CASE AUTH/2337/7/10

MERCK SERONO v SANDOZ

Press release and article on Omnitrope

Merck Serono complained about a global press release about Omnitrope (somatropin) issued in Germany by Sandoz and about an article which had allegedly been published in a UK patient support group newsletter entitled 'Biosimilars, NICE [National Institute for Health and Clinical Excellence] and Omnitrope'. Merck Serono supplied Saizen (somatropin). Both products were growth hormones. Omnitrope was a biosimilar.

The detailed response from Sandoz is given below.

With regard to the sentence in the press release 'Latest NICE cost-benefit guidance includes Sandoz's Omnitrope as one of seven recommended somatropin products to treat growth failure in children', Merck Serono stated that NICE referred to cost and effectiveness but no cost-benefit guidance was issued.

In the Panel's view the press release was subject to the UK Code. Whilst issued by Sandoz's German headquarters it discussed the UK NICE guidance and referred to cost savings to the NHS. Sandoz was thus responsible for the press release under the Code.

The Panel noted that the relevant NICE guidance referred to the acquisition cost of various somatropins their clinical effectiveness and cost-effectiveness. The Panel considered that most readers would assume that the term 'cost-benefit' meant more than separate analyses of the product's acquisition costs and clinical effectiveness. Given the detailed discussion of somatropins' cost-effectiveness the Panel did not consider that the term 'cost-benefit' misled as to the content of the NICE guideline on this point. No breach of the Code was ruled.

With regard to the sentence 'Guidance recommends that, where more than one product is suitable, the least costly option should be chosen', Merck Serono alleged that the NICE guidance had been misquoted to imply that cost was the key consideration in choosing growth hormone.

The Panel did not consider that the press release was misleading on this point. It did not state or imply that cost was the key consideration as alleged. It was made clear that only where more than one product was suitable then the least costly should be chosen. No breach of the Code was ruled.

Merck Serono alleged that the phrase 'no differences' in the sentence 'The guidance issued by the NICE Appraisal Committee noted that Omnitrope had undertaken head-to-head trials with the reference product as part of its regulatory submission to the European Medicines Agency (EMA) and found that there were no differences in terms of safety or efficacy between the products' was misleading and unsubstantiated.

The Panel noted that the press release began by introducing the NICE guidance and stating that it recommended the use of Sandoz's product Omnitrope as one of seven recommended products. It was the first time NICE had recommended the use of a biosimilar. This was followed by the sentence at issue. The press release continued by stating that biosimilars were approved by the EMA on the basis that they had demonstrated comparable quality, safety and efficacy to their reference product.

The Panel noted that the licensing approval process for Omnitrope, as a biosimilar, was discussed in the NICE guidance which noted that in general terms the originator biopharmaceutical product could not be copied exactly and that this might lead to different immunological effects and that biosimilar products might have a different safety profile from the originator product. It was noted that EMEA legislation on biosimilars defined the studies needed to demonstrate equivalent safety and efficacy to the pharmaceutical reference product. It was also noted that making specific recommendations around the safety of a medicine was outside NICE's remit, that no evidence had been submitted on differences between the biosimilar (Omnitrope) and the originator product in terms of safety or efficacy, and that the current prescribing advice referred to prescription of biopharmaceutical products by brand name. Based on the marketing authorization for Omnitrope NICE was satisfied that it could be considered for the treatment of growth failure alongside the other six somatropin products.

In relation to clinical effectiveness the NICE guidance stated that 'there appeared to be no difference in the clinical effectiveness of the various somatropin products available'. It was further noted that the studies submitted to the EMEA '… provided evidence on the equivalence [Omnitrope and the originator product]'. It did not state 'evidence of equivalence' as submitted by Sandoz. The guidance did not state that the somatropin products showed no differences in relation to efficacy nor that there were no differences on safety. It was expressly stated that making recommendations about safety was beyond NICE's remit. The Panel considered that the claim at issue was not an accurate reflection of the comments in

the NICE guidance about the product's safety and efficacy. The claim at issue was misleading in this regard and a breach of the Code was ruled.

Merck Serono alleged that the original NICE guidance had been paraphrased / misquoted to imply that cost was the first and key consideration in choosing growth hormone. In this regard it referred to the sentence 'NICE says that, when more than one product is suitable, the least costly option should be chosen. NICE recommended that a discussion should be held between a clinician and patient to choose the somatropin treatment received, based on therapeutic need and the likelihood of adherence to treatment'.

The Panel considered its ruling above was relevant here. The Panel did not consider that the claim at issue was misleading as alleged. No breach of the Code was ruled.

