CASE AUTH/2801/11/15

VOLUNTARY ADMISSION BY JANSSEN

Outdated prescribing information

Janssen-Cilag voluntarily admitted that its Stelara (ustekinumab) advertisement published in the Annals of Rheumatic Disease (ARD), October 2015, contained outdated prescribing information.

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 Janssen.

Janssen stated that its media booking agency notified it on 5 October that the publishing group wished to apologize for its error in placing the Stelara advertisement at issue. The publishing group had over printed the Stelara bound insert advertisement commissioned for the June 2015 issue of the ARD and had, without Janssen's knowledge, inserted them into the October 2015 edition.

The Stelara advertisement in the October 2015 edition of the ARD had been prepared, approved and certified in April 2015 and contained November 2014 prescribing information. The Stelara prescribing information was updated in June 2015 with the addition of wording for the plaque psoriasis paediatric indication; dosing information in paediatrics and the availability of a 45mg vial. This information would not be relevant to the ARD rheumatology audience. Janssen confirmed that the June 2015 prescribing information contained no additional/different safety information compared with the November 2014 prescribing information, and therefore the outdated prescribing information in the advertisement at issue had not risked patient safety. Janssen asked the publishing group to confirm that future advertisement placements would be confirmed with the relevant product manager at least 5 days prior to the journal closing.

Janssen acknowledged a breach because the expired prescribing information included in the advertisement was not consistent with the summary of product characteristics (SPC) at the time of publication.

Further details from Janssen are given below.

The Panel noted Janssen's submission that the publishing group had, without Janssen's prior knowledge, inserted the Stelara bound insert commissioned for the June 2015 issue of the ARD into the October 2015 edition. This advertisement had been prepared, approved and certified in April 2015 and contained the November 2014 prescribing information. The current prescribing information was dated June 2015. The Panel noted that after submitting its voluntary admission and receiving the PMCPA's letter, Janssen found out that the publishing group had placed another insert which was prepared in March 2015, and which also contained the November 2014 prescribing information, in BMJ Clinical Research, 5 September, again without the consent or prior knowledge of Janssen or its media booking agency. The Panel noted that the April 2015 advertisement was the subject of the voluntary admission.

The Panel noted that the first side of the advertisement related to use of Stelara in the treatment of moderate-to-severe plaque psoriasis. The reverse side referred to active psoriatic arthritis and contained the November 2014 prescribing information. The Panel noted Janssen's submission that the addition of the plaque psoriasis paediatric indication would not be relevant to the ARD rheumatology audience.

The Panel noted that the Stelara prescribing information was updated in June 2015 to reflect the addition of the paediatric (12 years and over) plaque psoriasis indication and included dosing information in the paediatric population and the availability of a 45mg vial. The November 2014 prescribing information stated that Stelara was not recommended in children under 18, whereas the June 2015 prescribing information stated that it was not recommended in children under 12 years. The Panel noted Janssen's submission that the June 2015 prescribing information contained no additional/different safety information. The Panel noted that the June 2015 prescribing information side effects, stated 'studies show adverse events reported in ≥ 12 year olds with plaque psoriasis were similar to those seen in previous studies in adults with plaque psoriasis'.

The Panel noted that although Janssen had been let down by the publishing group which had admitted full responsibility for the error, it was an established principle under the Code that pharmaceutical companies were responsible for third parties even if that third party acted outside the instructions from the pharmaceutical company.

The Panel noted that whilst the first side of the advertisement promoted Stelara for use in moderate-to-severe plaque psoriasis, it was not clear whether the advertisement was restricted to the adult population or not. In the Panel's view some readers might assume that the advertisement related to all patients with moderate-to-severe plaque psoriasis who could be treated with Stelara ie anyone from the age of 12. In the Panel's view, the prescribing information should thus have also included the paediatric indication and dosage information in line with the SPC. The advertisement contained out of date prescribing information which was not in line with the SPC. The Panel ruled a breach of the Code as acknowledged by Janssen.

The Panel noted Janssen's submission that following the update of the Stelara prescribing information in June 2015, all affected materials were withdrawn within the agreed timelines. However, the telephone

briefing of the media booking agency was not followed up in writing so the briefing had not been formally documented as required by the relevant standard operating procedure. The Panel further noted that Janssen had asked the publishing group to confirm that all future advertisement placements would be confirmed with the relevant product manager 5-14 days prior to the journal closing. The Panel noted that in addition to the advertisement at issue a further advertisement also containing outdated prescribing information had been published in a different BMJ publication. The Panel considered that high standards had not been maintained and a breach of the Code was ruled as acknowledged by Janssen.

