CASE AUTH/2925/1/17

HEALTH PROFESSIONAL v PFIZER

Websites

A health professional who until recently worked in the pharmaceutical industry complained about Pfizer's websites.

The complainant alleged that the prescribing information on a number of materials on the websites was out of date. The materials at issue were a Vfend (voriconazole) leavepiece, a Tygacil (tigecycline) leavepiece, an Ecalta (anidulafungin IV) leavepiece, and documents headed 'Prescribing Information' for Depo-Provera (medroxyprogesterone acetate) and Sayana Press (medroxyprogesterone acetate).

In response to a request for more information from the case preparation manager, the complainant explained that he/she had reviewed the date of creation of the prescribing information on the items compared with the latest versions on the electronic medicines compendium (eMC). The complainant focussed on when the information in Section 4.4 [Special warnings and precautions for use] had been updated, since it was highly likely to be of direct clinical impact.

The complainant referred to the prescribing information for Depo-Provera on the Pfizer website which was dated July 2015 whereas the eMC for Depo-Provera had been updated twice with the latest change stipulating an update to the adverse drug reaction (ADR) frequency. The date of the prescribing information for Sayana Press on the Pfizer website was May 2015 whereas the eMC had been updated once or twice since then. The complainant also referred to changes on the eMC for Ecalta and Tygacil.

The detailed response from Pfizer is given below.

The Panel noted that despite the prescribing information being updated in November 2015 and a new version of the Vfend leavepiece with the updated prescribing information being certified in January 2016, the previous version of the leavepiece with out-of-date prescribing information remained on the website when viewed by the complainant in January 2017. The out-of-date prescribing information did not inform the reader of a number of side effects. A breach of the Code was ruled.

The Panel noted Pfizer's submission that although there had been four revisions of the Tygacil SPC since the current prescribing information was approved in May 2015, none of those revisions had necessitated a change to the prescribing information. The May 2015 prescribing information thus remained up-to-date. The Tygacil leavepiece referred to by the complainant was certified in September 2015 and contained the current and up-to-date prescribing information that had been effective since May 2015. The Panel therefore ruled no breach of the Code.

The Panel noted Pfizer's submission that the Ecalta leavepiece at issue was certified in January 2016 and that it contained the current prescribing information that had been effective since July 2014. The only intervening change to the Ecalta SPC did not impact on the prescribing information. The Panel thus considered that the leavepiece contained the up-to-date prescribing information and so it ruled no breach of the Code.

The Panel noted Pfizer's submission that the prescribing information on the Sayana-Press website which was last updated in May 2016, and not May 2015 as referred to by the complainant, was current and up-to-date. The only revision to the SPC since that date involved Section 5.1 which did not necessitate a change to the prescribing information. The Panel therefore ruled no breach of the Code.

The Panel noted Pfizer's submission that the Depo-Provera SPC was updated in December 2016 such that three clinically non-serious side effects were moved to the 'Very Common' category from the 'Common' (and 'Other') categories. The Panel noted Pfizer's submission that the prescribing information had since been updated and that a new version was now effective on all materials but that at the time of the complaint the previous prescribing information was effective. The Panel noted Pfizer's submission that regulatory approval for the type II variation was received on 8 December 2016 and the SPC was updated the same day. The Panel further noted that according to the eMC, the updated SPC was displayed on Wednesday, 14 December 2016. The Panel noted that the general principle was that the prescribing information must be up-to-date, must comply with the Code and must not be inconsistent with the particulars given in the SPC. The Panel considered that the prescribing information seen by the complainant on 2 January when the complaint was received was not up-to-date and a breach of the Code.

The complainant stated that each instance might be technically following the requirements of the Code if the sections that had been updated had not altered the prescribing information but together pointed to a concerning picture when all four were out-of-date. The complainant queried whether the processes were sufficiently rigorous.

