CASE AUTH/3871/1/24

COMPLAINANT v ABBVIE

Allegation of error in the presentation of the SPC on the EMC website

CASE SUMMARY

This case was in relation to a missing 'dash' in the posology and method of administration section of the Summary of Product Characteristics (SPC) for Venclyxto (venetoclax), which had been published on the Electronic Medicines Compendium (EMC) website by a third-party on behalf of AbbVie.

The outcome under the 2021 Code was:

Breach of Clause 5.1	**Failing to maintain high standards**

No Breach of Clause 2	**Requirement that activities or materials must not bring discredit upon, or reduce confidence in, the pharmaceutical industry**

This summary is not intended to be read in isolation.
For full details, please see the full case report below.

FULL CASE REPORT

A complaint was received about AbbVie from an anonymous, non-contactable complainant who described themselves as a health professional.

COMPLAINT

The complaint wording is reproduced below, with typographical errors corrected:

> "I was reading the SPC [summary of product characteristics] of Venclyxto (venetoclax) 100mg. I noticed something erroneous with the dosing for the Acute Myeloid Leukaemia dosage. See screenshots attached. From the SPC it appears that the Azacitidine administration should be administered on 'Days 17 of each 28 day cycle'. However, the dosage should be days 1-7. The omission of the dash could cause some confusion and potentially incorrect dosing to patients. I hope this can get corrected."

When writing to AbbVie, the PMCPA asked it to consider the requirements of Clauses 2 and 5.1 of the 2021 Code.

ABBVIE'S RESPONSE

The response from AbbVie is reproduced below:

"Thank you for your letter of 19th January 2024 regarding a complaint received by the PMCPA related to concerns about an error in the presentation of the Summary of Product Characteristics ("**SmPC**") of one of our products on the EMC website.

We take our responsibility for compliance with all applicable laws and regulations including the ABPI Code of Practice ('**Code**') very seriously and we continuously endeavor to maintain these high standards in all our activities.

Complaint:

A healthcare professional (HCP) noticed a formatting error in section 4.2 of the SmPC for Venclyxto 100mg film-coated tablets. The healthcare professional is concerned a dash ('-') is missing between the numbers 1 and 7 referring to the days when Azacitidine should be administered with Venclyxto in patients with Acute Myeloid Leukaemia. The HCP is requesting this error to be corrected.

Response:

AbbVie make every effort to ensure that all regulatory documents and information pertaining to AbbVie medicines marketed in the UK are precise, complete, and fully compliant with all regulations applicable in the UK, including the Human Medicines Regulations 2012. We would like to thank the health professional and the PMCPA for bringing this formatting error to our attention.

Outside the Scope of the Code

The Code covers promotion of prescription only medicines to HCPs, in addition to other non-promotional activities, and explicitly calls out in Clause 1.17 that the SmPC is not considered promotional in and of itself, unless it is used for promotional purposes.

After careful consideration, AbbVie believes the Complaint does not fall within the scope of the Code as the requirements detailed in Clause 1.1, Clause 1.1 SI and Clause 1.17 have not been satisfied for the following reasons:

i) The SmPC is not considered a promotional item, it is an item covered by regulations as referenced in the Code (Clause 1.17).
ii) The SmPC has not been used for promotional purposes. It is a reference document for HCPs to provide them with the relevant information pertaining to the medicine, which has been approved by the MHRA. It is hosted on the EMC portal to enable easy access for HCPs, which is standard practice in the UK (further information on this outlined below).

AbbVie believe that, as a rule, regulatory documents such as SmPCs, in and of themselves, are outside the scope of the activities regulated by the ABPI Code.

AbbVie Investigation Regarding the Identified Formatting Error

AbbVie has reviewed the details of this case. Please find our analysis below.

Venclyxto 100mg film-coated tablets SmPC hosted on the EMC Website

On receipt of the complaint, AbbVie immediately reviewed the SmPC for Venclyxto 100mg film-coated tablets hosted on the EMC Website and confirmed the presence of blank space instead of a dash between numbers 1 and 7. AbbVie noticed the same discrepancy in the SmPC for Venclyxto 50mg film-coated tablets. The SmPC for Venclyxto 10mg film-coated tablets did not include the same formatting error.

AbbVie's SmPCs submission to EMC

AbbVie reviewed our internal records and confirmed the Venclyxto 50 and 100mg film-coated tablet SmPCs uploaded by AbbVie on the EMC website for publication by [third-party] (the party responsible for running the EMC website) were correct and fully aligned with the versions approved by the MHRA. Specifically, these included the 'dash' sign in the appropriate place. AbbVie believes the formatting errors have occurred during the process of converting the documents submitted by AbbVie into the versions available on the EMC website, which is a technical procedural step carried out by [third-party].

