CASE AUTH/3263/11/19

ANONYMOUS COMPLAINANT v ALMIRALL

Online promotion of Ilumetri

An anonymous, non-contactable individual alleged that claims about the dosing and efficacy of Ilumetri (tildrakizumab) on Almirall's company website were misleading. Ilumetri was indicated for the treatment of adults with moderate to severe plaque psoriasis who were candidates for systemic therapy.

The complainant noted that Almirall had provided information about prescription only medicines on a publicly available website. There was no statement that the website, which included prescribing information, was only intended for health professionals and thus it appeared to promote prescription only medicines to the public.

The complainant noted that there was a separate section on the website for 'Access for Professionals' where a health professional had to sign up. The complainant queried why, if the website was intended for health professionals, they had to sign-up separately.

The detailed response from Almirall is given below.

The Panel noted that the welcome page of the website clearly stated 'The information provided on this website is intended for use by Health Care Professionals qualified to prescribe and supply medications, thus requiring specific knowledge and training to interpret it correctly'. The target audience for the website was thus clearly identified. Readers were asked to choose between 'I'm a HCP' and 'I'm not a HCP'. The Panel considered that it would have been good practice and helpful to those who were not health professionals, to have clearly stated on the welcome page that if a reader clicked the 'I'm not a HCP' button, they would be re-directed to a non-promotional corporate website where information such as summaries of product characteristics (SPCs) and patient information leaflets were available. Otherwise they might assume that they would get no information and be tempted to access material aimed at health professionals. The Panel noted, however, that the landing page was a mechanism to direct two potential audiences (health professionals and the public) to information relevant to each audience which were identified.

The Panel did not consider that there was evidence that the website promoted prescription only medicines to the public as alleged and, based on the narrow allegation, no breaches of the Code were ruled.

The Panel noted that the website had been certified as promotional material and therefore no breaches of the Code were ruled.

The Panel noted that it was clear that it was Almirall's website and prescribing information for its products was provided. The Panel considered that there was no

evidence before it that the promotional nature of the website was disguised and no breach of the Code was ruled.

The Panel noted the complainant's vague allegations that claims about the dosing and efficacy of Ilumetri were misleading; no claims had been identified and no reasons given as to why they might be misleading. The Panel noted that a complainant had the burden of proving his/her complaint on the balance of probabilities; it was not for the Panel to make out a complainant's case for him/her. In the circumstances, the Panel decided that it would only consider the headline claims in the Ilumetri dosing and efficacy sections which Almirall had responded to; in the absence of any specific complaint, it was not for the Panel to examine every claim.

The Panel noted the claim 'Ilumetri is the only IL-23 inhibitor with just four doses per year and two dosing options'. A schematic beneath the claim showed that in the first year of treatment patients received six injections and it was not until the second year of treatment that they would only get four doses a year. The Panel considered that, with regard to the first year of treatment, the claim was misleading and incapable of substantiation. Breaches of the Code were ruled.

With regard to efficacy, the Panel noted the claim 'Ilumetri demonstrated superior efficacy to placebo at Week 12 and maintains control for >2.5 years in responders (PASI≥75)'. The Panel noted, however, that at 12 weeks approximately one third of patients were not classed as responders (Reich *et al* 2017). With regard to long-term response in those who were classed as responders at week 28, a pooled analysis over three years (Thaci *et al* 2018) reported a maintenance of response in over 90% of patients. The Panel thus considered that the first part of the claim 'Ilumetri demonstrated superior efficacy to placebo at Week 12' was not sufficiently complete such that readers would understand 'responders' only accounted for about two thirds of patients treated. In that regard, the Panel considered that the claim was misleading and incapable of substantiation and breaches of the Code were ruled.

The Panel noted the claim 'Ilumetri significantly improves quality of life' referenced to Reich *et al*. Below the claim was a schematic which appeared to show an improvement in quality of life between 0 and 12 weeks for 42% of patients. There was a plateau between 12 and 28 weeks when 52% of patients reported an improved quality of life and a further improvement between 28 and 52 weeks by which time 64% of patients had reported an improved quality of life. It appeared that the data within the schematic was taken from Thaci *et al*. The Panel thus noted that although 64% of patients reported an improvement in quality of life at 52 weeks, it was 64% of responders – not 64% of all patients treated. The Panel considered that the claim was not sufficiently complete such that readers would be able to form their own opinion of the therapeutic value of the medicine. In that regard, the Panel considered that the claim was misleading and incapable of substantiation and breaches of the Code were ruled.