The Panel noted its rulings above and considered that high standards had not been maintained. Up-to-date prescribing information had not been provided in the case of the Vfend leavepiece available on the Pfizer website. The out-of-date prescribing information did not refer to dermatological adverse events and higher frequency of liver enzyme elevations in the paediatric population in the Warnings and Precautions Section. It also did not include the addition of new very

common and common side effects. Further, out-of-date Depo-Provera prescribing information was provided at the time of the complaint such that three clinically non-serious side effects were not listed as 'Very Common'.

The Panel considered that Pfizer had failed to maintain high standards. A breach of the Code was ruled.

The complainant referred to a page on Pfizer's Champix (varenicline) website from which a copy of a new landmark study, EAGLES, the largest comparative randomised controlled trial of approved smoking cessation medicines could be downloaded. The complainant stated that although it was clear that the document was held on a different site, as health professionals were proactively encouraged to use the link, the complainant queried whether it was an independent item or whether it was promotional in nature.

The Panel noted Pfizer's submission that health professionals had, in effect, been invited to access the publication and that Pfizer had certified the e-print for promotional use. The Panel considered that upon visiting the website and possibly downloading the publication, relevant prescribing information should, at the same time, be available to the health professional and in that regard it noted that prescribing information could be accessed via a separate but prominent link in the same screenshot as the link to the publication. No breach of the Code was ruled.

A health professional, who until recently worked in the pharmaceutical industry complained about Pfizer Limited's websites. The complainant was concerned about a number of issues.

1 Prescribing information

COMPLAINT

The complainant alleged that the prescribing information on a number of materials on the websites was out of date. The materials at issue were a Vfend (voriconazole) leavepiece (ref VFE1771), a Tygacil (tigecycline) leavepiece (ref TYG162), an Ecalta (anidulafungin IV) leavepiece (ref ECA359), and documents headed 'Prescribing Information' for Depo-Provera (medroxyprogesterone acetate) (ref DP 13_0) and Sayana Press (medroxyprogesterone acetate) (ref PP-SAY-GBR-0071).

In response to a request for more information from the case preparation manager, the complainant explained that the parts he/she considered were missing from the prescribing information for the various medicines was based on a review of the date of creation of the prescribing information on the items compared with the latest versions on the electronic medicines compendium (eMC) (emc.org.uk). The complainant stated that he/she focussed on when the information in Section 4.4 [Special warnings and precautions for use] had been updated, since it was highly likely to be of direct clinical impact.

The complainant referred to the prescribing information for Depo-Provera on the Pfizer website which was dated July 2015 whereas the eMC for Depo-Provera had been updated twice with the latest change stipulating an update to the adverse drug reaction (ADR) frequency.

The date of the prescribing information for Sayana Press on the Pfizer website was May 2015 whereas the eMC had been updated once or twice since then.

The complainant also referred to changes on the eMC for Ecalta and Tygacil.

In writing to Pfizer, attention was drawn to the requirements of Clauses 4.1, 4.2 and 9.1 of the Code.

a) Vfend

RESPONSE

Pfizer stated that the Vfend prophylaxis leavepiece (ref VFE 1771), was certified in September 2015.

In May 2015, Pfizer submitted a type II variation to update the Vfend summary of product characteristics (SPC) to reflect new safety and efficacy data. Regulatory authority approval of this labelling change was received on 17 December 2015. As a result, the SPC was updated to the current version with changes to Sections 4.4 Special warnings and precautions for use, 4.8 Undesirable effects and 5.1, Pharmacodynamic properties.

Consequently, the previous version of the prescribing information (ref VF 23_0; 06/2014) was thus updated to the current version (ref VF 24_0; 11/2015) by incorporating additional material under 'Warnings and Precautions' and 'Side Effects' to reflect the SPC changes. The new material under 'Warnings and Precautions' involved dermatological adverse reactions and reference to the higher frequency of liver enzyme elevations in the paediatric population. The 'Side Effects' section was updated to include new material under the 'very common' and 'common' sub-sections.

