CASE AUTH/3106/10/18

VOLUNTARY ADMISSION BY JANSSEN

Use of out-of-date prescribing information

Janssen-Cilag Limited voluntarily admitted that an advertisement for Zytiga (abiraterone) (ref PHGB/ZYT/0716/0009(1)) had been published on two occasions with out-of-date prescribing information. Zytiga was indicated for the treatment of certain adult men with metastatic prostate cancer.

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Janssen stated that it had recently identified that a Zytiga advertisement which bore a superseded version of the prescribing information (November 2016) had been mistakenly placed in the September 2018 issue of The Journal of Clinical Oncology, Volume 30, Issue 9.

The prescribing information had been updated twice since November 2016, once in September 2017 and again in November 2017. The prescribing information for Zytiga dated November 2017 was the current version that should have been included in the advertisement.

The same advertisement was re-run in the October 2018 issue of the same journal without prior knowledge or authorisation of Janssen or its media buying agent. The publisher had taken it upon itself to repeat the advertisement.

The response from Janssen is given below.

The Panel noted that Janssen had informed its media buyer on 4 September 2017 that the Zytiga prescribing information had been updated and all advertisements bearing the November 2016 prescribing information should be withdrawn and destroyed. In the same email Janssen included the updated prescribing information dated September 2017. The advertisement in question (ref PHGB/ZYT/0716/0009(1)) fell within the scope of this instruction. Janssen received confirmation of deletion of materials from the media buyer on 11 September 2017 and confirmation that it had requested that its publishing partners do the same. The journal publisher confirmed to the media buyer on 13 September that it had deleted the copy from its systems.

The Panel noted that on 22 November Janssen issued another withdrawal and destruction notification to the media buyer relating to all materials containing the September 2017 prescribing information and included a copy of the updated Zytiga prescribing information dated November 2017, which continued to be current. The Panel noted Janssen's submission that there were no print advertisements in circulation at that time, so no formal destruction notice was required. The media buyer acknowledged the instruction by confirming Janssen's approach to managing the links to the prescribing information from digital assets.

The Panel noted that on 31 July 2018, the journal publisher requested confirmation from the media buyer as to the correct advertisement for print and attached the withdrawn advertisement (ref PHGB/ZYT/0716/0009(1)) to the email. Despite the media buyer checking with Janssen which advertisement was to be used and receiving confirmation of the correct one, the media buyer responded to the publisher and approved the incorrect advertisement. The withdrawn advertisement (ref PHGB/ZYT/0716/0009(1) bearing the out-of-date prescribing information was therefore published in the September 2018 issue of The Journal of Clinical Oncology.

The Panel noted that Janssen was also told on 26 September 2018 that the publisher decided independently of Janssen and the media buyer to run the same non-compliant advertisement in the October 2018 issue of the same journal. The publisher acknowledged its failure to locate and destroy copies of the withdrawn advertisement and confirmed that it had decided, independently, to run the advertisement in October.

The Panel noted that whilst Janssen had been let down by its media buyer and 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 advertisement published in the September 2018 issue of The Journal of Clinical Oncology 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 that the publisher had decided independently to re-run the advertisement in the October 2018 issue of The Journal of Clinical Oncology. The Panel noted that whilst Janssen had been let down by its 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 therefore ruled a breach of the Code as the advertisement containing out of date prescribing information was also published in the October issue.

Janssen-Cilag Limited voluntarily admitted that an advertisement for Zytiga (abiraterone) (ref PHGB/ZYT/0716/0009(1)) had been published on two

occasions with out-of-date prescribing information. Zytiga was indicated for the treatment of certain adult men with metastatic prostate cancer.

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 had recently identified that a Zytiga advertisement which bore a superseded version of the prescribing information (November 2016) had been mistakenly placed in the September 2018 issue of The Journal of Clinical Oncology, Volume 30, Issue 9.

The prescribing information had been updated twice since November 2016, once in September 2017 and again in November 2017. The prescribing information for Zytiga dated November 2017 was the current version that should have been included in the advertisement.