[Third-party] Quality Control Process

As per [third-party] EMC Content Policy and their SmPC Quality Control Guidelines, a quality control ('**QC**') check must be completed by [third-party] before any SmPC is published on the EMC website. The purpose of the QC check is to ensure that the SmPCs are not changed during the conversion process.

The QC control consists of the following checks:

1. Active ingredient name in document details
2. Table of contents and headings
3. Document presentation
4. Document formatting

The document presentation quality check (number 3 above) includes the check for converter issues. [Third-party] technical team is responsible for correcting the following errors, where these occur as a result of document conversion:

- Errors in line or paragraph spacing.
- Text spacing changes mid document.
- Font changes mid document.
- Fragmented tables.
- Text in columns or tables which is misaligned.
- Missing or incorrect display of symbols.
- Incorrect display of subscript or superscript characters

The QC check is a 2 stage process. AbbVie has visibility of the quality control results and the QC for the Venclyxto 50 and 100mg film-coated tablets passed without any

flags of any missing or incorrect display of symbols or any errors in line or paragraph spacing.

As per our contractual agreement with [third-party], AbbVie relies on [third-party] quality control process for correction of formatting errors caused by the document conversion process.

Corrective actions on receipt of the complaint

Upon completion and review of our records, AbbVie took immediate action and sent a letter to [third-party] to rectify the errors highlighted in our communication. [Third-party] confirmed the errors have been resolved and that they are prioritising the learnings of this incident and taking the necessary actions in their processes to prevent similar incidents occurring again.

AbbVie have requested [third-party] to provide further details of their corrective and preventative actions following on from this complaint.

SmPC on the EMC portal

The EMC portal is a platform used by the majority of UK pharmaceutical companies to host SmPCs for their products to be easily accessible by HCPs. [Reference to flowchart on ABPI website citing EMC registration provided].

[Third-party] provides an arm's length standardised service across the industry to host medicines SmPCs. It is standard practice for pharmaceutical companies in the UK to utilise this service and is the main point of reference for SmPCs. The EMC portal provides an easily searchable database of SmPCs for medicinal products. As noted below, product SmPCs are also hosted on the MHRA website, though this is less navigable. In certain cases, the MHRA provides direct links to the EMC, e.g. when providing safety updates. AbbVie believe that an individual company decision to refrain from using the EMC service would be out of kilter with the expectations of both healthcare professionals and other sector stakeholders.

In addition, all our product SmPCs are hosted on the MHRA website and, in the particular cases of the Venclyxto SmPCs, the versions available on the MHRA website are fully correct and include the 'dash' sign.

Missing Dash

AbbVie would also make the point that, even if the PMCPA would regard this matter as falling within its purview, we do not believe that the missing 'dash' sign has the potential to put patient safety at risk, given the following considerations:

i) Azacitidine is a medicine that has been available on the market for a very long time and clinicians would be very familiar with its administration and dosing, which is for the first 7 days of a 28-day treatment cycle. The SmPC states that 'Treatment with venetoclax should be initiated and supervised by a physician experienced in the use of anticancer medicinal products.' AbbVie do not believe healthcare professionals managing AML patients would

consider, upon reading that paragraph, that Azacitidine should be administered on the 17th day of the treatment cycle.

ii) The same dosing regimen for Azacitidine is also outlined in its individual SmPC.

iii) The SmPC sentence highlighted in the complaint clearly refers to 'days 1 7' *(emphasis added by the underlining of 's')* and includes a space between 1 and 7, which is clearly different from a reference to 'day 17' and is unlikely to be misinterpreted as 'day 17'.

iv) The SmPC sentence that immediately follows the sentence highlighted in the complaint refers to other medicines that can be used in combination to Venclyxto for the treatment of AML patients (i.e. Decitabine) and that sentence clearly states '*Decitabine should be administered at 20 mg/m^2 of BSA intravenously on Days 1-5 of each 28-day cycle beginning on Cycle 1 Day 1*', matching the format and structure of the sentence subject to the complaint.

Lastly, the SmPCs available on the MHRA website, materials developed by AbbVie, prescribing information, PILs, as well as available NICE guidance, all include correct and complete information about the dosing of Azacitidine when used in combination with Venclyxto for patients with AML. We would not expect the EMC version of the SmPC to be the single document that a clinician would use to inform their prescribing decisions.

Summary

In summary, AbbVie do not believe that this complaint falls within the scope of the Code and therefore is not in breach of Clause 2 or 5.1 of the Code. As explained above, AbbVie take all our responsibilities extremely seriously and have immediately addressed the formatting error."

PANEL RULING

The complaint concerned the Summary of Product Characteristics (SPC) for Venclyxto (venetoclax) 100mg film-coated tablets, which had been published on the Electronic Medicines Compendium (EMC) website by AbbVie's third-party. The SPC on the EMC website contained an error in Section 4.2 (Posology and method of administration) relating to the Acute Myeloid Leukaemia (AML) dose schedule in that the administration of azacitidine (a combination agent) was incorrectly stated as *"…Days 1 7 of each 28-day cycle…"* as opposed to *"Days 1-7"*.