Pfizer submitted that all promotional materials were updated with the new prescribing information including the Vfend prophylaxis leavepiece which was updated and recertified in January (ref VFE 1803; January 2016). The Vfend section of the Pfizer website was certified in December 2016 (ref PP-VFE-GBR-0035). Pfizer submitted that whilst it had taken care to ensure that the website itself provided access to the current and up-to-date Vfend prescribing information (ref VF 24_0), the older version of the Vfend prophylaxis leavepiece (ref VFE1771) containing the out-of-date prescribing information was erroneously incorporated instead of the updated piece containing the updated prescribing information. This was an entirely unintended oversight due to human error and was an isolated incident. All other promotional materials, including the leavepiece not on the website, were updated correctly with the new prescribing information, and as stated above, the website itself was updated with the new prescribing information. Pfizer accepted

that there had been a breach of Clauses 4.1 and 4.2 in this isolated incident which it sincerely regretted. Pfizer submitted that the error had been corrected.

PANEL RULING

The Panel noted that Clause 4.1 of the Code required the prescribing information listed in Clause 4.2 to be provided in a clear and legible manner. Clause 4.2 stated that the prescribing information consisted of, *inter alia*, a succinct statement of common side-effects likely to be encountered in clinical practice, serious side-effects and precautions and contra-indications relevant to the indications in the advertisement. The Panel noted that despite the prescribing information being updated in November 2015 and a new version of the Vfend leavepiece with the updated prescribing information being certified in January 2016, the previous version of the leavepiece with out-of-date prescribing information remained on the website when viewed by the complainant in January 2017. The out-of-date prescribing information did not inform the reader that a higher frequency of liver enzyme elevations was observed in the paediatric population and also referred to rare reports of serious cutaneous reaction whereas the updated prescribing information did not use the word rare and gave more details of the serious cutaneous reactions that could occur. The out-of-date prescribing information did not list any common side-effects and did not include respiratory distress in the list of very common side effects. It also did not include new material under the 'very common' and 'common' side effects sections.

The Panel noted that a breach of Clause 4.2 had been alleged. Clause 4.2 listed the components of prescribing information and it was a requirement of Clause 4.1 that such be provided. The Panel considered that as the prescribing information in the Vfend leavepiece available on the pfizerpro.co.uk was not up-to-date with regard to precautions and side-effects it did not comply with the Code. A breach of Clause 4.1 was ruled.

b) Tygacil

RESPONSE

Pfizer submitted that the Tygacil leavepiece at issue was certified in September 2015. This piece included the current and up-to-date prescribing information (ref TL 7_0) that had been effective since May 2015.

The complainant referred to revisions to the Tygacil SPC noted on the eMC. Pfizer stated that the SPC had been revised four times since the current prescribing information was approved in May 2015. However, none of those revisions had an impact on the prescribing information and as a result the prescribing information had remained unchanged.

With the first revision in June 2015, the changes were confined to Section 5.1 Pharmacodynamic properties, apart from minor administrative/formatting changes. The second revision in February 2016, impacted Sections 4.2 Posology and method of administration, 4.4 Special warnings and precautions for use, 4.6 Fertility, pregnancy and lactation and 4.8 undesirable effects. The changes to Sections 4.2 and 4.4 were non-content related reordering of text and additional headings. Changes to Section 4.6 did not include any additional warnings that impacted the prescribing information. The changes to Section 4.8 only involved reformatting undesirable effects into a table format.

The third revision in April 2016 involved the addition of 'hypofibrinogenaemia' as an undesirable effect (Section 4.8) under the 'frequency not known' category and thus did not warrant a prescribing information update. The fourth revision of the SPC undertaken in June 2016 only impacted Section 10 involving updates to dates of revision/approval. In summary, Pfizer submitted these SPC changes did not warrant any amendments to the prescribing information and hence there had not been any prescribing information updates. Since the prescribing information was current and up-to-date, Pfizer denied a breach of Clauses 4.1 or 4.2.