The Panel noted its rulings and comments above and considered that the promotional material had failed to comply with all relevant requirements of the Code including that high standards had not been maintained. Breaches of the Code were ruled.

The Panel noted its rulings above but did not consider that the particular circumstances in this case warranted a ruling of a breach of Clause 2 which was a sign of particular censure and reserved for such. No breach of Clause 2 was ruled.

An anonymous, non-contactable individual complained about Almirall's company website (Almirallmed.co.uk) and in particular about claims for Ilumetri (tildrakizumab). Ilumetri was a sub-cutaneous injection indicated for the treatment of adults with moderate to severe plaque psoriasis who were candidates for systemic therapy.

COMPLAINT

The complainant noted that Almirall had provided information about prescription only medicines on a website freely available to the public. There was no statement that the website was only intended for health professionals and it appeared to promote prescription only medicines to the public.

As prescribing information had been provided, it was clearly a promotional website.

The complainant noted that there was a separate section on the top right-hand corner of the website for 'Access for Professionals' where a health professional had to sign up. The complainant queried why, if the website was intended for health professionals, they had to sign-up separately.

The complainant noted that if readers clicked on any of the product tiles, they were taken to promotional claims for all the relevant products. The complainant alleged that the claims about the dosing and efficacy of Ilumetri appeared to be misleading. The complainant alleged breaches of Clauses 2, 7, 9, 12, 14 and 28.

When writing to Almirall, the Authority noted the clauses of the Code cited by the complainant. The case preparation manager identified the relevant sub-clauses on the information provided and asked Almirall to consider Clauses 7.2 and 7.4 in relation to the claims for Ilumetri, Clause 26.1 in relation to the alleged promotion to the public as well as Clauses 2, 9.1, 12.1, 14.1, 14.3 and 28.1.

RESPONSE

Almirall noted that the website at issue was a promotional website for health professionals; it was certified as such and contained the relevant mandatory information, including prescribing information which was one click away in the footer.

The website was accessible only after a visitor had confirmed that they were a health professional. This was one of the two choices available on a pop-up which appeared before entering the website. The pop-up appeared superimposed on a blurred background of the website homepage so that those who were not health professionals could not see the content of the site.

If visitors selected 'I'm a HCP', they accessed the site; if they confirmed they were not, they were referred back to a non-promotional corporate website where information on Almirall's products, such as summaries of product characteristics (SPCs) and patient information leaflets were available.

Almirall noted that computers could memorise passwords through cookies, etc, such that if a visitor had previously accepted the cookies and confirmed his/her choice, access to Almirallmed.co.uk for a health professional might appear seamless (ie no pop-up would appear again).

Accordingly, Almirall rejected all allegations related to public visibility of promotional content.

If an individual confirmed that he/she was a health professional then he/she had access to content such as product information, events calendar and patient materials. Health professionals could also register to log in ('Access for Professionals' section) and personalise their Almirallmed account by saving favourite Almirallmed pages, requesting patient and/or promotional materials and attending, or registering for, promotional meetings. By clicking on product tiles, health professionals would find relevant promotional information, claims and prescribing information.

Almirall submitted that the promotional claims for Ilumetri were certified after internal review in line with the requirements of Clause 14.1. With regard to the claim 'Ilumetri is the only IL-23 inhibitor with just four dosing options', Almirall submitted that tildrakizumab was the only IL-23 inhibitor with four doses per year in the maintenance phase (ref SPC). Ilumetri 100mg was the standard dose, compared with 100mg for guselkumab (more than 4 injections a year), and risankizumab (standard dose of 150mg delivered via two 75mg dose injections). Almirall considered, therefore, that the claim was objective, balanced, capable of substantiation and not misleading.

Almirall further submitted that the efficacy claims 'Ilumetri demonstrated superior efficacy to placebo at Week 12 and maintains control for >2.5 years in responders (PASI≥75)', 'Ilumetri met the co-primary endpoint of patients achieving PASI 75 and PGA response at Week 12 in Phase III trials' and 'Of the patients who had achieved PASI 75 at Week 28: 91% maintained PAI 75 to week 148, 68% achieved PASI 90 at Week 148, 80% were still on Ilumetri at the 148 week follow-up' (supported by Reich *et al* 2017 and Thaci *et al* 2018) were similarly objective, balanced, capable of substantiation and not misleading. Almirall submitted that the quality of life claims were substantiated by Reich *et al* and from data from the SPC.