Merck Serono referred to the quotation from a named consultant paediatrician that 'I have 10 years of clinical experience using Omnitrope with my paediatric patients and I believe it is both effective and well tolerated. I welcome the decision by NICE to recommend the option of a biosimilar; it will benefit patients by providing an alternative, equally effective treatment option as well as offering much needed cost savings to the NHS'. Merck Serono alleged that the quotation that Omnitrope was an 'equally effective treatment option' was misleading. Merck Serono was also concerned that this quotation referred to the paediatrician's 10 years of clinical experience with Omnitrope. This was unsubstantiated as was the reference to Omnitrope being able to 'offer much needed cost savings to the NHS'.

The Panel noted the submission that the quotation was the clinical opinion of a named paediatrician. The Panel noted that this was a company press release which it had decided was covered by the Code and thus its entire content must comply with the Code irrespective of whether any part of it represented the personal view of a clinician.

Merck Serono had alleged that the phrase 'an equally effective treatment option' was misleading but had not provided reasons. Other allegations above related to whether the descriptions in the press release fairly reflected the NICE guidance. It was not entirely clear whether the named doctor was referring to the concept of recommending a biosimilar in order to benefit patients by providing an alternative, equally effective treatment option and offer much needed cost savings to the NHS or attributing these qualities specifically to Omnitrope. The Panel noted its ruling above which had related to a slightly different point, namely whether the press release fairly reflected the NICE guidance in relation to the claim that there were 'no differences in terms of safety or efficacy between the products.' The Panel considered that if the phrase 'an equally effective treatment option' related to biosimilars as a class it was not necessarily a misleading description of a biosimilar. No comparative efficacy evidence had been submitted by either party in relation to Omnitrope and its reference product. The Panel noted that the complainant, Merck Serono, had to establish its case on the balance of probabilities. No breach of the Code was ruled.

The Panel noted Sandoz's submission that the named doctor had been involved in the early stage development of Omnitrope. The Panel did not consider that the phrase '10 years of clinical experience' was misleading as alleged. No breach of the Code was ruled.

The Panel noted that at the time of publication the price of Omnitrope had been reduced making it the least expensive growth hormone in the UK on list price. Sandoz also referred to clear positive, cost-benefits compared to other somatropin preparations. The Panel noted that the claim at issue was very general and simply referred to cost savings to the NHS, it did not state or imply that the cost savings would be greater than with all other somatropins. No breach of the Code was ruled.

Merck Serono alleged that the reference to Omnitrope in a patient newsletter clearly breached the Code. Merck Serono was also aware that this was sent to the patient group unsolicited.

Merck Serono alleged that the statement '…the NICE panel deemed it to be as safe and effective as the other Somatropin products …' implied that Omnitrope offered the same efficacy and safety as other somatropins. NICE guidance did not state that Omnitrope offered the same efficacy and safety as other somatropins.

Merck Serono alleged that the statement that 'Omnitrope is 26% less expensive than the most widely prescribed product in the UK' was unsubstantiated as was the statement 'Omnitrope … offers clear savings without compromising patient care or support'.

It was unclear whether the article had been written solely by the named consultant paediatrician or whether Sandoz was involved in the development of its content. There did not appear to be any declaration of the involvement of Sandoz in the production of this article.

Merck Serono further alleged that the combination of advertising medicines to the public, providing misleading information, claims and comparisons and not declaring sponsorship constituted a breach of Clause 2.

The Panel noted that the article at issue had not been published in the patient group newsletter or otherwise used by the company. A version which was clearly a draft had been distributed for comment. Given that the item was not in its final

form and had not been used as described above the Panel ruled no breach of the Code including Clause 2.

Merck Serono complained about a press release about Omnitrope (somatropin) issued by Sandoz and about an article which had allegedly been published in a patient support group newsletter entitled 'Biosimilars, NICE [National Institute for Health and Clinical Excellence] and Omnitrope'. Inter-company dialogue had failed to resolve the matter. Merck Serono supplied Saizen (somatropin). Both products were growth hormones. Omnitrope was a biosimilar.

A Press release

Sandoz explained that the item was a global press release, issued by its head office in Germany, as was apparent from the press release. The press release was not certified but it was examined to ensure that it did not breach the Code or relevant statutory requirements. When Merck Serono raised its initial concerns on 14 June it was advised that this was a global press release and that it should discuss the matter with Sandoz's global headquarters. Merck insisted on dealing locally and so, to show good will and aid inter-company dialogue, Sandoz agreed to discuss the matter.

1 Claim 'Latest NICE cost-benefit guidance includes Sandoz's Omnitrope as one of seven recommended somatropin products to treat growth failure in children'

COMPLAINT

Merck Serono stated that the NICE referred to cost and effectiveness but no cost-benefit guidance was issued. A breach of Clause 7.2 was alleged.

