HEALTH PROFESSIONAL v ABBVIE

Promotion of Humira

A health professional who until recently worked in the pharmaceutical industry complained about a Humira (adalimumab) journal advertisement issued by AbbVie.

The complainant stated that the two page advertisement included the claim 'Fast symptom relief from week 1 (CD) and week 2 (UC)'. The complainant considered that 'fast' was a relative term and stated that there were other treatments that were as fast or faster as symptoms could be varied. Opiates and antispasmodics could provide symptom relief within hours.

The detailed response from AbbVie is given below.

The Panel noted AbbVie's submission that the claim related solely to the effect of Humira, with no comparisons being made to other treatments. The Panel further noted AbbVie's submission that the promotion of Humira for the treatment of moderately to severely active adult Crohn's disease (CD) and ulcerative colitis (UC) was in accordance with the terms of its marketing authorisation and was not inconsistent with the particulars listed in the summary of product characteristics (SPC). The Panel noted that unlike the advertisement the SPC did not describe the product as providing fast symptom relief from week 1 in Crohn's disease and week 2 in ulcerative colitis. The Humira SPC stated 'Available data in ulcerative colitis suggest that clinical response is usually achieved within 2-8 weeks of treatment.'

The Panel noted that the complainant referred to opiates and antispasmodics but provided no data in support of his/her contention. The Panel noted that AbbVie had not responded in detail with regard to the action of opiates and antispasmodics effects on symptom relief other than to state that these two medicines were not listed as agents with the ability to provide induction of remission for patients with inflammatory bowel disease (IBD) according to NICE or within guidance issued by the British Society of Gastroenterology (BSG). In contrast, NICE referred to biologic agents as therapies which could be used to induce and maintain remission in IBD.

The Panel noted that the complainant was concerned about the alleged comparative nature of the word 'fast'. However, overall and on balance the Panel did not consider that the claim at issue 'Fast symptom relief from week 1 (CD) and week 2 (UC)' within the context of the advertisement was a comparison. Neither the headline nor the visual were comparative. The claims beneath did not refer to other products. None of the three studies referenced included any comparator products although this was not made clear in the advertisement. The Panel did not consider that the complainant had proven on the balance of probabilities that the claim was a comparison with other medicines including opiates or antispasmodics and that such a comparison was unfair and misleading. Based on the very narrow allegation, the Panel ruled no breach of the Code.

Noting its comments above the Panel did not consider that the use of the word 'fast' exaggerated the clinical comparative efficacy of Humira as alleged. No breach of the Code was ruled.

A health professional who until recently worked in the pharmaceutical industry, albeit in a different therapeutic area, complained about an advertisement (ref AXHUG160440b(2)) for Humira (adalimumab) issued by AbbVie Ltd. The advertisement was published in Gastrointestinal Nursing, September 2016.

Humira was indicated, *inter alia*, for the treatment of moderately to severely active Crohn's disease, in adult patients who had not responded despite a full and adequate course of therapy with a corticosteroid and/or an immunosuppressant; or who were intolerant to or had medical contraindications for such therapies and for the treatment of moderately to severely active ulcerative colitis in adult patients who had an inadequate response to conventional therapy including corticosteroids and 6-mercaptopurine (6-MP) or azathioprine (AZA), or who were intolerant to or had medical contraindications for such therapies.

COMPLAINT

The complainant stated that the two page advertisement included the claim 'Fast symptom relief from week 1 (CD) and week 2 (UC)'. The complainant considered that 'fast' was a relative term and stated that there were other treatments that were as fast or faster as symptoms could be varied. Opiates and antispasmodics could provide symptom relief within hours.

When writing to AbbVie the Authority asked it to respond in relation to the requirements of Clauses 7.2 and 7.10 of the Code.

RESPONSE

AbbVie submitted that the claim in question was fully substantiated using accurate data representing the most up to date published information. The claim related solely to the effect of Humira, with no comparisons being made to other treatments. It was consistent with the use of Humira within the licensed population of patients with moderately to severely active Crohn's disease or ulcerative colitis.

AbbVie explained that Humira was an anti-tumour necrosis factor (TNF) biologic agent with multiple

indications, including inflammatory bowel disease (IBD). AbbVie submitted that moderate to severely active IBD, followed a chronic, relapsing, remitting disease course. According to the National Institute for Health and Care Excellence (NICE) quality standards for IBD, the aim of treatment was 'either to heal the inflammation and so reduce symptoms during a flare-up (inducing remission) or to prevent flare-ups happening in the future (maintaining remission)'.