PANEL RULING

The Panel noted Pfizer's submission that although there had been four revisions of the SPC since the current prescribing information was approved in May 2015, none of those revisions had necessitated a change to the prescribing information. The May 2015 prescribing information thus remained up-to-date. The Tygacil leavepiece referred to by the complainant was certified in September 2015 and contained the current and up-to-date prescribing information that had been effective since May 2015. The Panel therefore ruled no breach of Clause 4.1.

c) Ecalta

RESPONSE

Pfizer submitted that the Ecalta leavepiece at issue was certified in January 2016 and had the current and up-to-date prescribing information that had been effective since July 2014.

Pfizer noted that although the complainant referred to revisions to the Ecalta SPC noted on the eMC, the only change had been a change to Section 6.5 Nature and contents of container, which had no impact on the prescribing information. Since the prescribing information was current and up-to-date, Pfizer denied any breach of Clauses 4.1 or 4.2.

PANEL RULING

The Panel noted Pfizer's submission that the Ecalta leavepiece at issue was certified in January 2016 and that it contained the current prescribing information that had been effective since July 2014. The only intervening change to the Ecalta SPC had been to Section 6.5 Nature and contents of container, which did not impact on the prescribing information. The Panel thus considered that the leavepiece contained the up-to-date prescribing information and so it ruled no breach of Clause 4.1.

d) Sayana-Press

RESPONSE

Pfizer submitted that the website had the current and up-to-date prescribing information which had been effective since May 2016. Pfizer noted that the date of the prescribing information as shown against 'Last Updated' was May 2016 and not 'May 2015' as the complainant had stated. Further, the complainant had stated that the eMC showed again that the prescribing information had been updated once or twice since the available prescribing information. Pfizer submitted, however, that the eMC only referred to changes to the SPC (and not the prescribing information) and only showed one revision to the SPC since the date of approval of the current prescribing information. This revision involved Section 5.1, Pharmacodynamic properties/mode of action and thus had no impact on the prescribing information. Therefore Pfizer did not accept there had been any breach of Clauses 4.1 or 4.2.

PANEL RULING

The Panel noted Pfizer's submission that the prescribing information on the Sayana-Press website which was last updated in May 2016, and not May 2015 as referred to by the complainant, was current and up-to-date. The only revision to the SPC since that date involved Section 5.1 which did not necessitate a change to the prescribing information. The Panel therefore ruled no breach of Clause 4.1.

e) Depo-Provera

RESPONSE

Pfizer submitted that the Depo-Provera prescribing information on the website had been effective since July 2015. Pfizer noted that the complainant referred to the eMC to support the claim that the prescribing information had been updated twice since then. Pfizer submitted, however, that the eMC only referred to SPC updates and the complainant had incorrectly concluded them to be prescribing information updates. Not all SPC updates required revisions to the prescribing information.

The first of the two SPC updates (February 2016) involved Section 5.1, Pharmacodynamic properties and thus had no impact on the prescribing information. The second resulted from a type II variation that was submitted to the regulatory authority to primarily update Section 4.8 of the SPC in line with the Company Core Data Sheet. The update involved relocation of three clinically non-serious side effects under the 'Very Common' category (they were moved from 'Common' and 'Other' categories) as well as clinically non-significant changes to other sections. The regulatory approval for this variation was received in December 2016 and as a result the SPC was updated. The prescribing information had also been updated to reflect these changes to a new version which was now effective on all materials but at the time of the complaint the previous prescribing information was effective. Therefore Pfizer did not accept there had been any breach of Clauses 4.1 or 4.2.

In response to a request for further information, Pfizer submitted that regulatory approval for the type II variation referred to above was received on the 8 December 2016 and accordingly the SPC was updated the same day. A copy of the updated Depo-Provera prescribing information (ref DP 14-0) was provided. Pfizer submitted that it was the master copy and therefore a certificate of approval did not form part of the document in accordance with Pfizer's global process for the management of all regulatory labelling documentation (including the prescribing information) which was created, maintained and stored in its regulatory document management system. The prescribing information was approved by medical affairs to ensure compliance with Clause 4 of the Code. The approved prescribing information itself was not certified until the document was attached to a promotional item. At this stage, the prescribing information would be certified as an integral part of the promotional item through Pfizer's approval and certification management system.

