ASSOCIATE DIRECTOR PHARMACY POLICY & PRESCRIBING v MERCK SHARP & DOHME AND SCHERING-PLOUGH

Ezetrol journal advertisement

The Associate Director Pharmacy Policy & Prescribing at a teaching primary care trust complained about an advertisement for Ezetrol (ezetimibe) in Pulse in September issued by Merck Sharp & Dohme and Schering-Plough.

The complainant noted the headline claim 'New NICE [National Institute for Health and Clinical Excellence] technology appraisal recommends ezetimibe alone or in combination with initial statin therapy'. The NICE technology appraisal cited in support of the claim, and stated in very small font size in a footnote to the prescribing information, was the NICE technical appraisal 132, November 2007 – Ezetimibe for the treatment of primary (heterozygous-familial and non-familial) hypercholesterolaemia. Those reading the advertisement, however might reasonably assume that the 'New' NICE guidance referred to was the Clinical Guideline 67 – Lipid Modification. This guideline clearly gave a very different (and much less significant) place in treatment for ezetimibe for lipid modification in primary and secondary prevention of cardiovascular disease than did technology appraisal 132. The advertisement did not refer to familial hypercholesterolaemia. The complainant alleged that the advertisement was misleading.

The detailed response from Merck Sharp & Dohme and Schering-Plough is given below.

The Panel noted that the headline to the advertisement stated 'New NICE technology appraisal recommends ezetimibe alone or in combination with initial statin therapy'. The cited reference was the NICE technology appraisal guidance 132 published in November 2007. The advertisement was published in September 2008. In May 2008 NICE had issued Clinical Guideline 67 on Lipid Modification. The advertisement was clearly about lipid control and the Panel considered that a reference to something 'new' from NICE might be assumed by some readers to be the document issued four months earlier (the clinical guideline) and not the document issued ten months previously (the technology appraisal). Nonetheless the heading clearly referred to the technology appraisal and so in that regard the Panel considered that the advertisement was not misleading and no breach was ruled.

The Panel noted that the technology appraisal guidance 132 (Ezetimibe for the treatment of primary (heterozygous – familial and non-familial) hypercholesterolaemia) was solely about ezetimibe and its place in therapy. The medicine was recommended for use either alone or in combination with initial statin therapy. It was noted, however, that, *inter alia*, a clinical guideline on lipid modification was under development and that the technology appraisal guidance should be read in the context of the relevant clinical guideline when available. The lipid modification clinical guideline was published in May 2008.

The clinical guidance examined the whole therapy area and the use of lipid modification therapy, not just the use of ezetimibe. The clinical guideline was concerned with 'Cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease'. In a section looking at treatment pathways for primary and secondary prevention it was stated that one of the treatment choices for patients who could not tolerate statins for primary prevention was ezetimibe. Readers were referred to the NICE technology appraisal guidance 132 for the treatment of primary (heterozygous-familial and non familial) hypercholesterolaemia. The clinical guideline was silent upon the use of combination therapy of any kind.

The Panel noted the complainant's comments that the clinical guideline gave a less significant place in treatment for ezetimibe in primary and secondary prevention than the technology appraisal. The two documents had to be considered together. The clinical guideline had not rendered the ezetimibe technology appraisal irrelevant. The advertisement at issue was about the use of Ezetrol not about the broad therapy area of lipid lowering. The Panel considered that it was true to state that, if and when ezetimibe was to be prescribed, NICE had recommended its use either alone or in combination with initial statin therapy. In that regard the Panel considered that the headline claim was not misleading as alleged and that it could be substantiated. No breach of the Code was ruled.

