CASE AUTH/2698/1/14

VOLUNTARY ADMISSION BY ASTELLAS

Declaration of sponsorship

Astellas Pharma voluntarily admitted that there was an error in the declaration of sponsorship on the front cover of a promotional item linked to the recent launch of Vesomni (tamsulosin HCl, solifenacin succinate). 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 Astellas.

Astellas explained that the Lower Urinary Tract Symptoms (LUTS) Consensus Statement was certified and the instruction to print given before comments in relation to pre-vetting had been received from the Medicines and Healthcare Products Regulatory Agency (MHRA). The MHRA subsequently requested that the acknowledgement of Astellas' involvement on the front page be expanded to explain that Astellas had been fully involved with the initiation, meeting organisation and author nomination for the consensus statement. Astellas tried to recall the item but it had already been distributed with the BMJ. Astellas submitted that it had not maintained high standards and acknowledged breaches of the Code.

The detailed response from Astellas is given below.

The Panel noted Astellas' submission that the MHRA requested that the declaration of sponsorship on the front page 'This edition is funded and has been checked for factual accuracy by Astellas Pharma Ltd' be changed to explain that Astellas had been fully involved with the initiation, meeting organisation and author nomination for the consensus statement. The Panel also noted the acknowledgements section on page 7 of the consensus statement read 'The consensus group meeting was organised and funded by Astellas Pharma Ltd. Editorial support was provided by a named communications agency and the final content was reviewed by Astellas Pharma Ltd'. The Panel was unsure of the role of the communications agency given the final statement on page 1 of the document was 'Medicine matters strives to bring you topical opinion from all clinical specialities. We also want to know what subjects matter to you. Email us at the [given communication agency's email address] with your suggestions'.

The Panel noted the Code required that care be taken with company sponsored reports of meetings and the like to ensure that they were not disguised promotion and that the declaration of sponsorship be sufficiently prominent to ensure that readers were aware of it at the outset. The wording of the declaration must be unambiguous so that readers would immediately understand the extent of the company's involvement and influence over the material. This was particularly important when companies were involved in the production of material which was circulated by an otherwise wholly independent party such as supplements to health journals'. In that regard the Panel noted that the item had been distributed as a supplement with the BMJ.

The Panel considered that the design of the front cover was such that the reader's eye was caught by the title, 'Medicine matters', the heading 'Optimal management of lower urinary tract symptoms (LUTS) in primary care: a consensus statement' and the subheading 'Consensus group members'. The declaration of sponsorship at the bottom of the left hand column on a light blue background was less prominent.

The fact that the consensus statement resulted from a meeting of eight health professionals that was organised and entirely funded by Astellas was not immediately clear at the outset. The Panel considered that the initial impression was that the 'consensus' was reached by an independent clinical authority, rather than an Astellas advisory board. The reference to prescribing information in small type font at the bottom of the front cover was not sufficiently prominent to dispel the initial impression. In the Panel's view the initial impression was compounded by the declaration of sponsorship in the bottom left hand column that 'This edition is funded and has been checked for factual accuracy by Astellas Pharma Ltd'; it implied that the consensus statement was independently produced material and that was not so. This was misleading and in the Panel's view amounted to disguised promotion. A breach of the Code was ruled.

The Panel considered that the declaration of sponsorship was misleading; it did not provide an unambiguous account of Astellas' involvement and misleadingly implied that the company had only funded a consensus statement written by a group of independent clinicians. A breach of the Code was ruled.

The Panel noted its comments above. In addition the Panel was extremely concerned that the material was certified and instruction given to print before the MHRA had provided its comments as part of the pre-vetting process. This was unacceptable. High standards had not been maintained and a breach of the Code was ruled as acknowledged by Astellas.

Astellas voluntarily admitted that there was an error in the declaration of sponsorship on the front cover of a promotional item, the Lower Urinary Tract Symptoms (LUTS) Consensus Statement. The item had already been the subject of a complaint from the Medicines and Healthcare Products Regulatory Agency (MHRA) which had requested that Astellas

print a corrective statement outlining its full involvement.

Astellas' product Vesomni (tamsulosin HCl, solifenacin succinate) was indicated for the treatment of moderate to severe storage symptoms and voiding symptoms associated with benign prostatic hyperplasia (BPH) in men who were not adequately responding to monotherapy.

