CASE AUTH/2577/2/13

VOLUNTARY ADMISSION BY ABBVIE

Out-of-date prescribing information

Abbvie voluntarily admitted that out-of-date prescribing information had been linked to an online Humira (adalimumab) banner advertisement and included in a hard copy Humira journal advertisement. The materials at issue, which were published in December 2012, promoted Humira for the treatment of moderate to severe, active rheumatoid arthritis.

The detailed response from Abbvie is given below.

The Panel noted that as the banner advertisement had appeared on a UK website and the journal advertisement had been published in international journals which were based in the UK, they both came within the scope of the Code. Although the material had been placed by Abbvie's global group, it was a well established principle under the Code that UK companies were responsible for the acts or omissions of overseas parents or affiliates that came within the scope of the Code.

The Code stated that the prescribing information consisted of, *inter alia*, a succinct statement of common side-effects likely to be encountered in clinical practice, serious side-effects and precautions and contra-indications relevant to the indications in the advertisement. The Panel noted that the prescribing information at issue was last revised in May 2011 and did not include two common side-effects and two serious, uncommon side-effects of Humira that were included in the December 2012 prescribing information. The Panel considered that as the prescribing information linked to the banner advertisement and included in the journal advertisements was not up-to-date with regard to precautions and side-effects it did not comply with the Code. High standards had not been maintained. Breaches of the Code were ruled.

Abbvie Ltd voluntarily admitted that out-of-date prescribing information had been linked to an online Humira (adalimumab) advertisement (ref AXHUR111644a) and included in a hard copy Humira advertisement (ref AXHUR111644) which was published in four journals. The material at issue promoted Humira for the treatment of moderate to severe, active rheumatoid arthritis.

As Paragraph 5.6 of the Constitution and Procedure required the Director to treat a voluntary admission as a complaint, the matter was taken up with Abbvie.

COMPLAINT

Abbvie submitted that it had become aware of a potential breach of the Code and drew attention to an online banner advertisement for Humira placed on rheumatology.org.uk on 17 December 2012 by the global rheumatology team. The advertisement had been approved by the UK affiliate in October 2011. On inspection it became clear that the linked prescribing information was now out-of-date (ie version 23) contrary to Clause 4.2 of the Code.

Abbvie contacted the publisher and requested the immediate removal of the banner advertisement. The advertisement was taken down within an hour of Abbvie knowing about the breach. Abbvie also contact the advertising agencies involved and its global colleagues. Both confirmed that there was no other online advertising using the same out-of-date prescribing information.

In the course of these communications, Abbvie also became aware that on 17 December 2012 the global rheumatology team had commissioned the printed advertisements. These advertisements had also been approved by the UK affiliate in October 2011, but also now included prescribing information which was out-of-date (version 23). The advertisements were scheduled to appear in Annals of Rheumatic Disease, Rheumatology, International Rheumatology and Clinical Rheumatology. The first two of these journals were based in the UK.

On becoming aware of this, Abbvie requested the print run to be stopped but was unfortunately too late to stop the out-of-date advertisements appearing in the January 2013 editions of the journals, in breach of Clause 4.2. The advertisement had been withdrawn from all future issues.

In summary, Abbvie submitted that it became aware of two incidents where outdated prescribing information was included in an online advertisement and printed journal advertisements for Humira. The online advertisement was withdrawn as a matter of urgency and the printed advertisements had been withdrawn from future issues.

After an investigation, including a review of processes involved, Abbvie believed that this was an isolated incident. The incident was an individual's error, rather than Abbvie processes which were not followed by a new employee. Retraining of the employee was underway.

In terms of further preventative measures, an updated global standard operating procedure (SOP) was in development. This would mandate that global marketing could not make promotional advertisements on behalf of an affiliate, and only an affiliate could make a placement in its local market.

Abbvie considered that there was no risk to patient safety arising from this incident and the correct prescribing would have been available through

many other sources. Abbvie took its obligations to transparency under the Code very seriously and so wanted to bring this matter to the Authority's attention.

When writing to Abbvie, the Authority asked it to respond to Clauses 4.2 and 9.1 of the Code.

RESPONSE

Abbvie submitted that global colleagues requested UK approval of advertisements which were to be run in rheumatology journals and online in October 2011. Electronic copies were provided which included the then Humira prescribing information (version 23). Abbvie noted that the advertisements were used again on 17 December 2012. These advertisements had been commissioned by Abbvie global, without further approval from the UK. The correct Humira prescribing information in December 2012 was version 27. The advertisements were placed on rheumatology.org.uk and printed in Annals of Rheumatic Disease, Rheumatology, International Rheumatology and Clinical Rheumatology.