RESPONSE

Sandoz stated that the press release did not quote the NICE guidance document directly. Sandoz's interpretation of cost-benefit and cost-effectiveness was that the two terms had the same inference.

The NICE website listed the following point as one of the definitions of what NICE guidance was:

'Good value for money, weighing up the cost and benefits of treatments'

Section 4.2 'Cost effectiveness' of the NICE guidance [Human growth hormone (somatropin) for the treatment of growth failure in children] clearly included a detailed assessment of the cost-effectiveness of somatropin. Furthermore the guidance increased the access to patients through two newly approved indications, small for gestational age (SGA) and short stature homeobox-containing gene (SHOX) deficiency, based on cost vs patient benefit. Sandoz therefore did not see why the use of the term 'Latest NICE cost-benefit guidance' would be misleading.

PANEL RULING

The Panel noted Sandoz's general comments about the international nature of the press release and was concerned that it appeared only to have agreed to discuss Merck Serono's concerns on a local UK level merely to show good will. In the Panel's view the press release was subject to the UK Code. Whilst issued by Sandoz's German headquarters it discussed the UK NICE guidance and referred to cost savings to the NHS. Sandoz was thus responsible for the press release under the Code and obliged to enter into inter-company dialogue at a UK level.

The Panel noted that the relevant NICE guidance not only referred to the acquisition cost of various somatropins (Section 3.5) but also discussed their clinical effectiveness (Section 4.1) and cost-effectiveness (Section 4.2). The Panel considered that most readers would assume that the term 'cost-benefit' meant more than separate analyses of the product's acquisition costs and clinical effectiveness. Given the detailed discussion of somatropins' cost-effectiveness the Panel did not consider that the term 'cost-benefit' misled as to the content of the NICE guideline on this point. No breach of Clause 7.2 was ruled.

2 Claim 'Guidance recommends that, where more than one product is suitable, the least costly option should be chosen'

COMPLAINT

Merck Serono alleged that the NICE guidance had been misquoted to imply that cost was the key consideration in choosing growth hormone. A breach of Clause 7.2 was alleged.

RESPONSE

Sandoz noted that the press release did not state that the guidance recommended that the least costly option should be chosen. It expressly contained a pre-condition for such choice by stating that, '**where** more than one product **is suitable**, the least costly option should be chosen' (emphasis added). It was in the nature of such a pre-condition that it must be fulfilled before cost was taken into account. The press release also gave a detailed explanation of the term 'suitable' by stating that 'NICE recommended that a discussion should be held between a clinician and patient to choose the somatropin treatment received, based on therapeutic need and the likelihood of adherence to treatment'.

It stated that the least costly option should be chosen where more than one product was suitable, implying it was still an important factor.

PANEL RULING

The Panel did not consider that the press release was misleading on this point. It did not state or

imply that cost was the key consideration as alleged. It was made clear that only where more than one product was suitable then the least costly should be chosen. No breach of Clause 7.2 was ruled.

3 Claim 'The guidance issued by the NICE Appraisal Committee noted that Omnitrope had undertaken head-to-head trials with the reference product as part of its regulatory submission to the European Medicines Agency (EMA) and found that there were no differences in terms of safety or efficacy between the products'

This claim was referenced to the NICE guidance and the Omnitrope European Public Assessment Report (EPAR).

COMPLAINT

Merck Serono alleged that the phrase 'no differences' was misleading and unsubstantiated in breach of Clause 7.2.

RESPONSE

Sandoz stated that Section 4.3.5 of the NICE guidance used the phrase 'evidence of equivalence'. The claim at issue was from the guidance, Section 4.3.5 stated that, 'The Committee agreed that there appeared to be no differences in the clinical effectiveness of the various somatropin products available'.

Therefore, Sandoz believed the claim at issue was substantiated.

PANEL RULING

The Panel noted that the press release began by introducing the NICE guidance and stating that it recommended the use of Sandoz's product Omnitrope as one of seven recommended products. It was the first time NICE had recommended the use of a biosimilar. This was followed by the sentence at issue. The press release continued by stating that biosimilars were approved by the EMA on the basis that they had demonstrated comparable quality, safety and efficacy to their reference product.