Almirall submitted that as per the evidence above, claims on dosing and efficacy for Ilumetri were accurate, balanced, fair, objective and unambiguous and were based on up-to-date data; it denied a breach of Clause 7.2. The claims could be substantiated; the company denied a breach of Clause 7.4.

Almirall submitted that the promotional website at issue was not disguised as a non-promotional website. A pop-up was in place before a visitor could enter the website. Those who declared that they were health professionals were allowed to access the content of the promotional website – if they were not health professionals they were re-directed to the non-promotional corporate website where appropriately presented information on Almirall products could be found. Almirall denied a breach of Clause 12.1.

The promotional website was certified before use and so the company denied a breach of Clauses 14.1 and 14.3 which Almirall considered to be out of scope.

The website was a promotional website for health professionals. Those who were not health professionals were re-directed to the non-promotional corporate website where they could find appropriate information on Almirall products. Almirall denied a breach of Clauses 26.1 and 28.1.

Almirall submitted that the evidence and explanations above confirmed its commitment to compliance with the letter and the spirit of the Code.

Almirall aimed to conduct itself in a manner which constituted the highest standards which it expected of itself and in line with expected industry standards and the Code; it was committed to conducting promotional activities in the interest of patient safety and in line with Code. The website complied with the requirements of the clauses cited and so the company denied a breach of Clause 9.1. Further, patient safety had not been compromised and so the company denied a breach of Clause 2.

PANEL RULING

The Panel noted that Clause 26.1 prohibited the advertising of prescription only medicines to the public. Clause 26.2 permitted information to be supplied directly or indirectly to the public but such information had to be factual and presented in a balanced way. The Panel also noted the reference to a library resource in the supplementary information to Clause 26.2.

The Panel noted that Clause 28 covered the Internet and other digital platforms, its supplementary information, Access, stated that unless access to promotional material about prescription only medicines was limited to health professionals and other relevant decision makers, a pharmaceutical company website or a company sponsored website must provide information for the public as well as promotion to health professionals with the sections for each target audience clearly separated and the intended audience identified. This was to avoid the public needing to access material for health professionals unless they chose to.

The Panel noted the complainant's submission that there was no statement that the website was only intended for health professionals, however, the welcome page of the Almirall website (Almirallmed.co.uk) clearly stated 'The information provided on this website is intended for use by Health Care Professionals qualified to prescribe and supply medications, thus requiring specific knowledge and training to interpret it correctly'. The target audience for the website was thus clearly identified. Readers were asked to choose between 'I'm a HCP' and 'I'm not a HCP'. In that regard, the Panel noted Almirall's submission that the website in question was a promotional website for health professionals; no information had been provided by either party as to the likelihood of patients/public finding the website on an Internet search. The Panel noted that if a reader identified as a health professional, he/she could access the promotional website. The Panel considered that it would have been good practice and helpful to those who were not health professionals, to have clearly stated on the welcome page that if a reader clicked the 'I'm not a HCP' button, they would be re-directed to a non-promotional corporate website where information on Almirall's products, such as summaries of product characteristics (SPCs) and patient information leaflets, were available. Otherwise they might assume that they would get no information and be tempted to access material aimed at health professionals. The Panel noted, however, that the landing page was a mechanism to direct two potential audiences (health professionals and the public) to information relevant to each audience which were identified.

Whilst the Panel noted Almirall's submission that to improve the visitor experience the website used cookies that would remember a visitor's choice (ie if they accessed the website in the past and selected the option 'I'm a HCP', no pop-up would appear when accessing the website again and they would automatically access the site), the Panel did not consider that there was evidence that the website promoted prescription only medicines to the public as alleged and, based on the narrow allegation, the Panel therefore ruled no breach of Clauses 26.1 and 28.1.

The Panel noted that the website had been certified as promotional material and therefore no breach of Clause 14.1 was ruled. As the material at issue was promotional, Clause 14.3 was not relevant and so the Panel ruled no breach of that clause.

The Panel noted that promotional material did not need to be labelled as such, however, it must not be disguised, and the identity of the responsible pharmaceutical company must be obvious at the outset. The Panel noted that it was clear that it was Almirall's website and prescribing information for its products was provided. The Panel considered that there was no evidence before it that the promotional nature of the website was disguised and no breach of Clause 12.1 was ruled.