The online banner advertisement was withdrawn immediately but the journal advertisement had already gone to print and appeared in the January 2013 editions of the journals listed above. Printed advertisements had been withdrawn from all future issues.

Annals of Rheumatic Disease and Rheumatology were both published in the UK. The Humira advertisement at issue would only be seen by subscribers in the UK and Europe. As previously stated, Abbvie believed these journals would be subject to the Code. Clinical Rheumatology and Rheumatology International were international journals published in Germany. Abbvie did not consider that these journals were subject to the Code.

By chance, an Abbvie UK employee noted that the date of preparation of the online banner advertisement was October 2011 and checked the prescribing information; the matter was then escalated to the medical department.

Abbvie provided internal policy documents current when the advertisements were published and also provided details of the dates when the Humira prescribing information had been updated from version 23 (included on the material at issue) to the current version (version 27, revised December 2012). Abbvie submitted that the prescribing information was extensively rewritten and simplified in December 2012 so a direct comparison of version 27 with version 23 was not possible.

The major changes between versions 23 and 27 were:

- Version 23 did not contain the ulcerative colitis, paediatric Crohn's or nonradiographic-axial spondyloarthropathy indications.
- Version 23 did not refer to the following adverse events: nerve root compression, pyrexia (both common), specific wording regarding Merkel cell carcinoma and liver failure (both serious uncommon). Previous versions of the prescribing information included general statements regarding increased risk of malignancy.
- Under Precautions, the time relating to monitoring patients for infections has reduced from 5 months to 4 months in version 27.

When prescribing information was updated, regulatory affairs emailed the marketing department which then had to update materials or withdraw and notify all parties and ensure the return of any outstanding hard copy material for destruction. Unfortunately, due to an individual error in this case, a new employee did not follow this process. The employee had been trained on the policy in September 2011 and Abbvie had not identified any other examples where the individual in question had made the same error. Action regarding retraining the employee was underway. The promotional materials in question were withdrawn in October 2012.

Abbvie considered that this was an isolated incident and reflected an individual's error rather than Abbvie processes which were not followed by a new employee.

PANEL RULING

The Panel noted that the banner advertisement at issue had appeared on a UK website (rheumatology.org.uk) and the hard copy advertisement at issue had been published in international journals which were based in the UK (Annals of Rheumatic Disease and Rheumatology). The Panel thus considered that the materials came within the scope of the Code. Although the material had been placed by Abbvie's global group, it was a well established principle under the Code that UK companies were responsible for the acts or omissions of overseas parents or affiliates that came within the scope of the Code.

The Panel noted that Clause 4.1 of the Code required the prescribing information listed in Clause 4.2 to be provided in a clear and legible manner. Clause 4.2 stated the prescribing information consisted of, *inter alia*, a succinct statement of common side-effects likely to be encountered in clinical practice, serious side-effects and precautions and contra-indications relevant to the indications in the advertisement. The Panel noted that the prescribing information included on the online advertisement and in the journal advertisements was last revised in May 2011 and did not include the common side-effects of nerve root compression and pyrexia; nor were the serious, uncommon side-effects of Merkel cell carcinoma and liver failure included. Under precautions the prescribing information on the online advertisement and in the journal advertisements stated that because of the susceptibility of Humira patients to serious infections compounded by possible impaired lung function, patients should be closely monitored for infections, including tuberculosis, before, during and for 5 months after treatment with Humira. The prescribing information had been changed such that the

monitoring period had been reduced to 4 months. The Panel further noted that although the prescribing information at issue did not refer to three particular indications, it did refer to rheumatoid arthritis which was the subject of the advertisements at issue. Clause 4.2 also stated that at least one authorized indication for use had to be given and this had been done. However, the Panel considered that as the prescribing information linked to the banner advertisement and included in the journal advertisements was not up-to-date with regard to precautions and side-effects it did not comply with the Code. As Clause 4.1 required that the prescribing information be provided a breach of that clause was ruled.

The Panel noted its rulings above and considered that high standards had not been maintained. Up-to-date prescribing information had not been provided. A breach of Clause 9.1 was ruled.

Complaint received **6 February 2013**

Case completed **14 March 2013**