CASE AUTH/2184/11/08

PRIMARY CARE TRUST HEAD OF MEDICINES MANAGEMENT AND GP MEDICAL ADVISOR/GENERAL PRACTITIONER v PFIZER

Lipitor journal advertisement

The head of medicines management at a primary care trust and a GP medical advisor/general practitioner complained jointly about a journal advertisement for Lipitor (atorvastatin) placed by Pfizer.

The advertisement was headed 'New NICE [National Institute for Health and Clinical Excellence] lipid modification & Type 2 diabetes guidelines published' beneath which was the claim that 'New NICE guidelines recommend lowering cholesterol to <4mmol/L Total-cholesterol or <2mmol/L LDL-cholesterol to improve cardiovascular outcomes for patients with established CVD [cardiovascular disease] or Type 2 diabetes'. This was followed by claims that 'Economic modelling estimates that only 37% of patients with established CVD, with or without diabetes, achieve a Total-cholesterol <4mmol/L with simvastatin 40mg' and 'An estimated 82% of these patients would achieve a Total-cholesterol <4mmol/L with a simvastatin 40mg – Lipitor titration strategy'.

The complainants stated that the prominence of the heading that new NICE guidelines recommended lowering cholesterol to 4 and 2 was misleading as this only applied to NICE guidance for cholesterol management in secondary prevention in patients with established CVD or type 2 diabetes. Although this was implied, the way that the sentence was broken to fit around the prominent graphic of cholesterol levels of 4 and 2 was misleading and was deliberately designed to imply that the NICE guidance was a total cholesterol <4mmol/L and an LDL-cholesterol <2mmol/L for all patients. There was no reference to the NICE lipid modification recommendations in patients for primary prevention which was the vast majority of patients that required lipid modification therapy.

The second point implied that only 37% of patients with established CVD would achieve the recommended cholesterol targets with simvastatin, whereas 82% of patients would achieve the target with the Lipitor titration strategy. This claim was referenced to data on file. The complainants, however, were concerned that the data related to a study that had not been published or peer reviewed and was an economic profiling study, not a study done in actual patients but an implied benefit using cholesterol prevalence data from UK population data and statin lowering efficacy data from a different study conducted in the USA. This data was not robust enough to support the claims made.

Lastly, the complainants alleged that the advertisement implied that Lipitor was endorsed by the NICE guideline on lipid modification which was incorrect. The NICE guideline stipulated that if a patient failed to reach target then simvastatin 80mg, or a medicine of similar efficacy and cost, should be used. As atorvastatin was six times the cost of simvastatin it could not satisfy the NICE recommendations as a medicine of similar efficacy and cost.

The detailed response from Pfizer is given below

The Panel considered that the combination of the heading and the claim that immediately followed made it clear that the advertisement referred to new NICE guidelines on lipid modification for patients with established CVD or type 2 diabetes. The Panel did not consider that the advertisement implied that NICE had recommended a total cholesterol of <4mmol/L and an LDL-cholesterol of <2mmol/L for all patients. It was acceptable for an advertisement to refer to a subset of patients ie in this case those with established CVD or type 2 diabetes, and not the vast majority of patients provided this was made clear. The Panel did not consider the advertisement was misleading as alleged and no breach of the Code was ruled.

The Panel was concerned about the claim relating to economic modelling estimates. However it was not a breach of the Code per se to cite 'data on file'. The Code required that claims were capable of substantiation. The Panel noted that the economic analysis used data from two sources. Firstly, the THIN database gave the baseline cholesterol levels. Secondly the lipid lowering efficacy data for each statin was based on the CURVES study. The Panel noted that the advertisement made clinical claims based on the economic modelling data. This was reinforced by the way the claims were presented in that '37%' and '82%' were in large bold type. The figures thus appeared to be proven absolutes. The reference to 'estimates' did not negate this impression. Further, the heading to the advertisement referred to clinical data. The Panel considered that given their context the claims at issue were misleading and not capable of

substantiation. Pfizer had not submitted clinical data to support the quoted percentages of patients achieving a total cholesterol of <4mmol/L. The Panel ruled breaches of the Code.

The Panel noted that the heading and first part of the advertisement referred to NICE guidelines targets and then in a different colour text referred to the lipid lowering efficacy of simvastatin and Lipitor. The claim 'Lipitor is an evidence-based choice when your patients with established CVD or Type 2 diabetes with CVD need intensive cholesterol-lowering for improved cardiovascular outcomes' did not refer to NICE. The context in which a claim appeared, however, was important; the two claims which headed the advertisement at issue referred to NICE guidelines. Nonetheless, on balance, the Panel did not consider that the advertisement implied that Lipitor was endorsed by the NICE guideline on lipid modification as alleged. The advertisement was thus not misleading in that regard and the Panel ruled no breach of the Code.

The head of medicines management at a primary care trust and a GP medical advisor/general practitioner complained jointly about a journal advertisement (ref LIP3055c) for Lipitor (atorvastatin) placed by Pfizer Limited in Guidelines in Practice, volume II, 7 July.