AbbVie noted that the two medicines mentioned by the complainant, opiates and anti-spasmodics, were not listed as agents with the ability to provide induction of remission for patients with IBD according to NICE or within guidance issued by the British Society of Gastroenterology (BSG). In contrast, NICE referred to biologic agents as therapies which could be used to induce and maintain remission in IBD.

The information contained within the advertisement regarding the promotion of Humira for treatment of moderately to severely active adult Crohn's disease (CD) and ulcerative colitis (UC) was in accordance with the terms of its marketing authorisation and was not inconsistent with the particulars listed in the summary of product characteristics (SPC). It was not inappropriate in promotional material for Humira, to make reference to the time at which symptom relief occurred, as this would be of interest to specialists treating patients with IBD.

A named consultant gastroenterologist described the significance of symptom reduction in this population of patients as:

> 'Adalimumab improves quality of life and reduces rectal bleeding within 2 weeks when used for ulcerative colitis and symptom improvement starts within a week when treating Crohn's disease. This fast onset of action benefits patients who have objective evidence of active inflammation.'

AbbVie therefore submitted that using the term 'fast' to describe a 1-2 week response time to onset of symptom relief was appropriate and fully understood by IBD specialists. Clinical data for Humira focussed on the importance of symptom relief, both from a clinical and patient perspective. The references used to substantiate the claim described both:

1 Time to significant reduction in clinical symptoms, using comprehensive disease-related symptom scores (Crohn's disease activity index (CDAI) for CD and simple clinical colitis activity index (SCCAI) for UC). These clinical symptom scores were used in clinical trials, by the regulatory authorities and were widely recognised by clinicians treating IBD.

2 **Patient-reported symptom relief** using validated questionnaires specific to patients with IBD (inflammatory bowel disease questionnaire (IBDQ) and short IBDQ (SIBDQ) for CD and UC, respectively). These scales were widely used in studies of IBD and recommended by the regulatory authorities.

AbbVie submitted that there was no breach of Clause 7.2, as the term 'fast' was being used in an accurate, objective and qualified manner to reflect the impact of treatment on clinical and patient reported symptoms in the moderately to severely active CD and UC population at early time points. No absolutes such as 'immediate' had been used which ensured the claim was neither misleading, nor a hanging comparison.

AbbVie denied a breach of Clause 7.10 as the claim did not exaggerate the properties of Humira, as the relevant timings (ie week 1 and week 2) were clearly stated and all information was fully substantiated within the references provided. The claim also did not use any superlatives, such as 'faster' or 'fastest'.

AbbVie concluded that it had not breached Clauses 7.2 or 7.10. The advertisement was accurate and clearly substantiated, describing the outcomes of using Humira when considering the rational use in the licensed populations of patients with moderately to severely active Crohn's disease and ulcerative colitis.

AbbVie confirmed that the advertisement was displayed across two adjacent pages of the journal and when viewed was similar in size to A3.

PANEL RULING

The Panel noted the complainant's concern that the word 'fast', which appeared in the claim 'Fast symptom relief from week 1 (CD) and week 2 (UC)' within the Humira advertisement, was a relative term. According to the complainant there were other treatments that were as fast or faster as symptoms could be varied. The complainant stated that opiates and antispasmodics could provide symptom relief within hours.

The Panel noted AbbVie's submission that the claim related solely to the effect of Humira, with no comparisons being made to other treatments. The Panel further noted AbbVie's submission that the promotion of Humira for the treatment of moderately to severely active adult Crohn's disease (CD) and ulcerative colitis (UC) was in accordance with the terms of its marketing authorisation and was not inconsistent with the particulars listed in the SPC. The Panel noted that unlike the advertisement the SPC did not describe the product as providing fast symptom relief from week 1 in Crohn's disease and week 2 in ulcerative colitis. The Humira SPC stated 'Available data in ulcerative colitis suggest that clinical response is usually achieved within 2-8 weeks of treatment.'

The Panel noted that Crohn's disease and ulcerative colitis were the 2 main forms of inflammatory bowel disease. The NICE Quality Standard on inflammatory bowel disease stated that in Crohn's disease, inflammation of the digestive system led to diarrhoea, abdominal pain, tiredness and weight loss. Symptoms of active disease or relapse of ulcerative colitis included bloody diarrhoea, an urgent need to defecate and abdominal pain. According to NICE the aim when treating

inflammatory bowel disease was either to heal the inflammation and so reduce symptoms during a flare-up (inducing remission) or to prevent flare-ups happening in the future (maintaining remission).