PANEL RULING

The Panel noted Pfizer's submission that the Depo-Provera SPC was updated in December 2016 such that three clinically non-serious side effects were moved to the 'Very Common' category from the 'Common' (nervousness) and 'Other' (weight increase, weight decrease) categories. The Panel noted Pfizer's submission that the prescribing information had since been updated to reflect these changes and that a new version was now effective on all materials but that at the time of the complaint (2 January) the previous prescribing information was effective. The Panel noted Pfizer's submission that regulatory approval for the type II variation was received on Thursday, 8 December 2016 and the SPC was updated the same day. The Panel further noted that according to the eMC, the updated SPC was displayed on Wednesday, 14 December 2016. The Panel noted that the general principle was that the prescribing information (defined in Clause 4.2) must be up-to-date, must comply with Clauses 4.1 and 4.2 of the Code and must not be inconsistent with the particulars given in the SPC. The Panel considered that the prescribing information seen by the complainant on 2 January when the complaint was received was not up-to-date. The website thus contained out-of-date prescribing information for Depo-Provera which was not in line with the SPC and the Panel ruled a breach of Clause 4.1.

f) Summary

COMPLAINT

The complainant stated that each instance might be technically following the requirements of the Code if the sections that had been updated had not altered the prescribing information but together pointed to a concerning picture when all four were out-of-date. The complainant queried whether the processes were rigorous enough to prevent this from happening.

RESPONSE

Pfizer regretted that there had been a breach of Clauses 4.1 and 4.2 due to an isolated incident as

a result of human error on the Vfend leavepiece (ref VFE1771). However, all other materials for all products referred to by the complainant had the correct and up-to-date prescribing information and there were no breaches of Clauses 4.1 or 4.2 in these examples. Thus Pfizer strongly believed that high standards had been maintained in compliance with Clause 9.1.

PANEL RULING

The Panel noted its rulings above and considered that high standards had not been maintained. Up-to-date prescribing information had not been provided in the case of the Vfend leavepiece available on the Pfizer website. The out-of-date prescribing information did not refer to dermatological adverse events and higher frequency of liver enzyme elevations in the paediatric population in the Warnings and Precautions Section. It also did not include the addition of new very common and common side effects. Further, out-of-date Depo-Provera prescribing information was provided at the time of the complaint such that three clinically non-serious side effects were not listed as 'Very Common'.

The Panel noted the above and considered that Pfizer had failed to maintain high standards. A breach of Clause 9.1 was ruled.

2 Champix reprint

COMPLAINT

The complainant referred to a page on Pfizer's Champix (varenicline) website from which a copy of a new landmark study, EAGLES, the largest comparative randomised controlled trial of approved smoking cessation medicines could be downloaded. The complainant stated that although it was clear that the document was held on a different site, as health professionals were proactively encouraged to use the link, the complainant queried whether it was an independent item or whether it was promotional in nature.

RESPONSE

Pfizer submitted that with regard to the complainant's query about the link to an e-reprint hosted on the Elsevier website about Champix, the hyperlinked publication was part of the same material that was referenced by the complainant as health professionals had, in effect, been invited to access the publication. All requirements of the Code had been met with regard to the page and the associated e-reprint. The requirements of Clauses 4.1 and 4.2 were met through the provision of prescribing information on the website as a clickable link in close proximity to the link to the e-reprint.

As the Elsevier website that hosted the e-reprint was not itself owned by Pfizer, a clear statement to that effect was provided to comply with data privacy requirements.

PANEL RULING

The Panel noted Pfizer's submission that health professionals had, in effect, been invited to access the publication and that Pfizer had certified the e-print for promotional use. The Panel considered that upon visiting the website and possibly downloading the publication, relevant prescribing information should, at the same time, be available to the health professional and in that regard it noted that prescribing information could be accessed via a separate but prominent link in the same screenshot as the link to the publication. No breach of Clause 4.1 was ruled.

Complaint received **3 January 2017**

Case completed **3 April 2017**