The advertisement in question was headed 'New NICE [National Institute for Health and Clinical Excellence] lipid modification & Type 2 diabetes guidelines published' beneath which was the claim that 'New NICE guidelines recommend lowering cholesterol to <4mmol/L Total-cholesterol or <2mmol/L LDL-cholesterol to improve cardiovascular outcomes for patients with established CVD [cardiovascular disease] or Type 2 diabetes'. This was followed by claims that 'Economic modelling estimates that only 37% of patients with established CVD, with or without diabetes, achieve a Total-cholesterol <4mmol/L with simvastatin 40mg' and 'An estimated 82% of these patients would achieve a Total-cholesterol <4mmol/L with a simvastatin 40mg – Lipitor titration strategy'.

COMPLAINT

The complainants alleged that the advertisement appeared to contravene Clauses 7.2, 7.3 and 7.4 of the Code.

The complainants stated that the prominence of the heading that new NICE guidelines recommended lowering cholesterol to 4 and 2 was misleading as this only applied to NICE guidance for cholesterol management in secondary prevention in patients with established CVD or type 2 diabetes. Although this was implied, the way that the sentence was broken to fit around the prominent graphic of cholesterol levels of 4 and 2 was misleading and was deliberately designed to imply that the NICE guidance was a total cholesterol <4mmol/L and an LDL-cholesterol <2mmol/L for all patients. There was no reference to the NICE lipid modification recommendations in patients for primary prevention which was the vast majority of patients that required lipid modification therapy.

The second point implied that only 37% of patients with established CVD would achieve the recommended cholesterol targets with simvastatin, whereas 82% of patients would achieve the target with the Lipitor titration strategy. This claim was referenced to data on file. The complainants, however, were concerned that the data related to a study that had not been published or peer reviewed and was an economic profiling study, not a study in actual patients but an implied benefit using cholesterol prevalence data from UK population data and statin lowering efficacy data from a different study conducted in the USA. This data was not robust enough to support the claims in the advertisement.

Lastly, the complainants alleged that the advertisement implied that Lipitor was endorsed by the NICE guideline on lipid modification. This was incorrect, the NICE guideline stipulated that if a patient failed to reach target then simvastatin 80mg, or a medicine of similar efficacy and cost, should be used. As atorvastatin was six times the cost of simvastatin it could not satisfy the NICE recommendations as a medicine of similar efficacy and cost, therefore it was not recommended by the NICE guidelines on lipid modification.

RESPONSE

Pfizer stated that the advertisement aimed to raise awareness of the newly published NICE lipid modification and type 2 diabetes clinical guidelines with regard to the recommendation to achieve lower cholesterol levels of total cholesterol <4mmol/L in high risk patients with established CVD and type 2 diabetes.

Pfizer submitted that it had been explicit throughout the advertisement about the population of patients the recommendations were for ie patients with established CVD and those with type 2 diabetes. The sentence below the graphic of <4mmol/L total cholesterol or <2mmol/L LDL cholesterol referred to improving cardiovascular outcomes for patients with established CVD and type 2 diabetes. In addition, the advertisement referred throughout only to patients with established CVD and type 2 diabetes. For example, economic modelling estimates were presented for patients with established CVD, with or without diabetes. The boxed statement highlighted the role of Lipitor in reducing cholesterol in patients with established CVD or type 2 diabetes.

The objective of the advertisement was to raise awareness of recommended cholesterol levels in secondary prevention patients and type 2 diabetics. The NICE lipid modification clinical guidance did not

recommend a target level for total or LDL cholesterol for primary prevention and as such it would be inappropriate to refer to this population of patients in this advertisement which focused on the recommendations of lowering total cholesterol to <4mmol/L or LDL-cholesterol to <2mmol/L. In addition, it might be potentially misleading to include the primary prevention population in Lipitor advertising as NICE had explicitly recommended simvastatin 40mg (or a medicine of similar efficacy or cost) for the treatment of these patients and did not recommend intensifying lipid lowering therapy thereafter.

Finally, whilst Pfizer agreed that the vast majority of patients who required lipid modification therapy were primary prevention patients, it was entirely reasonable for advertising to focus on a specific population of patients and not the majority.

With regard to the complainants' concerns about the claims 'Economic modelling estimates that only 37% of patients with established CVD, with or without diabetes, achieve a total cholesterol <4mmol/L with simvastatin 40mg' and 'An estimated 82% of these patients would achieve a total cholesterol <4mmol/L with a simvastatin 40mg - Lipitor titration strategy', Pfizer submitted that these estimates were based on analysis obtained from the Titration Outcomes Cost-effectiveness Model (TOCEM). A description of the methodology underpinning this tool was provided.