The Panel noted that the main part of the advertisement did not refer to familial hypercholesterolaemia; the indications for ezetimibe were stated in the prescribing information ie primary (heterozygous familial and non-familial) hypercholesterolaemia, homozygous familial hypercholesterolaemia and homozygous sitosterolaemia. The NICE technology appraisal

guidance referred to in the headline was about the use of ezetimibe for the treatment of primary-(heterozygous familial and non-familial) hypercholesterolaemia. The Panel considered that the prescribing information was adequate with regard to the stated use of ezetimibe and that the advertisement was not misleading in that regard. No breach was ruled.

The Associate Director Pharmacy Policy & Prescribing at a teaching primary care trust complained about an advertisement (ref 08-09 EZT.08.GB.751108.J) for Ezetrol (ezetimibe) in Pulse, 22 September, issued by Merck Sharp & Dohme Limited and Schering-Plough Limited.

COMPLAINT

The complainant noted the headline claim 'New NICE [National Institute for Health and Clinical Excellence] technology appraisal recommends ezetimibe alone or in combination with initial statin therapy'.

The NICE technology appraisal cited in support of the claim, and stated in very small font size in a footnote to the prescribing information, was the NICE technical appraisal 132, November 2007 – Ezetimibe for the treatment of primary (heterozygous-familial and non-familial) hypercholesterolaemia. Those reading the advertisement, however might reasonably assume that the 'New' NICE guidance referred to was the Clinical Guideline 67 – Lipid Modification. This guideline clearly gave a very different (and much less significant) place in treatment for ezetimibe for lipid modification in primary and secondary prevention of cardiovascular disease than did technology appraisal 132. The advertisement did not refer to familial hypercholesterolaemia.

The complainant alleged that the advertisement was misleading.

When writing to the companies, the Authority asked them to respond in relation to Clauses 7.2 and 7.4 of the Code which were the same in the 2006 and 2008 Codes.

RESPONSE

Merck Sharp & Dohme and Schering-Plough submitted a joint response.

The companies were surprised that the complainant found the advertisement to be misleading and that those reading the advertisement might reasonably assume that the 'New' NICE guidance referred to was the Clinical Guideline 67 - Lipid Modification, as the title 'NEW NICE **TECHNOLOGY APPRAISAL**' [emphasis added] was very prominent; it was written in capital letters, bold type and font size and the statements and claims immediately below it were all taken from this official document.

Immediately after 'appraisal' a subscript '1' referred the reader to reference number 1, located at the end of the prescribing information. This reference clearly stated that the information related to NICE single technology appraisal of ezetimibe (November 2007). The reference was of the same font size as the prescribing information, namely a lower case 'x' was no less than 1mm in height. This was in accordance with the supplementary information to Clause 4.1, which stated that the prescribing information must be given in a clear and legible manner which assisted readability. By default, the same should hold true for the legibility of references. The Code, in any case, allowed for statements and claims to be made without the need for references - the only exception being where references were made to published studies (Clause 7.6).

In using the word 'New' the companies had taken into account Clause 7.11 which allowed the word 'New' to be used for any 'product, presentation or therapeutic indication' for a period of no longer than 12 months. As the complainant acknowledged, the technology appraisal was issued in November 2007, and the advertisement appeared in the 22 September 2008 edition of Pulse, so 'New' was used well within the 1 year timeframe allowed by the Code.

NICE classified its guidance according to type, which was given on its website as follows:

> 'Technology appraisals
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> Technology appraisals are recommendations on the use of new and existing medicines and treatments within the NHS in England and Wales, such as:
> • medicines
> • medical devices (for example, hearing aids or inhalers)
> • diagnostic techniques (tests used to identify diseases)
> • surgical procedures (for example, repairing hernias)
> • health promotion activities (for example, ways of helping people with diabetes manage their condition).
>
> Clinical guidelines
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> Clinical guidelines are recommendations on the appropriate treatment and care of people with specific diseases and conditions within the NHS in England and Wales. Clinical guidelines are based on the best available evidence. Guidelines help healthcare professionals in their work, but they do not replace their knowledge and skills.'

