available on www.sanofi.co.uk) to launch Lyxumia. Various cost saving claims were made in the press release in relation to Lyxumia, without naming or providing any information on the comparative efficacy and safety of similar available treatments. Claims included:

- 'Costing 25% less than similar treatments …'
- A quotation 'It is encouraging that effective and innovative Type 2 diabetes treatments are made available more cheaply to the NHS and the patients it treats'
- A quotation: 'The price is one that represents real value to both the NHS and Sanofi'.

As the press release was embargoed until 00.01 on Wednesday, 1 May 2013, and given the impact such a release could have, Novo Nordisk's considered that Sanofi had had time to amend the cost saving claims in light of its commitment made to Novo Nordisk on 29 April in relation to cost saving claims in the Health Service Journal advertisement.

Novo Nordisk alleged that the claims 'Lyxumia leads to even greater costs savings' and 'Turn to the GLP-1 that minimises costs' were misleading, inaccurate and unfair comparisons, in breach of Clauses 7.2 and 7.3.

RESPONSE

Sanofi stated that whilst Lyxumia was the cheapest GLP-1 receptor agonist available in the UK (15% cheaper than exenatide 10mcg twice daily, 26% cheaper than exenatide 2mg weekly and Victoza 1.2mg daily, 51% cheaper than Victoza 1.8mg daily), Sanofi understood as how these claims might be considered to imply wider savings than the cost of the medicine alone. This was not intended, but taking into account this concern the advertisement was withdrawn from further use. Sanofi had honoured a commitment not to use these claims further.

With respect to the advertisement at issue, Sanofi considered that inter-company dialogue reached a definitive conclusion. The advertisement was withdrawn and claims of 'cost saving or cost minimisation' had not been used again. In respect to these actions Sanofi therefore submitted that all the requirements of the Code had been upheld.

Sanofi was therefore exceedingly disappointed that Novo Nordisk had referred the matter to the PMCPA after an apparently successful resolution, at the very least without any further recourse to inter-company discussion in an attempt to resolve any new concerns.

Although Novo Nordisk referred to new claims that appeared in a subsequent press release, Novo Nordisk had not complained to Sanofi or the PMCPA about the item itself. Although no complaint has been made, Sanofi was confident that the content of the press release could be substantiated and met the requirements of the Code, and it would defend these points rigorously were such a complaint forthcoming.

Before it was issued the press release was examined to ensure that the commitment mentioned above was respected. No explicit nor implicit claim that Lyxumia would achieve 'cost savings' or 'cost minimisation' beyond the cost of the medicine itself was made. Instead, the press release reflected the fact that Lyxumia was cheaper than the other GLP-1 receptor agonists at the equivalent dosage for the same indication, as required by Clause 7.2. The quotations from the press release cited by Novo Nordisk reflected the simple message of cheaper cost; not one implied the potential to achieve savings beyond the cost of the medicine alone. The quotations simply reported that Lyxumia cost '… less than similar treatments …' or was available '… more cheaply to the NHS …'.

In summary, Sanofi agreed with Novo Nordisk that the advertisement at issue could have been interpreted more widely than intended, and withdrew it as a consequence of inter-company dialogue. At the same time a commitment was given that further claims regarding the cheaper cost would avoid any such ambiguity. Sanofi considered that

inter-company dialogue had reached a successful conclusion with respect to this item and these claims.

For Novo Nordisk now to introduce a matter, upon which Sanofi had had no opportunity to comment, was disappointing. Sanofi recognised that the complaint had been made only in reference to the original journal advertisement. Regardless, Sanofi would be willing to respond to Novo Nordisk regarding any element of the press release, but would expect the first approach to be in the form of inter-company dialogue as required by the Code.

Sanofi looked forward to receiving the Panel's conclusion regarding the advertisement in due course, albeit that the advertisement was already withdrawn and the company's commitment made (and respected) not to repeat potentially ambiguous claims in the future.

PANEL RULING

The Panel noted that in a letter to Novo Nordisk dated 29 April, Sanofi had agreed that the cost saving comparison in the advertisement at issue might invite conclusions beyond acquisition cost alone and had committed to amend the claim. Sanofi had also acknowledged Novo Nordisk's concerns about the comparison with Victoza. Sanofi stated in that letter that it had instructed its agency not to use the advertisement forthwith. The Panel further noted, however, that a press release which was embargoed until 00.01, Wednesday 1 May featured the claim 'Lyxumia is a new, cost-effective option….'. The Panel thus disagreed with Sanofi's submission that the press release made no explicit or implicit claim that Lyxumia would achieve 'cost savings' or 'cost minimisation' beyond the cost of the medicine itself. The Panel considered that the term 'cost-effective' clearly implied savings beyond the acquisition cost alone and in that regard inter-company dialogue had been unsuccessful and the matter should proceed.

The Panel noted that the claim 'Turn to the GLP-1 that minimises costs' appeared in bold, dark type in the bottom left-hand corner of the advertisement. In the Panel's view the claim would be read as an indirect comparison of Lyxumia with all other GLP-1 receptor agonists. The claim 'Lyxumia leads to *even greater cost savings* of:' appeared in the body of the advertisement above two stab points which referred respectively to a 26% saving vs Bydureon (exenatide) 2mg once-weekly and Victoza 1.2mg once-daily and a 51% saving vs Victoza 1.8mg once-daily. The Panel considered that without the benefit of more information, it was not clear that the claims were only based on acquisition costs and not a cost-effectiveness analysis or similar. In that regard the Panel considered that the claims were misleading and a breach of Clause 7.2 was ruled. The comparisons were thus also misleading and a breach of Clause 7.3 was ruled. The Panel noted that the advertisement had already been withdrawn.

Complaint received **13 May 2013**

Case completed **26 June 2013**