CONSULTANT ONCOLOGIST AND A PHARMACIST v LILLY

Oncology handbook

In Case AUTH/2849/6/16 a consultant oncologist and a pharmacist, raised a new matter when asked for further information about their original complaint about the 8th edition of the Handbook of Systemic Treatments for Cancer produced by Eli Lilly & Company. The complainants were advised that the new matter could only be considered if it were the subject of a fresh complaint. The complainants subsequently submitted the present complaint.

The complainants were concerned that the handbook was not up-to-date in relation to newly licensed medicines for the treatment of the cancers referred to in the handbook. For example the omission of, *inter alia*, nivolumab (lung cancer) and ramucirumab (gastric cancer) was misleading and unbalanced and did not therefore reflect the purpose of the handbook, as an authoritative reference text which provided relevant, accurate and up-to-date information on the treatment of various cancers.

The detailed response from Lilly is given below.

The Panel noted that the 8th Edition of the handbook had been withdrawn prior to completion of Case AUTH/2849/6/16.

Turning to this case, the Panel noted that the date of preparation of the handbook, February 2014, was stated on the bottom right hand corner of the even numbered pages. The Panel also noted the disclaimer that the publisher had tried to ensure that the information was accurate and up-to-date at the time of publication and the reference to the need to check the summary of product characteristics (SPC). The disclaimer further reminded the user that the handbook was not a substitute for each product's SPC and went on to provide the user with a link to the electronic medicines compendium. A list of monographs appearing in the handbook was included.

The Panel noted Lilly's submissions regarding the decision to compare cancer agents included in the 7th Edition with those whose launch had been notified to MIMS by the end of November 2013 and that ramucirumab and nivolumab were not approved for use in the UK until 10 and 14 months after that date respectively.

The handbook was clear regarding the date of publication. The intended audience would be aware that it was likely that new medicines would be approved after the publication date.

The Panel did not consider that the omission of ramucirumab and nivolumab from the 8th Edition of the handbook, published months before either were approved, was misleading or unbalanced as alleged. The company had not failed to maintain high standards. The Panel therefore ruled no breaches of the Code including no breach of Clause 2.

In Case AUTH/2849/6/16 the complainants, a consultant oncologist and a pharmacist, raised a new matter when asked for further information about their original complaint which concerned the 8th edition of the Handbook of Systemic Treatments for Cancer 2014 (ref UKONC00326) produced by Eli Lilly & Company Limited. The complainants were advised that the new matter could only be considered if it were the subject of a fresh complaint. The complainants subsequently submitted the present complaint.

In Case AUTH/2849/6/16, the handbook was ruled in breach of Clauses 2, 7.2, 7.4 and 9.1 of the Code as the inclusion of an error, which listed the intramuscular dose of Vitamin B_{12} at 1g instead of 1mg when used before and during treatment with Lilly's Alimta (pemetrexed), meant that the information in the handbook was inaccurate, misleading and not capable of substantiation and high standards had not been maintained. The error reduced confidence in the pharmaceutical industry.

COMPLAINT

The complainants stated that they ceased using the handbook in their hospital unit because they were concerned that it was not up-to-date in relation to other newly licensed medicines available for the treatment of the cancers referred to in the handbook whilst it was being promoted by Eli Lilly. For example, the omission of, *inter alia*, nivolumab (lung cancer) and ramucirumab (gastric cancer) was misleading and unbalanced and did not therefore reflect the purpose of the handbook, as an authoritative reference text which provided relevant, accurate and up-to-date information on the medical treatment of various cancers. The complainants noted that in its response Lilly stated 'The handbook was conceived and published by Lilly to assist health professionals in their day-to-day patient management by providing concise information as guidelines for the administration of medicines commonly used for the treatment of cancer'. To achieve the latter objective would have necessitated inclusion of information pertaining to all cancer medicines that were licensed in the UK whilst the handbook was being 'widely distributed' and promoted by Lilly; this was evidently not the case.

When writing to Lilly, the Authority asked it to consider the requirements of Clauses 2, 7.2 and 9.1.

RESPONSE

Lilly stated that the handbook was a non-promotional educational item as stated on the back. It accepted full responsibility for the handbook and all previous editions.

Lilly submitted that the 8th Edition was published in February 2014, two years after the publication

of the 7th Edition. Lilly had worked with a named hospital to publish the first edition around 20 years earlier. Since then each subsequent edition of the handbook had been produced in consultation with key pharmacy staff at that hospital.

The handbook was conceived and published by Lilly to assist health professionals in their day-to-day patient management by providing concise information and guidelines for the administration of commonly used medicines for the treatment of cancer. Subsequent editions included new anticancer agents as these came to market. In the 7th edition, additional information to support the care of cancer patients was added, including the 'Oncology/ Haematology Helpline Triage Tool' developed by the UK Oncology Nursing Society and endorsed by MacMillan Cancer Support. This information was also included in the 8th Edition.

The handbook was widely distributed by Lilly to cancer-treating institutions in the NHS, with chemotherapy nurses and cancer nurse specialists were the primary users. Consistent feedback confirmed that the handbook in its various editions over the years was a well-regarded and valued resource among health professionals.