The heading in the advertisement clearly related to information contained within a technology appraisal, as opposed to clinical guidelines and, as explained above, the technology appraisal was clearly referenced.

The complainant had also noted that the

advertisement did not refer to familial hypercholesterolemia. The main body of the advertisement did not mention this as this condition was not part of the scope of the NICE technology appraisal for ezetimibe. However, the prescribing information included the licensed indications for the product and stated, for instance, that Ezetrol was indicated as adjunctive therapy to diet for use in patients with primary (heterozygous familial and non-familial) hypercholesterolemia who were not appropriately controlled with a statin alone. Further, the appropriate management of patients with this condition was covered in a separate guideline (CG71) identification and management of familial hypercholesterolaemia, which was not a feature of this advertisement.

In summary the companies did not believe that the advertisement was either misleading or incapable of substantiation and therefore neither in breach of Clause 7.2 nor 7.4.

PANEL RULING

The Panel noted that the headline to the advertisement stated 'New NICE technology appraisal recommends ezetimibe alone or in combination with initial statin therapy.' The cited reference was the NICE technology appraisal guidance 132 published in November 2007. The advertisement was published in September 2008. In May 2008 NICE had issued Clinical Guideline 67 on Lipid Modification. The advertisement at issue was clearly about lipid control and the Panel considered that a reference to something 'new' from NICE might be assumed by some readers to be the document issued four months earlier (the clinical guideline) and not the document issued ten months previously (the technology appraisal). Nonetheless the heading clearly referred to the technology appraisal and so in that regard the Panel considered that the advertisement was not misleading and no breach of Clause 7.2 was ruled.

The Panel noted that the technology appraisal guidance 132 (Ezetimibe for the treatment of primary (heterozygous – familial and non-familial) hypercholesterolaemia) was solely about ezetimibe and its place in therapy. The medicine was recommended for use either alone or in combination with initial statin therapy. It was noted, however, that, *inter alia*, a clinical guideline on lipid modification was under development and that the technology appraisal guidance should be read in the context of the relevant clinical guideline when available. The lipid modification clinical guideline was published in May 2008.

The lipid modification document examined the whole therapy area and the use of lipid modification therapy, not just the use of ezetimibe. The title page stated that the clinical guideline was concerned with 'Cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease'. In a section looking at treatment pathways for primary and secondary prevention it was stated that one of the treatment choices for patients who could not tolerate statins for primary prevention was ezetimibe. Readers were referred to the NICE technology appraisal guidance 132 for the treatment of primary (heterozygous-familial and non familial) hypercholesterolaemia. The clinical guideline was silent upon the use of combination therapy of any kind.

The Panel noted the complainant's comments regarding the clinical guideline and that it gave a less significant place in treatment for ezetimibe in primary and secondary prevention than the technology appraisal. The two documents had to be considered together. The clinical guideline had not rendered the ezetimibe technology appraisal irrelevant. The advertisement at issue was about the use of Ezetrol not about the broad therapy area of lipid lowering. The Panel considered that it was true to state that, if and when ezetimibe was to be prescribed, NICE had recommended its use either alone or in combination with initial statin therapy. In that regard the Panel considered that the headline claim was not misleading as alleged and that it could be substantiated. No breach of Clauses 7.2 and 7.4 was ruled.

The Panel noted that the main part of the advertisement did not refer to familial hypercholesterolaemia; the indications for ezetimibe were stated in the prescribing information ie primary (heterozygous familial and non-familial) hypercholesterolaemia, homozygous familial hypercholesterolaemia and homozygous sitosterolaemia. The NICE technology appraisal guidance referred to in the headline was about the use of ezetimibe for the treatment of primary-(heterozygous familial and non-familial) hypercholesterolaemia. The Panel considered that the prescribing information was adequate with regard to the stated use of ezetimibe and that the advertisement was not misleading in that regard. No breach of Clause 7.2 was ruled.

Complaint received **3 November 2008**

Case completed **23 December 2008**