The front page of the consensus statement bore the title 'Medicine matters' above the prominent heading 'Optimal management of lower urinary tract symptoms (LUTS) in primary care: a consensus statement'. Immediately beneath this was the subheading 'Consensus group members' in a highlighted dark blue box, followed by a list of clinicians who were consensus group members. The declaration of sponsorship appeared at the bottom of the left hand column and read 'This edition is funded and has been checked for factual accuracy by Astellas Pharma Ltd'. The statement 'Prescribing information for Betmiga (mirabegron) and Vesomni (solifenacin 6mg/tamsulosin 0.4mg) can be found on page 8 of this publication' appeared as a footnote to page 1. The acknowledgements on page 7 stated 'The consensus group meeting was organised and funded by Astellas Pharma Ltd. Editorial support was provided by a named communications agency and the final content was reviewed by Astellas Pharma Ltd'. Prescribing information for Vesomni and Betmiga appeared on the final page.

COMPLAINT

Astellas submitted that a cessation of vetting notice was issued to Astellas on 2 December 2013 with one outstanding item required for submission to the MHRA, the Lower Urinary Tract Symptoms (LUTS) Consensus Statement, which was submitted on 17 January 2014. Due to human error the item was certified on 13 January 2014 and the instruction to print the item given before any comments had been received from the MHRA. The MHRA had no objections to the actual consensus statement but in comments received on 22 January it requested that the acknowledgement of Astellas' involvement statement on the front page be expanded to explain that Astellas had been fully involved with the initiation, meeting organisation and author nomination for the consensus statement and not just an arm's length agreement which could have been inferred from the printed acknowledgement.

Until then Astellas had an excellent record with pre-vetting and no item had previously been certified before final comments had been received from the MHRA. However, on this occasion, perhaps due to the long gap between receiving the cessation notice and the item being ready for final approval with a holiday period in between, there was a breakdown in communication and a misunderstanding arose that the item was to be sent to the MHRA for reference purposes only (as sometimes is genuinely the case with cessation of vetting notices). However, the cessation of vetting notice clearly stated that the MHRA wished to see the consensus statement before it could be used.

Astellas tried to recall the item on 22 January but it had already been distributed with the BMJ and could not be recalled. Astellas had agreed to enclose a corrective statement with the BMJ on Saturday, 8 February in the form of a letter which had been agreed with the MHRA. Astellas would also individually contact anyone who had been handed a copy of the consensus statement and give them a copy of the corrective statement. The item was last used on 27 January. In addition, Astellas was reviewing its processes to ensure that this could not happen again and the individuals concerned had received additional training.

Astellas acknowledged a breach of Clauses 12.1 (disguised promotion) and 9.1 as clearly it had not maintained high standards in this case.

Astellas was asked to respond in relation to Clauses 9.1 and 9.10 of the 2014 Code.

RESPONSE

Astellas submitted that although Vesomni was not a black triangle product, Astellas was mindful of the possibility that a new combination product might be subject to pre-vetting and made contact with the MHRA in April 2013. The initial response was that the MHRA was not minded to vet advertising for Vesomni but might review the product in the future to consider whether vetting would be required. As the granting of a marketing authorization approached, Astellas sent a further email to the MHRA and it received a vetting invitation letter one week later.

Astellas had previously completed MHRA pre-vetting exercises for three newly launched products, Dificlir, Betmiga and Xtandi, during which a best working practice was established. Astellas provided copies of two separate presentations which had been developed and used by the medical information team and the Vesomni Brand team outlining the pre-vetting process and requirements. However, a formal standard operating procedure (SOP) had not been written or implemented describing this process.

Materials which were subject to MHRA pre-vetting review were usually handled by Astellas in the following way:

Medical information was the primary contact with the MHRA for the pre-vetting of materials. All correspondence was sent via the relevant medical information scientist covering the product within the department who also submitted materials for review. The progression of those submissions was documented on the materials tracking spreadsheet which was similarly maintained by the medical information scientist.

It was acknowledged that the MHRA expected that the material submitted for review should have undergone a full set of internal quality control and compliance checks and sign-off. Therefore, there had been an understanding that materials submitted to the MHRA for pre-vetting were required to have

reached the pre-certification stage. Materials were then sent by email to the MHRA assessor along with supporting references and a covering letter describing the purpose of the item. Once a response was received from the MHRA, it was circulated to the review team (marketing manager, product manager, medical adviser, medical information scientist) and further action undertaken incorporating any comments received.