The same advertisement was re-run in the October 2018 issue of the same journal without prior knowledge or authorisation of Janssen or its media buying agent. The publisher had taken it upon itself to repeat the advertisement.

Janssen submitted that it had investigated the circumstances that led to the incident and it provided a summary of the sequence of events. An email trail between Janssen, its media buyer and the publisher of the journal, was provided.

Janssen stated that it informed its media buyer on 4 September 2017 that the Zytiga prescribing information had been updated and all advertisements bearing the November 2016 prescribing information should be withdrawn and destroyed. In the same email Janssen included the updated prescribing information dated September 2017. The advertisement in question (ref PHGB/ZYT/0716/0009(1)) fell within the scope of this instruction. Janssen received confirmation of destruction from the media buyer on 11 September 2017.

The journal publisher confirmed to the media buyer on 13 September that it had deleted the copy from its systems.

On 22 November 2017 Janssen issued another withdrawal and destruction notification to the media buyer relating to all materials containing the September 2017 prescribing information and included a copy of the updated Zytiga prescribing information dated November 2017, which continued to be current. Janssen submitted that there were no print advertisements in circulation at that time, so no formal destruction notice was required. The media buyer acknowledged the instruction by confirming Janssen's approach to managing the links to the prescribing information from digital assets.

At that time Janssen believed that all artwork and copies of previous print advertisements which bore either the November 2016 or the September 2017 prescribing information had been destroyed in line with previous instructions.

On 31 July 2018, the journal publisher requested confirmation from the media buyer as to the correct advertisement for print and attached the withdrawn advertisement (ref PHGB/ZYT/0716/0009(1)) to the email.

Despite the media buyer checking with Janssen which advertisement was to be used and receiving confirmation of the correct one, the media buyer responded to the publisher and approved the incorrect advertisement, the withdrawn advertisement (ref PHGB/ZYT/0716/0009(1). Janssen stated that it was not party to the communication chain between the media buyer and the publisher.

Because of the media buyer's error, the publisher printed the incorrect Zytiga advertisement bearing the out-of-date prescribing information in the September 2018 issue of The Journal of Clinical Oncology. Janssen became aware of this mistake when file copies of the journal were received from the media buyer in late September. This triggered the internal investigation and a decision to self-report.

Janssen was also told on 26 September 2018 that the publisher decided independently of Janssen and the media buyer to run the same non-compliant advertisement in the October 2018 issue of the same journal. At that time, it was too late to halt production as the issue had already been despatched to recipients.

Janssen asked the publisher to clarify why it had printed an incorrect advertisement in the September issue and to confirm that neither Janssen nor the media buyer instructed any advertisement to be placed in the October edition. In an email of 3 October, the publisher acknowledged its failure to locate and destroy all copies of the withdrawn advertisement and confirmed that it had decided, independently, to run the advertisement in October.

Janssen stated that the main changes compared with the incorrectly published November 2016 prescribing information included:

- September 2017 prescribing information
  - Removal of the availability of a 250mg tablet and any information relating to its presentation, pack size and NHS cost.
  - Addition of allergic alveolitis to the list of 'other side-effects'.

- November 2017 prescribing information
  - Addition of an indication for adult men with newly diagnosed high risk metastatic hormone sensitive prostate cancer in combination with androgen deprivation therapy (ADT).
  - Additional clarification of the steroid dose to be used with the new indication.
  - Reclassification of abnormalities of liver function test from common to very common.
  - Addition of 'other arrhythmias' to the list of 'other side-effects'.

Janssen did not consider that the failure to provide the most current prescribing information had any significant implications for patient safety. The prescribing information stated that the summary of product characteristics (SPC) needed to be referred to before prescribing. Allergic alveolitis was rare and 'other arrhythmias' was listed in the SPC as uncommon. With regard to the common potential for abnormal liver function tests, prescribers were already very informed of this given the longstanding requirement to monitor liver function upon initiation of treatment and regularly thereafter.