Janssen-Cilag Ltd voluntarily admitted that the October 2015 edition of the Annals of Rheumatic Disease (ARD) published a two page bound insert advertisement for Stelara (ustekinumab) (ref PHGB/STE/0415/0010) that contained outdated prescribing information.

Stelara was indicated for the treatment of moderate-to-severe plaque psoriasis in adults who failed to respond to, or who had a contraindication to, or were intolerant to other systemic therapies including ciclosporin, methotrexate (MTX) or PUVA (psoralen and ultraviolet A). Stelara was also indicated for the treatment of moderate-to-severe plaque psoriasis in adolescents from the age of 12 years who were inadequately controlled by, or were intolerant to, other systemic therapies or phototherapies. Stelara was also indicated alone or in combination with MTX for the treatment of active psoriatic arthritis in adults when the response to previous non-biological disease-modifying anti-rheumatic medicine therapy had been inadequate.

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 Janssen.

VOLUNTARY ADMISSION

Janssen stated that it received notification from its media booking agency, on 5 October that the publishing group wished to apologize for its error in placing a Stelara advertisement in the October 2015 edition of ARD. The publishing group had over printed the Stelara bound insert advertisement commissioned for the June 2015 issue of the ARD and had, without Janssen's prior knowledge, inserted them into the October 2015 edition.

The Stelara marketing team regularly communicated with the media booking agency to ensure that all published advertisements were fully copy approved, certified and complied with the Code. However, the decision by the publishing group to run the advertisement of its own volition, and without prior permission from Janssen or the booking agency, meant that there was no opportunity to discuss the particular advertisement placement.

The October 2015 edition of the ARD was distributed on 21 September 2015 including the Stelara advertisement at issue which was originally prepared, approved and certified in April 2015 and contained the November 2014 prescribing information. The Stelara prescribing information was updated in June 2015 to reflect the addition of the paediatric plaque psoriasis indication, which would not be relevant to the ARD rheumatology audience. The changes to the prescribing information included wording for the paediatric plaque psoriasis indication; dosing information in the paediatric population and the availability of a 45mg vial formulation. Janssen confirmed that the June 2015 prescribing information contained no additional/different safety information compared with the November 2014 prescribing information, and therefore the outdated prescribing information in the advertisement at issue had not risked patient safety. Janssen provided a copy of the November 2014 Stelara prescribing information and an annotated version of the June 2015 prescribing information indicating the changes. Janssen requested confirmation from the publishing group that all future advertisement placements would be confirmed with the relevant Janssen product manager 5-14 days prior to the journal closing. The Stelara marketing team and the media booking agency would also continue to communicate regularly to ensure it met the Code standards.

Janssen admitted a breach of Clause 4.1 because the expired prescribing information included in the advertisement was not consistent with the summary of product characteristics (SPC) at the time of publication. Janssen submitted that it had voluntarily contacted the PMCPA about the incident; it had not received any complaint from the ARD readership or companies. Janssen submitted that it took responsibilities under the Code very seriously and sincerely regretted the actions taken by the publishing group. Janssen registered its dissatisfaction with the publishing group which confirmed that any future advertisements would only be placed with prior agreement from Janssen.

When writing to confirm that the matter would be taken up under the Code, the Authority asked Janssen to provide any further comments it might have in relation to Clauses 4.1 and 9.1.

RESPONSE

Janssen submitted that following the June 2015 prescribing information update, the changes were confirmed with the media booking agency and Janssen provided direction to ensure that all subsequent planned advertisement placements included the updated text. In addition, following notification of the unauthorised placement of the Stelara advertisement at issue, Janssen received written confirmation from the publishing group that all future advertisement placements would be confirmed with Janssen prior to the journal closing date. Janssen provided a copy of its standard operating procedure (SOP) for the Withdrawal of Materials. The procedure was followed in principle, after the Stelara prescribing information was updated in June 2015 ie all affected materials were withdrawn within the agreed timelines. However, the briefing of

the media booking agency by teleconference was not followed up in writing, therefore there was no formal documentation of the briefing as required by the SOP. The relevant Janssen employees had since been reminded of their responsibility in ensuring that they appropriately document all evidence of withdrawal following a prescribing information update. The Stelara prescribing information was updated in June 2015 to reflect the addition of the paediatric plaque psoriasis indication. The changes to the prescribing information included:

- Wording for the paediatric plaque psoriasis indication
- Dosing information in the paediatric population and the availability of a 45mg vial.

The June 2015 prescribing information contained no additional/different safety information compared with the November 2014 prescribing information. Janssen therefore submitted that the inclusion of the outdated prescribing information in the Stelara advertisement at issue, had not risked patient safety. Janssen submitted that after receiving the PMCPA's letter, its media booking agency informed it that a double-page insert containing the November 2014 prescribing information was also placed by the publishing group in the 5 September 2015 edition of the BMJ Clinical Research (CR) journal. This was again without the consent or prior knowledge of Janssen.