This process was followed for all other materials that were submitted for Vesomni and resulted in a swift conclusion of MHRA pre-vetting. Astellas received a cessation of vetting letter dated 2 December 2013, with the stipulation that the output of the consensus group meeting would be submitted to the MHRA when available. A copy of this letter was circulated via email to the Vesomni review team. The piece was submitted to the MHRA on 17 January 2014. Due to human error, the item was certified on 13 January and the instruction to print the item given before the final piece was submitted to the MHRA and any subsequent comments received.

Astellas had until then an excellent record with pre-vetting and no item had previously been certified before final comments had been received from MHRA. Unfortunately, there was no mechanism in existence for retaining the material that was subject to MHRA pre-vetting within the electronic approval system whilst awaiting final comments and the release of the certified material was reliant upon human recall/tracking of the progress of these individual materials.

Clause 9.1

Astellas was committed to adhering to the MHRA pre-vetting process and had ensured implementation of all MHRA recommendations for all other materials associated with this product and for a number of other products which had previously been through the pre-vetting process. Astellas was aware of the possibility of pre-vetting early on and actively sought advice on this matter from the MHRA.

Once the error was identified, immediate remedial action was taken by Astellas. The MHRA was notified and agreed to the issue of the corrective statement in a letter circulated with the BMJ on 8 February. The MHRA also agreed with the actions proposed by Astellas to ensure the error was not repeated. Astellas self-reported the case to the PMCPA on the same day that agreement was reached with the MHRA.

Astellas acknowledged that the pre-vetting process should have been documented in a formal standard operating procedure (SOP). Its existing copy approval SOP would be updated to emphasise the importance of this process and a pre-vetting SOP was currently being formulated.

Astellas submitted that it took immediate action to further retrain the individuals directly involved and would also highlight the importance of the MHRA vetting process and the requirement to quarantine materials undergoing review by the MHRA in its next compliance training update meeting to all brand teams.

Astellas engaged Zinc Ahead to create an additional process stamp, 'Pending MHRA Approval', which would be uploaded (electronically) onto the original piece of material subject for review by the originator. This stamp was configured to electronically prevent those materials bearing the stamp to be uploaded to the certification stage of approval. Materials could only progress to certification once external written authority was received from the MHRA. This written authority must be scanned and added to the piece and a request made to the compliance manager or medical director via the Zinc helpdesk. The purpose was to reduce issues arising from human error or misunderstanding and informed all reviewers that the piece was currently under MHRA pre-vetting scrutiny.

The material tracking spreadsheet would be hosted on an internal shared drive enabling access for all members of the review team to check progression of the materials subject to pre-vetting.
Within the current copy approval process, medical information would also now be involved in an additional review cycle for MHRA pre-vetting materials.

Astellas submitted that it had remained committed to maintaining high standards throughout all of the steps and actions detailed above but acknowledged that this unfortunate incident may have, regrettably, resulted in a failure to demonstrate that.

Clause 9.10

Astellas reassured the Panel that this item was developed entirely in good faith following the format of the 'Medicine Matters' template. Many previously published supplements in this series, sponsored by other companies, had used a similar declaration where their level of support and involvement had been comparable. There was no intention to mislead the readership as to the involvement of Astellas in the development of the document, and despite the additional disclosure of the nature and extent of its involvement in the acknowledgements section at the end of the material, Astellas recognised that the wording of the declaration on the front cover, which it believed to have been 'sufficiently prominent to ensure that readers of sponsored material were aware of it at the outset', may not have been sufficiently 'unambiguous such that the readers would have immediately understood the extent of the company's involvement and influence over the material'.

Clause 12.1

In response to a request by the Panel for comment on Clause 12.1, Astellas submitted that Clause 12.1 simply stated that 'Promotional material and activities must not be disguised'. The supplementary information went on to state that 'promotional material in journals must not resemble independent

editorial matter'. In a recent case (AUTH/2610/6/13) the company was found in breach of Clause 12.1 by having promotional material closely resembling the main journal house style and in another recent case (AUTH/2622/7/13) a representative's email was not explicit enough about the nature of an invitation to a promotional webcast and there was no prescribing information attached to the email. Astellas had a clear declaration of funding on the front cover of the LUTS consensus statement (albeit not as complete as it would have wished), an acknowledgement at the end of the article which also mentioned funding the actual meeting where the consensus statement was agreed and there was prescribing information on the last page indicating that this was clearly a promotional piece. Astellas submitted that there was certainly no attempt to disguise the consensus statement and make it appear as anything other than a promotional item. Astellas submitted that it was also worth noting that the MHRA found the consensus statement to be balanced as it had no issues with the content, just the declaration on the front cover. It was therefore hard to know if a breach of Clause 12.1 did occur on this narrow point of interpretation of the word 'disguise'. Astellas however as previously stated accepted that on this occasion high standards had not been maintained and acknowledged a breach of Clause 9.1.