The Panel noted that the licensing approval process for Omnitrope, as a biosimilar, was discussed at Section 4.3.4 of the NICE guidance. The guidance noted that in general terms the originator biopharmaceutical product could not be copied exactly and that this might lead to different immunological effects and that biosimilar products might have a different safety profile from the originator product. It was noted that EMEA legislation on biosimilars defined the studies needed to demonstrate equivalent safety and efficacy to the pharmaceutical reference product. It was noted that making specific recommendations around the safety of a medicine was outside NICE's remit, that no evidence had been submitted on differences between the biosimilar (Omnitrope) and the originator product in terms of safety or efficacy, and that the current prescribing advice referred to prescription of biopharmaceutical products by brand name. Based on the marketing authorization for Omnitrope NICE was satisfied that it could be considered for the treatment of growth failure alongside the other six somatropin products.

In relation to clinical effectiveness, Section 4.3.5 of the NICE guidance stated that 'there **appeared to be** no difference in the clinical effectiveness of the various somatropin products available.' (emphasis added). It was further noted that the studies submitted to the EMEA '… provided evidence on the equivalence [Omnitrope and the originator product]'. It did not state 'evidence of equivalence' as submitted by Sandoz. Section 4.3.5 did not state that the somatropin products showed no differences in relation to efficacy nor that there were no differences on safety. Section 4.3.4 expressly stated that making recommendations about safety was beyond NICE's remit. The Panel considered that the claim at issue was not an accurate reflection of the comments in the NICE guidance about the product's safety and efficacy. The claim at issue was misleading in this regard and a breach of Clause 7.2 was ruled.

4 Claim 'NICE says that, when more than one product is suitable, the least costly option should be chosen. NICE recommended that a discussion should be held between a clinician and patient to choose the somatropin treatment received, based on therapeutic need and the likelihood of adherence to treatment'

COMPLAINT

Merck Serono alleged that the original NICE guidance had been paraphrased / misquoted to give the impression that cost was the first and key consideration in choosing growth hormone in breach of Clause 7.2.

RESPONSE

Sandoz stated that this point had already been addressed in response to point A2 above. Sandoz endeavoured to ensure that the press release was a fair representation of the guidance with respect to accuracy and content. As noted above, Sandoz consulted NICE before the piece was published.

PANEL RULING

The Panel considered its ruling at point A2 above was relevant here. The Panel did not consider that the claim at issue was misleading as alleged. No breach of Clause 7.2 was ruled.

5 Claim 'a named consultant paediatrician …said: "I have 10 years of clinical experience using

Omnitrope with my paediatric patients and I believe it is both effective and well tolerated. I welcome the decision by NICE to recommend the option of a biosimilar; it will benefit patients by providing an alternative, equally effective treatment option as well as offering much needed cost savings to the NHS."'

COMPLAINT

Merck Serono alleged that the reference to Omnitrope being an 'equally effective treatment option' was misleading. Merck Serono was also concerned that this quotation referred to the named paediatrician's 10 years of clinical experience with Omnitrope. This was unsubstantiated as was the reference to Omnitrope being able to 'offer much needed cost savings to the NHS'. A breach of Clause 7.2 was alleged.

RESPONSE

Sandoz stated that this was the named paediatrician's clinical opinion, which it supported. Furthermore, the consultant paediatrician was involved in the early stage development of Omnitrope, which began in 1998. He was involved in the first human trials, in February 2000, which gave him a unique standpoint on which to comment. He had not been briefed by Sandoz; this was his personal opinion having used the product for many years, and his in-depth understanding of biosimilars being involved in the trials. Sandoz therefore had no reason to believe that the consultant's opinion would be incorrect or misleading.

Section 4.3.5 of the NICE guidance supported the equivalence of the two products. The named consultant paediatrician was only supporting this claim in his statement.

With regard to the statement about much needed cost savings to the NHS, while this was a personal opinion, Sandoz added that from relative cost comparison per mg as in Section 3.5 of the NICE guidance, there were clear, positive, cost-benefits with use of Omnitrope compared with some of the other somatropin preparations. In addition, at the time of publication the price of Omnitrope had been further reduced making it the least expensive growth hormone in the UK on list price.

A copy of 'A Report Detailing the Economic Value of Omnitrope in England and Wales' was provided.

PANEL RULING

The Panel noted the submission that the quotation at issue was the clinical opinion a named consultant paediatrician which the company supported and that he had not been briefed by Sandoz. The Panel noted that this was a company press release which it had decided was covered by the Code and thus its entire content must comply with the Code irrespective of whether any part of it represented the personal view of a clinician.