Janssen submitted that it took its responsibilities under the Code very seriously and sincerely regretted its oversight in not appropriately documenting the briefing of the media booking agency and also the actions taken by the publishing group in publishing Stelara advertisements in both the ARD and the BMJ CR containing outdated prescribing information. Janssen stressed that it would not have allowed either of the advertisements to go to press had it been aware of them in advance. While Janssen maintained that the events had not risked patient safety, the failure of the relevant employees to fully document its SOP regarding the withdrawal of advertisements and its recent finding that a second advertisement was placed with outdated Stelara prescribing information, that a breach of Clause 9.1 be considered for failing to maintain its usual high standards.

Janssen submitted that it had taken further steps to look at how it could further optimise its process and training of employees to ensure that it fully document the process related to the briefing of agencies.

PANEL RULING

The Panel noted Janssen's submission that the publishing group had, without Janssen's prior knowledge, inserted the Stelara bound insert commissioned for the June 2015 issue of the ARD into the October 2015 edition. This advertisement at issue was originally prepared, approved and certified in April 2015 and contained the November 2014 prescribing information. The current prescribing information was dated June 2015. The Panel noted that after submitting its voluntary admission and receiving the PMCPA's letter, Janssen was informed by its media booking agency that another insert (ref PHGB/STE/0515/0011) which was prepared in March 2015 and also contained the November 2014 prescribing information had been published by the publishing group in BMJ Clinical Research on 5 September, again without the consent or prior knowledge of Janssen or its media booking agency. The Panel noted that the April 2015 advertisement was the subject of the voluntary admission.

The Panel noted that the first side of the advertisement related to use of Stelara in the treatment of moderate-to-severe plaque psoriasis. The reverse side referred to active psoriatic arthritis and contained the November 2014 prescribing information. The Panel noted Janssen's submission that the addition of the paediatric plaque psoriasis indication would not be relevant to the ARD rheumatology audience.

The Panel noted that the Stelara prescribing information was updated in June 2015 to reflect the addition of the paediatric (12 years and over) plaque psoriasis indication to include dosing information in paediatrics and the availability of a 45mg vial. The November 2014 prescribing information stated that Stelara was not recommended in children under 18, whereas the June 2015 prescribing information was updated to state that it was not recommended in children under 12 years. The Panel noted Janssen's submission that the June 2015 prescribing information contained no additional/different safety information. The Panel noted that the June 2015 prescribing information side effects, stated 'studies show adverse events reported in ≥ 12 year olds with plaque psoriasis were similar to those seen in previous studies in adults with plaque psoriasis'.

The Panel noted Janssen's submission that the publishing group had admitted full responsibility for the error. Whilst Janssen had been let down by the publisher, it was an established principle under the Code that pharmaceutical companies were responsible for third parties even if that third party acted outside the instructions from the pharmaceutical company.

The Panel noted that Clause 4.2 required the prescribing information to include a succinct statement of the information in the SPC relating to the dosage and method of use relevant to the indications quoted in the advertisement and, where not otherwise obvious, the route of administration. The supplementary information to Clause 4.1 required that the prescribing information be consistent with the SPC for the medicine.

The Panel noted that whilst the first side of the advertisement promoted Stelara for moderate-to-severe plaque psoriasis, it was not clear whether the advertisement was restricted to the adult population or not. In the Panel's view some readers might assume that the advertisement related to the entire patient population for whom the product was indicated for the treatment of moderate-to-severe plaque psoriasis ie both adults and adolescents from the age of 12. In the Panel's view, the prescribing information should thus have also included the

paediatric indication and dosage information in line with the SPC. The advertisement contained out of date prescribing information which was not in line with the SPC. The Panel ruled a breach of Clause 4.1 as acknowledged by Janssen.

The Panel noted Janssen's submission that following the update of the Stelara prescribing information in June 2015, all affected materials were withdrawn within the agreed timelines. However, the briefing of the media booking agency by teleconference was not followed up in writing so there was no formal documentation of the briefing, as required by the relevant SOP. The Panel further noted that Janssen had requested confirmation from the publishing group that all future advertisement placements would be confirmed with the relevant Janssen product manager 5-14 days prior to the journal closing. The Panel noted that in addition to the advertisement at issue a further advertisement also containing outdated prescribing information had been published in a different BMJ publication. The Panel considered that high standards had not been maintained and a breach of Clause 9.1 was ruled as acknowledged by Janssen.

Complaint received **3 November 2015**

Case completed **21 December 2016**