As the complexity of information included in the handbook increased, Lilly decided to outsource its production to a third party while maintaining the close association with key pharmacy staff at the hospital. Two of the three authors of the 8th Edition were from the hospital.

Lilly submitted that the publication date was clearly stated on every even page of the handbook, and the disclaimer, which appeared prominently on page 3, stated that the publisher had tried to ensure that the information contained in the handbook was accurate and up-to-date at the date of publication. The disclaimer also stated clearly in bold and underlined text that it was the user's responsibility to ensure that they checked for any variation in the product summary of product characteristics (SPC). The disclaimer further reminded the user that the handbook was not a substitute for each product SPC and went on to provide the user with a link to the electronic medicines compendium (eMC).

The editorial decision taken by the third party when compiling the 8th Edition was to compare those cancer drugs included in the 7th Edition with those whose launch had been notified to MIMS by the end of November 2013. It stood to reason that only medicines approved at that date were included; ramucirumab and nivolumab were not approved for use in the UK until December 2014 and April 2016 respectively. Lilly understood from users of the handbook over the last 20 years; that this was fully understood. Had there been a 9th Edition then any newly licensed anti-cancer agents would have been included.

Lilly referred to the text of the disclaimer:

> 'Welcome to the 8th edition of the Lilly Handbook of Systemic Treatments for Cancer (2014).
>
> The intent of this handbook is to assist healthcare professionals in their day-to-day patient management by providing concise information and guidelines for the administration of commonly used pharmacological agents for the treatment of cancer.
>
> The contents of this handbook have been developed collaboratively by nurse and pharmacist teams at [named hospital and named authors], on behalf of Eli Lilly and Company Ltd ("Lilly") and the publisher, [named].
>
> Lilly's role, as the sponsor of this handbook, has been limited to checking the factual accuracy of information on Lilly products and ensuring compliance with the PMCPA Code of Practice for the Pharmaceutical Industry.
>
> Save for the above, and the compilation of the 'Appendices' section, the updated contents of the handbook have been developed independently by the authors in collaboration with the publisher.
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> The monographs in this handbook were compiled from manufacturers' summaries of product characteristics (SPCs) and other established resources. Some of the information presented may reflect local practice and the clinical expertise of the healthcare professionals involved.
>
> The monographs of the products contained herein are not intended to be a substitute for the manufacturers' SPCs. Only adverse events deemed to be of particular relevance are included. The publisher has tried to ensure that the information contained in this handbook is accurate and up-to-date at the time of publication. It is the user's responsibility to check for any variation in the product SPC subsequently. These can be found at www.medicines.org.uk/emc. It is important not to use copies of the handbook that are out of date or pass on old editions.
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> The practice guidance presented in this handbook is offered as recommendations, and does not diminish the requirement for clinical judgment. Readers are strongly advised to check these recommendations against their local protocols and guidelines and to make their own further enquiries of manufacturers or specialists in relation to particular drugs, treatments or advice. Lilly, the publisher and the authors cannot accept liability for errors or omissions, and disclaim any liability arising out of the use of this handbook in practice.'

For the reasons set out above, Lilly denied that it breached Clauses 7.2, 9.1 or 2 in relation to this particular complaint. The date of publication of the handbook was clear, and users would have understood that it contained references to medicines approved at the date of publication.

PANEL RULING

The Panel noted that the 8th Edition of the handbook had been withdrawn prior to completion of the previous case.

Turning to this case, the Panel noted that the date of preparation of the handbook was February 2014 which was stated on the bottom right hand corner of the even numbered pages. The Panel also noted the disclaimer that the publisher had tried to ensure that the information contained in the handbook was accurate and up-to-date at the time of publication and the reference to the need to check the SPC on page 3. The disclaimer further reminded the user that the handbook was not a substitute for each product SPC and went on to provide the user with a link to the eMC. A list of monographs appearing in the handbook was included on page 30 for readers to refer to.

The Panel noted Lilly's submission regarding the decision to compare those cancer agents included in the 7th Edition with those whose launch had been notified to MIMS by the end of November 2013. It also noted Lilly's submission that ramucirumab and nivolumab were not approved for use in the UK until after the cut-off date (December 2014 and April 2016 respectively).

The handbook was clear regarding the date of publication. The intended audience would be aware that it was likely that new medicines would be approved after the publication date.

The Panel did not consider that the omission of ramucirumab and nivolumab from the 8th Edition of the handbook, published 10 months before ramucirumab was approved and 14 months before nivolumab was approved, was misleading or unbalanced as alleged. The Panel therefore ruled no breach of Clause 7.2.

The Panel noted its ruling of no breach of Clause 7.2 and in this regard did not consider that Lilly had failed to maintain high standards in relation to the omission of ramucirumab and nivolumab from the 8th Edition of the handbook and no breach of Clause 9.1 was ruled. The Panel noted its rulings above and ruled no breach of Clause 2.

Complaint received **12 September 2016**

Case completed **9 November 2016**