Merck Serono had alleged that the phrase 'an equally effective treatment option' was misleading but had not provided reasons. Other allegations above related to whether the descriptions in the press release fairly reflected the NICE guidance. It was not entirely clear whether the consultant paediatrician was referring to the concept of recommending a biosimilar in order to benefit patients by providing an alternative, equally effective treatment option and offer much needed cost savings to the NHS or attributing these qualities specifically to Omnitrope. The Panel noted its ruling in point A3 which had related to a slightly different point, namely whether the press release fairly reflected the NICE guidance in relation to the claim that there were 'no differences in terms of safety or efficacy between the products.' The Panel considered that if the phrase 'an equally effective treatment option' related to biosimilars as a class it was not necessarily a misleading description of a biosimilar. No comparative efficacy evidence had been submitted by either party in relation to Omnitrope and its reference product. The Panel noted that the complainant, Merck Serono, had to establish its case on the balance of probabilities. No breach of Clause 7.2 was ruled.

The Panel noted Sandoz's submission that the consultant paediatrician had been involved in the early stage development of Omnitrope. The Panel did not consider that the phrase '10 years of clinical experience' was misleading as alleged. No breach of Clause 7.2 was ruled.

The Panel noted that at the time of publication the price of Omnitrope had been reduced making it the least expensive growth hormone in the UK on list price. Sandoz also referred to clear positive, cost-benefits compared with other somatropin preparations. The Panel noted that the claim at issue was very general and simply referred to cost savings to the NHS, it did not state or imply that the cost savings would be greater than with all other somatropins. No breach of Clause 7.2 was ruled.

B Article in patient support group newsletter 'Biosimilars, NICE and Omnitrope'

This article was attributed to the named consultant paediatrician.

COMPLAINT

Merck Serono alleged that the reference to Omnitrope in a patient newsletter clearly breached Clause 22.1. Merck Serono was also aware that this was sent to the patient group unsolicited.

Merck Serono alleged that the statement '…the NICE panel deemed it to be as safe and effective as the other Somatropin products …' implied that Omnitrope offered the same efficacy and safety as other somatropins. NICE did not issue any guidance that said that Omnitrope offered the same efficacy

and safety as other somatropins. Merck Serono alleged a breach of Clause 7.2.

Merck Serono alleged that the statement that 'Omnitrope is 26% less expensive than the most widely prescribed product in the UK' was unsubstantiated in breach of Clause 7.2 as was the statement 'Omnitrope … offers clear savings without compromising patient care or support'.

It was unclear whether the article had been written solely by the named consultant paediatrician or whether Sandoz was involved in the development of its content. There did not appear to be any declaration of the involvement of Sandoz in the production of this article. Merck Serono alleged a breach of Clause 9.10.

Merck Serono further alleged that the combination of advertising medicines to the public, providing misleading information, claims and comparisons and not declaring sponsorship constituted a breach of Clause 2.

RESPONSE

Sandoz stated that it first met the chairman of the patient support group when he gave advice on behalf of the group at the NICE committee meeting reviewing its guidance document, 'Human growth hormone (somatropin) for the treatment of growth failure in children' and indicated that Sandoz was the only company that had never engaged with the patient group. At that time the chairman knew little about biosimilars and the patient group would not be in a position to recommend them to its members. Following these comments Sandoz and the patient group agreed to meet and discuss the principles behind biosimilars.

The patient group chairman, the consultant paediatrician (invited by the chairman) and Sandoz met on 2 June 2010 and following a short discussion about biosimilars, the chairman decided it would be applicable for the consultant paediatrician to clarify some of the misconceptions surrounding them and write a piece for the patient group newsletter. Therefore this piece was not solicited by Sandoz.

Before the consultant's piece was published, the patient group distributed the article (as a word document and not in its final form) to all other growth hormone suppliers to ensure that it was not a biased or unfair representation. A copy was provided. The other companies were able to comment on the proposed article. The consultant paediatrician had added a Sandoz employee to the authors list as he was present at the original meeting. Sandoz was not fully aware of this. To reiterate, when the consultant's article was sent out for comment it was not approved in its final form and had not been published.

As soon as Sandoz realised that this could breach the Code, it informed the consultant that the piece should be withdrawn immediately to avoid any risk that it would be seen as disguised promotion. This was before the item went through the certification procedure. The consultant informed the patient group and the article was withdrawn. The article was not published and Sandoz did not intend to publish it in the future. A copy of an email of 7 July 2010 from the patient group confirming that the consultant had requested the proposed article to be withdrawn was provided.

Sandoz did not consider that it had breached the Code as this material had never been publicly available.

PANEL RULING

The Panel noted that the article at issue had not been published in the patient group newsletter or otherwise used by the company. A version which was clearly a draft had been distributed for comment. Given that the item was not in its final form and had not been used as described above the Panel ruled no breach of Clauses 2, 7.2, 9.10 and 22.1 of the Code.

Complaint received **28 July 2010**

Case completed **25 October 2010**