The Panel noted that the complainant had only vaguely alleged that claims about the dosing and efficacy of Ilumetri were misleading; no claims had been identified and no reasons given as to why they might be misleading. As the complainant was non-contactable, he/she could not be asked to provide further details. The Panel noted that a complainant had the burden of proving his/her complaint on the balance of probabilities; it was not for the Panel to make out a complainant's case for him/her. In the circumstances, the Panel decided that it would only consider the headline claims in the Ilumetri dosing and efficacy sections which Almirall had responded to; in the absence of any specific complaint, it was not for the Panel to examine every claim.

The Panel noted the claim 'Ilumetri is the only IL-23 inhibitor with just four doses per year and two dosing options'. A schematic beneath the claim showed that in the initial phase patients received an injection at week 0 and again at week 4 and thereafter they received injections every twelve weeks, ie at weeks 16, 28, 40 and 52. In the second year they would receive injections at weeks 12, 24, 36 and 48. Thus it was not until the second year of treatment that patients would only get four doses a year. Almirall had submitted that tildrakizumab was the only IL-23 inhibitor with four doses per year in the maintenance phase. The Panel noted that claims in promotional material must be capable of standing alone with regard to accuracy etc and that in general claims should not be qualified by the use of footnotes and the like. The Panel noted that in the first year of treatment a patient would receive 6 injections, not 4 as implied. The Panel considered that the claim was misleading and incapable of substantiation. A breach of Clauses 7.2 and 7.4 was ruled.

With regard to efficacy, the Panel noted that claim 'Ilumetri demonstrated superior efficacy to placebo at Week 12 and maintains control for >2.5 years in responders (PASI≥75)'. The claim was referenced to Reich *et al* (2017) and Thaci *et al* (2018). The Panel noted that Reich *et al* reported the results for tildrakizumab vs placebo or etanercept for chronic plaque psoriasis (reSURFACE 1 and reSURFACE 2). Results at 12 weeks showed that in the two trials, 62% and 66% of patients respectively given 200mg tildrakizumab responded to therapy and 64% and 61% of patients respectively given 100mg tildrakizumab responded to therapy. Approximately one third of patients were thus not classed as responders, ie achieving PASI 75. Thaci *et al* was a pooled analysis over three years of the long-term efficacy and safety of tildrakizumab in

patients with moderate to severe psoriasis who were responders at week 28 in reSURFACE 1 and reSURFACE 2. The authors reported that maintenance of PASI 75 response over 148 weeks of follow up was observed in 91% and 92% of patients that received tildrakizumab 100mg and 200mg, respectively. The Panel considered that the first part of the claim 'Ilumetri demonstrated superior efficacy to placebo at Week 12' was not sufficiently complete such that readers would understand 'responders' only accounted for about two thirds of patients treated. In that regard, the Panel considered that the claim was misleading and incapable of substantiation and a breach of Clauses 7.2 and 7.4 was ruled.

The Panel noted the claim 'Ilumetri significantly improves quality of life' which was referenced to the Reich *et al*. Below the claim was a schematic which appeared to show an improvement in quality of life between 0 and 12 weeks for 42% of patients. There was a plateau between 12 and 28 weeks when 52% of patients reported an improved quality of life and a further improvement between 28 and 52 weeks by which time 64% of patients had reported an improved quality of life. It appeared that the data within the schematic was taken from Thaci *et al*. It was stated in the Ilumetri SPC that at week 12 and across studies, tildrakizumab was associated with statistically significant improvement in health-related quality of life as assessed by the dermatology life quality index (DLQI). Improvements were maintained over time with at week 52, 63.7% (100mg) and 73.3% (200mg) in reSURFACE 1, and 68.8% (100mg) and 72.4% (200mg) in reSURFACE 2 of patients who were PASI 75 responders at week 28 having a DLQI of 0 or 1. The Panel thus noted that although 64% of patients reported an improvement in quality of life at 52 weeks, it was 64% of responders – not 64% of all patients treated. The Panel considered that the claim was not sufficiently complete such that readers would be able to form their own opinion of the therapeutic value of the medicine. In that regard, the Panel considered that the claim was misleading and incapable of substantiation and breaches of Clauses 7.2 and 7.4 were ruled.

The Panel noted its rulings and comments above and considered that the promotional material had failed to comply with all relevant requirements of the Code. A breach of Clause 28.1 was ruled. Almirall had failed to maintain high standards and a breach of Clause 9.1 was ruled.

The Panel noted its rulings above but did not consider that the particular circumstances in this case warranted a ruling of a breach of Clause 2 which was a sign of particular censure and reserved for such. No breach of Clause 2 was ruled.

Complaint received **17 October 2019**

Case completed **5 August 2020**