The Panel noted that 'fast' might be considered by some to be a relative term and thus the claim could potentially be read as a comparison with other products. The Panel noted that the complainant referred to opiates and antispasmodics but had provided no data in support of his/her contention. The Panel noted that AbbVie had not responded in detail with regard to the action of opiates and antispasmodics effects on symptom relief other than to state that the two medicines mentioned by the complainant were not listed as agents with the ability to provide induction of remission for patients with IBD according to NICE or within guidance issued by the British Society of Gastroenterology (BSG). In contrast, NICE referred to biologic agents as therapies which could be used to induce and maintain remission in IBD. The claim in question referred to symptom relief from weeks 1 and 2 and was referenced to Hanauer *et al* 2006 and Sandborn *et al* 2007 with regard to Crohn's disease and Travis *et al* 2016 with regard to ulcerative colitis.

Hanauer *et al* was a randomized, double-blind, placebo-controlled, dose-ranging trial to evaluate the efficacy of adalimumab induction therapy in patients with moderated to severe Crohn's disease naïve to anti-TNF therapy. The primary endpoint was demonstration of a significant difference in the rates of remission at week 4. The rates of remission at week 4 in the SPC recommended 80mg/40mg adalimumab dose group was 24% (p=0.06). The Panel noted that the study stated that significant responses compared with placebo were demonstrated as early as week 1 in this dose group; patients in the 80mg/40mg treatment group (75 patients) had significantly lower mean Crohn's disease activity index (CDAI) scores and higher mean inflammatory bowel disease questionnaire (IBDQ) total scores than patients in the placebo group. The study authors acknowledged that it was a short 4-week trial and there was insufficient data to determine whether an 80mg loading dose followed by 40mg every other week would be effective for induction and maintenance of remission in patients with Crohn's disease.

Sandborn *et al*, was also a 4 week, randomized, double-blind, placebo-controlled trial in which patients were randomly assigned to receive induction doses of adalimumab, 160mg and 80mg, at weeks 0 and 2, respectively or placebo at the same time points. The primary end point was induction of remission at week 4. At week 4, 21% of patients in the adalimumab group compared with 7% of patients in the placebo group achieved remission (p<0.001) whilst patients in the adalimumab group had statistically significantly lower mean CDAI total scores at weeks 1, 2 and 4 than did patients in the placebo group. The Panel noted that the Humira SPC stated that the recommended dose for adult patients with moderately to severely active Crohn's disease was 80mg at week 0 followed by 40mg at week 2. The SPC further stated that if there was a need for a more rapid response to therapy then 160mg at week 0 and 80mg at week 2 could be used with the awareness that the risk for adverse events was higher during induction. After induction treatment, the recommended dose was 40mg every other week via subcutaneous injection.

Travis *et al* was a poster presented at the European Crohn's and Colitis Organisation (ECCO) in March 2016 which detailed a single-arm, multi-country, open-label study that evaluated the effect of adalimumab on clinical outcomes, health-related quality of life (HRQoL), and costs of clinical care in patients with ulcerative colitis treated according to usual clinical pratice. Patients received 160mg/80mg adalimumab at week 0/2 followed by 40mg every other week at week 4 through week 26. Data from 461 patients were analysed and at week 2, 74% achieved Simple Clinical Colitis Activity Index (SSCAI) response, defined as a decrease of ≥ 2 points compared to baseline, at week 2 and 27% achieved SCCAI remission.

The recommended Humira induction dose regimen for adult patients with moderate to severe ulcerative colitis was 160mg at week 0 and 80mg at week 2. After induction treatment, the recommended dose was 40mg every other week via subcutaneous injection.

The Panel noted that the complainant was concerned about the alleged comparative nature of the word 'fast'. However, overall and on balance the Panel did not consider that the claim at issue 'Fast symptom relief from week 1 (CD) and week 2 (UC)' within the context of the advertisement was a comparison. Neither the headline nor the visual were comparative. The claims beneath did not refer to other products. None of the three studies referenced included any comparator products although this was not made clear in the advertisement. The Panel did not consider that the complainant had proven on the balance of probabilities that the claim was a comparison with other medicines including opiates or antispasmodics and that such a comparison was unfair and misleading. Based on the very narrow allegation, the Panel ruled no breach of Clause 7.2.

Noting its comments above the Panel did not consider that the use of the word 'fast' exaggerated the clinical comparative efficacy of Humira as alleged. No breach of Clause 7.10 was ruled.

Complaint received **21 September 2016**

Case completed **10 January 2017**