Scope of the Code

The first matter for the Panel to consider was whether an SPC on the EMC website was within the scope of the Code.

Clause 1.17 of the Code excluded from the definition of promotion, among other things, the labelling on medicines and accompanying package leaflets and stated that their contents were covered by regulations. While the Panel considered that complaints about the content of an SPC as approved by the licensing authority were not within the scope of the Code, the use and presentation of that SPC by the company may be within the scope of the Code.

The Panel noted AbbVie's submission that the missing 'dash' was an error in the way the SPC was presented on the EMC website and there was no such error in the SPC on the MHRA website. The Panel considered that if a company made its SPC available on a third-party platform such as the EMC website, the company had a responsibility to ensure that the SPC was presented accurately and was up-to-date. Furthermore, it was established in Case AUTH/3042/6/18 that a pharmaceutical company's oversight of its SPCs on the EMC website was within the scope of the Code. The Panel therefore concluded that the matter of complaint was within the scope of the Code.

Clause 5.1

The Panel noted from the material provided by the complainant that within Section 4.2 (Posology and method of administration) of the Venclyxto 100mg SPC on the EMC website, in relation to AML, it stated:

> *"Azacitidine should be administered at 75 mg/m^2 of Body Surface Area (BSA) either intravenously or subcutaneously on Days 1 7 of each 28 day cycle beginning on Cycle 1 Day 1."*

The complainant alleged that there was a missing 'dash' between the numbers 1 and 7 which could lead to confusion and potentially incorrect dosing as it erroneously appeared from the SPC that azacitidine should be administered on Days 17 of each 28 day cycle.

AbbVie submitted that the same error was also present in the SPC for Venclyxto 50mg film-coated tablets.

The Panel took account of AbbVie's submission that the SPCs it provided to the third-party for publication on the EMC website were correct and aligned with the versions approved by the MHRA. AbbVie believed the missing 'dash' between numbers 1 and 7 occurred during the process of converting documents for publication, which was a technical procedural step carried out by the third-party. AbbVie submitted that it had relied on the third-party's quality control process for the correction of formatting errors caused by the document conversion process.

Clause 1.24 included that companies were responsible under the Code for the acts and omissions of their third parties, even if they acted contrary to the instructions which they had been given. The Panel accepted that the versions of the SPCs provided to the third party by AbbVie contained the 'dash' in the correct place. The Panel considered, however, that AbbVie should have checked how the SPCs appeared when they were published on the EMC website. The Panel was concerned that AbbVie's response to the complaint did not state that such a check would be part of its standard process in the future as a preventative measure. The Panel considered that it was crucial that health professionals and others could rely on the SPC published on the EMC website to be accurate.

The Panel considered that other material relating to Venclyxto, including AbbVie material, likely contained links to these incorrect SPCs. In the Panel's view, that such an error occurred in both the 50mg and 100mg Venclyxto SPCs added to the potential for confusion.

The Panel noted that the 100mg and 50mg Venclyxto SPCs were published on the EMC website on the 1st and 2nd of February 2023, respectively. The complaint to the PMCPA was received on 18th January 2024. The Panel concluded that the error in two SPCs had been

present on the EMC website for almost one year and that it had only come to AbbVie's attention following a complaint to the PMCPA. Taking everything into account, the Panel considered that high standards had not been maintained and a **breach of Clause 5.1** was ruled.

Clause 2

Clause 2 was a sign of particular censure and reserved for such use. The Panel noted that the Venclyxto SPC stated that venetoclax should be initiated and supervised by a physician experienced in the use of anticancer medicinal products. AbbVie submitted that health professionals managing AML patients would be familiar with azacitidine's administration and dosing, which was for the first 7 days of a 28-day treatment cycle as outlined in its own SPC, as the medicine had been available on the market for a long time.

The Panel noted that the sentence with the 'Days 1 7' error went on to state 'beginning on Cycle 1 Day 1'. Furthermore, the plural 'Days' and the space between the 1 and the 7 would likely signal to readers that this was a formatting error. The Panel also took account of the sentence immediately before the sentence with the error, which contained reference to azacitidine being initiated on Cycle 1 Day 1. This same section of the Venclyxto SPC referred the health professional to view the azacitidine prescribing information.

The versions of the Venclyxto SPCs which AbbVie had provided to the third party for publication were correct and the error was introduced by the third party, which the Panel considered had let AbbVie down. For the aforementioned reasons, the Panel considered that, on balance, and in the particular circumstances of this case, the complainant had not established that AbbVie had brought discredit upon or reduced confidence in the industry. The Panel therefore ruled **no breach of Clause 2**.

Complaint received **18 January 2024**

Case completed **10 February 2025**