In conclusion, Janssen stated that it had acted in good faith to comply with the requirements of the Code but was let down by its agents. Nevertheless, Janssen accepted its accountability for complying with the letter and spirit of the Code even where that extended to the actions of its agents. As such, it acknowledged a failure to provide up-to-date prescribing information and thus a breach of Clause 4.1 relating to the publication of the advertisement in the September 2018 issue of the Journal of Clinical Oncology.

Janssen did not consider that it should be held accountable for the second advertisement placed in the October 2018 issue of the Journal of Clinical Oncology given this was done without any knowledge or instruction from Janssen or its media buyer.

Janssen stated that it would review its relationship and ways of working with all its media buying agents to reduce the likelihood of a recurrence of a similar breach of the Code.

In considering this matter, the Authority asked Janssen to consider the requirements of Clause 4.1 as cited by the company.

RESPONSE

Janssen stated that it had no further comments.

PANEL RULING

The Panel noted that Janssen had informed its media buyer on 4 September 2017 that the Zytiga prescribing information had been updated and all advertisements bearing the November 2016 prescribing information should be withdrawn and destroyed. In the same email Janssen included the updated prescribing information dated September 2017. The advertisement in question (ref PHGB/ZYT/0716/0009(1)) fell within the scope of this instruction. Janssen received confirmation of deletion of materials from the media buyer on 11 September 2017 and confirmation that it had requested that's its publishing partners do the same. The journal publisher confirmed to the media buyer on 13 September that it had deleted the copy from its systems.

The Panel noted that the updated September 2017 prescribing information included the removal of the availability of a 250mg tablet and any information relating to its presentation, pack size and NHS cost and the addition of allergic alveolitis to the list of 'other side-effects'.

The Panel noted that on 22 November Janssen issued another withdrawal and destruction notification to the media buyer relating to all materials containing the September 2017 prescribing information and included a copy of the updated Zytiga prescribing information dated November 2017, which continued to be current. The Panel noted Janssen's submission that there were no print advertisements in circulation at that time, so no formal destruction notice was required. The media buyer acknowledged the instruction by confirming Janssen's approach to managing the links to the prescribing information from digital assets.

The updated November 2017 prescribing information included addition of an indication for adult men with newly diagnosed high risk metastatic hormone sensitive prostate cancer in combination with androgen deprivation therapy (ADT); additional clarification of the steroid dose to be used with the new indication; reclassification of abnormalities of liver function test from common to very common; and addition of 'other arrhythmias' to the list of 'other side-effects'.

The Panel noted that on 31 July 2018, the journal publisher requested confirmation from the media buyer as to the correct advertisement for print and attached the withdrawn advertisement (ref PHGB/ZYT/0716/0009(1)) to the email. Despite the media buyer checking with Janssen which advertisement was to be used and receiving confirmation of the correct one, the media buyer responded to the publisher and approved the incorrect advertisement. The withdrawn advertisement (ref PHGB/ZYT/0716/0009(1) bearing the out-of-date prescribing information was therefore published in the September 2018 issue of The Journal of Clinical Oncology.

The Panel noted that Janssen was also told on 26 September 2018 that the publisher decided independently of Janssen and the media buyer to run the same non-compliant advertisement in the October 2018 issue of the same journal. The publisher acknowledged its failure to locate and destroy copies of the withdrawn advertisement and confirmed that it had decided, independently, to run the advertisement in October.

The Panel noted that whilst Janssen had been let down by its media buyer and 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 advertisement published in the September 2018 issue of The Journal of Clinical Oncology 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 that the publisher had decided independently to re-run the advertisement in

the October 2018 issue of The Journal of Clinical Oncology. The Panel noted that whilst Janssen had been let down by its 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 therefore ruled a breach of Clause 4.1 as the advertisement containing out of date prescribing information was also published in the October issue.

During the consideration of this case, the Panel was concerned to note Janssen's submission that it did not consider that its failure to provide the current prescribing information had any significant implications for patient safety. The Panel noted the changes included the addition and re-classification of side-effects which, in the Panel's view, failure to include could have potential patient safety implications. The Panel requested that Janssen be advised of its concerns.

Voluntary admission received **24 October 2018**

Case completed **28 January 2019**