PANEL RULING

The Panel noted that Astellas and the case preparation manager referred to a number of clauses of the 2014 Code. This came into operation on 1 January 2014 with a transition period for newly introduced requirements. The clauses cited, 9.1, 9.10 and 12.1, were the same in the 2014 and Second 2012 Edition (amended) Codes, thus the Panel used the 2014 Code.

The Panel noted Astellas' submission that the MHRA requested that the declaration of sponsorship on the front page 'This edition is funded and has been checked for factual accuracy by Astellas Pharma Ltd' be changed to explain that Astellas had been fully involved with the initiation, meeting organisation and author nomination for the consensus statement. The Panel also noted the acknowledgements section on page 7 of the consensus statement read 'The consensus group meeting was organised and funded by Astellas Pharma Ltd. Editorial support was provided by a named communications agency and the final content was reviewed by Astellas Pharma Ltd'. The Panel was unsure of the role of the named communications agency given the final statement on page 1 of the document was 'Medicine matters strives to bring you topical opinion from all clinical specialities. We also want to know what subjects matter to you. Email us at [the given communication agency's email address] with your suggestions'.

The Panel noted the supplementary information to Clause 12.1 Disguised Promotional Material stated, *inter alia*, that 'Care must be taken with company sponsored reports of meetings and the like to ensure that they are not disguised promotion. Sponsorship must be declared in accordance with Clause 9.10'. The supplementary information to Clause 9.10, Declaration of Sponsorship stated that 'the declaration of sponsorship must be sufficiently prominent to ensure that readers are aware of it at the outset. The wording of the declaration must be unambiguous so that readers will immediately understand the extent of the company's involvement and influence over the material. This is particularly important when companies are involved in the production of material which is circulated by an otherwise wholly independent party such as supplements to health journals'. In this regard the Panel noted that the item had been distributed as a supplement with the BMJ.

The Panel considered that the design of the front cover was such that the reader's eye was caught by the title, 'Medicine matters', the heading 'Optimal management of lower urinary tract symptoms (LUTS) in primary care: a consensus statement' and the subheading 'Consensus group members'. The declaration of sponsorship at the bottom of the left hand column on a light blue background was less prominent.

The fact that the consensus statement resulted from a meeting of eight health professionals that was organised and entirely funded by Astellas was not immediately clear at the outset. The Panel considered that the initial impression created by the heading and the overall design of the page was that the 'consensus' was reached by an independent clinical authority, rather than an Astellas advisory board. The reference to prescribing information in small type font at the bottom of the front cover was not sufficiently prominent to dispel the initial impression. In the Panel's view the initial impression was compounded by the declaration of sponsorship in the bottom left hand column that 'This edition is funded and has been checked for factual accuracy by Astellas Pharma Ltd'; it implied that the consensus statement was independently produced material and that was not so. This was misleading and in the Panel's view amounted to disguised promotion. A breach of Clause 12.1 was ruled.

The Panel considered that the declaration of sponsorship was misleading; it did not provide an unambiguous account of Astellas' involvement and misleadingly implied that the company had only funded a consensus statement written by a group of independent clinicians. A breach of Clause 9.10 was ruled.

The Panel noted its comments above. In addition the Panel was extremely concerned that the material was certified and instruction given to print before the MHRA had provided its comments as part of the pre-vetting process. This was unacceptable. High standards had not been maintained and a breach of Clause 9.1 was ruled as acknowledged by Astellas.

During its consideration of this case the Panel noted Astellas' submission that the MHRA had 'no objection to the actual consensus statement …'. The Panel noted that this was not so. The MHRA stated in a letter dated 22 January that it had not

carried out a detailed review of the consensus statement itself but would not object in principle to this material. The accuracy of the statistics, disease and background information were Astellas' responsibility. The Panel considered that the company's submission on this point was misleading and not a fair reflection of the MHRA's position as stated in its letter dated 22 January. It was essential that the Authority was able to rely on the accuracy of a company's submission. The Panel requested that the company be advised of its views.

Complaint received **30 January 2014**

Case completed **16 April 2014**