Whilst Pfizer acknowledged that TOCEM had not been published, in response to a request from NICE this year, a working, fully executable version of this model was shared with NICE. Pfizer did not know what NICE had used the model for but had always ensured that it was fully transparent with all the cost-effectiveness models it developed and had always been prepared to answer any questions about the workings of the model.

It had been made explicitly clear in the advertisement that the claims referred to an economic analysis and therefore, were not misleading. Whilst the majority of statin clinical trials compared a fixed dose of a statin against another, in the real world, clinicians often utilised a range of statins and doses to lower cholesterol. At present, there was limited literature on the impact of different statin titration strategies on the attainment of post-treatment total cholesterol thresholds. TOCEM was an innovative model which attempted to simulate real-life cholesterol management in the UK and used inputs from both published clinical trial and observational data. The observational data used were the UK baseline cholesterol values from The Health Improvement Network (THIN) database which had been published in a peer-reviewed journal.

TOCEM utilised UK baseline cholesterol values from the THIN database, the results of which had been published in a peer-reviewed publication. In addition, Pfizer noted that cholesterol values from its analysis had been adopted by NICE; the assumption of an average cholesterol level of 6.1mmol/L for non-diabetic CVD patients based on a distribution of patients taken from the THIN database was a key assumption underpinning the cost-effectiveness model within the NICE lipid modification clinical guideline.

Statin lowering efficacy data was obtained from the CURVES meta-analysis of statin trials, performed in the US and across Europe. Furthermore, the use of a large meta-analysis of clinical trials was recognised by NICE as level 1 evidence. The CURVES meta-analysis was chosen as a reference for statin lowering efficacy data because it was the largest meta-analysis of statin trials showing average total cholesterol reductions for individual statins and doses with associated p-values.

Pfizer did not agree that the advertisement implied that the NICE lipid modification guideline endorsed Lipitor, when NICE actually recommended that simvastatin 80mg (or a medicine of similar efficacy or cost) be used if a patient did not achieve the recommended cholesterol levels with simvastatin 40mg. The advertisement simply raised awareness of the new lower cholesterol levels recommended by NICE and went on to state how, by titrating up to Lipitor from simvastatin 40mg, more patients could achieve these levels. The final claim in the advertisement stated 'Lipitor is an evidence-based choice when your patients with established CVD or Type 2 diabetes with CVD need intensive cholesterol-lowering for improved cardiovascular outcomes'. This was to remind prescribers that Lipitor 20mg/40mg/80mg provided greater lipid lowering than simvastatin 40mg and had robust clinical data showing that it lowered cholesterol effectively to improve cardiovascular outcomes.

For the reasons outlined above, Pfizer denied breaches of Clauses 7.2, 7.3 and 7.4.

PANEL RULING

The Panel considered that the combination of the heading and the claim that immediately followed made it clear that the advertisement referred to new NICE guidelines on lipid modification for patients with established CVD or type 2 diabetes. The Panel did not consider that the advertisement implied that NICE had recommended a total cholesterol of <4mmol/L and an LDL-cholesterol of <2mmol/L for all patients. It was acceptable for an advertisement to refer to a subset of patients ie in this case those with established CVD or type 2 diabetes, and not the vast majority of patients provided this was made clear. The Panel did not consider the advertisement was misleading as alleged and no breach of Clause 7.2 was ruled.

The Panel was concerned about the claim relating to economic modelling estimates. However it was not a breach of the Code *per se* to cite 'data on

file' in support of promotional claims. The Code required that claims were capable of substantiation. The Panel noted that the economic analysis used data from two sources. Firstly, the THIN database gave the baseline cholesterol levels. Secondly the lipid lowering efficacy data for each statin was based on the CURVES study. The Panel noted that the advertisement made clinical claims based on the economic modelling data. This was reinforced by the way the claims were presented in that '37%' and '82%' were in large bold type which stood out compared to the rest of the text. The figures thus appeared to be proven absolutes. The reference to 'estimates' did not negate this impression. Further, the heading to the advertisement referred to clinical data. The Panel considered that given their context the claims at issue were misleading and not capable of substantiation. Pfizer had not submitted clinical data to support the quoted percentages of patients achieving a total cholesterol of <4mmol/L. The Panel ruled breaches of Clauses 7.2, 7.3 and 7.4.

The Panel noted that the heading and first part of the advertisement referred to NICE guidelines targets and then in a different colour text referred to the lipid lowering efficacy of simvastatin and Lipitor. The claim 'Lipitor is an evidence-based choice when your patients with established CVD or Type 2 diabetes with CVD need intensive cholesterol-lowering for improved cardiovascular outcomes' did not refer to NICE. The context in which a claim appeared, however, was important; the two claims which headed the advertisement at issue referred to NICE guidelines. Nonetheless, on balance, the Panel did not consider that the advertisement implied that Lipitor was endorsed by the NICE guideline on lipid modification as alleged. The advertisement was thus not misleading in that regard and the Panel ruled no breach of Clause 7.2.

Case received **14 November 2008**

Case completed **8 January 2009**