CASE AUTH/3642/5/22

COMPLAINANT v NOVARTIS

Promotion of Entresto (sacubitril, valsartan)

CASE SUMMARY

This case was in relation to concerns around the compliance culture at Novartis, particularly with regard to five Entresto promotional articles which were initiated and funded by Novartis Pharmaceuticals UK Ltd.

The Panel ruled a breach of the following Clause of the 2019 Code, as acknowledged by Novartis, in relation to each of the 5 articles, because whilst the adverse event reporting statement was included within the prescribing information, which was available via a link on each of the articles in question, it was not included within the body of the supplement or the articles themselves in line with the requirement of the Code:

Breach of Clause 4.9	**Failing to include information about how to report adverse events**

The Panel ruled no breach of the following Clauses of the 2019 Code as it did not consider that the complainant had established that:

- **there was an error in the approval process**
- **the articles had not been certified**
- **the inclusion of the black triangle for Entresto on the 2019 articles, as they appeared on the BJC website, was inaccurate or misleading**
- **Novartis did not have a dedicated signatory team or that compliance at Novartis had been substandard**

No Breach of Clause 7.2	**Requirement that information must be accurate, up-to-date and not misleading**
No Breach of Clause 9.1	**Requirement to maintain high standards**
No Breach of Clause 14.1	**Requirement to certify promotional material**

Although the Panel considered that it was unacceptable to omit the adverse event reporting statement within the articles in question, it could, nonetheless, be viewed on the prescribing information when accessed from the link within each of the five articles in question and thus the Panel did not consider, in relation to the allegations overall, that Novartis had failed to maintain high standards or that this case warranted a ruling of a breach of Clause 2 and it ruled no breach of the following Clauses of the 2019 Code:

No Breach of Clause 9.1	**Requirement to maintain high standards**

No Breach of Clause 2	Requirement that activities or material 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

An anonymous, contactable complainant who described him/herself as a cardiac specialist had concerns around the compliance culture at Novartis.

COMPLAINT

The complainant stated that Novartis had commissioned 5 promotional articles around Entresto which were not accurate as they all had a black triangle next to Entresto which was not correct as it was not a black triangle product, there was no adverse event reporting on the page and there was no certification for any of these articles (links to the five articles were provided).

The complainant stated that all of the articles had a disclaimer – This sponsored supplement was initiated and funded by Novartis Pharmaceuticals UK Ltd. Editorial control, however, was retained by the authors and editors but Novartis reviewed the supplement for technical accuracy and compliance with relevant regulatory requirements before publication. The complainant stated that, therefore, it was wholly inappropriate to not have the mandatory promotional requirements. All the articles had an identical code and date which would highly indicate an error in approvals process – Date of preparation: July 2019 Job bag number: ENT19-C029.

The complainant stated that a former peer who worked at Novartis had told him/her in confidence that Novartis did not have a dedicated signatory team focused purely for copy approval. In addition, Novartis wanted everyone on site at all times instead of a full remote working signatory team to focus purely on high quality approvals meaning that compliance had been substandard. Talent retention and experienced personnel recruitment was a major factor for compliance errors as junior members were not fully familiar with compliance importance either. Breaches of the Code: 8.1 (a total of five times) as not certified; 6.1 (a total of five times) as not black triangle product; 5.1 (for maintaining low standards); 12.9 (a total of five times) as no adverse event reporting; 2 (for bringing industry into disrepute).

When writing to Novartis, the Authority noted the complainant had referred to the requirements of the 2021 Code but, given that all of the articles were published in 2019, it appeared that the complaint ought to be considered under the requirements of the equivalent clauses of the 2019 Code. The Authority therefore asked Novartis to consider the requirements of Clauses 2, 9.1, 7.2, 14.1 and 4.9 of the 2019 Code which were the equivalent clauses to those cited by the complainant.

RESPONSE

Novartis stated that the complaint caused the company concern and it had taken its content seriously. Novartis highlighted that the company was committed to operating in accordance with the required standards and meeting the relevant requirements and expectations.

The relevant background to this supplement was as follows: The online and print supplements were initiated and funded by Novartis Pharmaceuticals UK Ltd, but editorial control was retained by the relevant authors. Novartis reviewed the supplement for technical accuracy and compliance before its publication. The print version consisted of a total of 5 supplements published together in The British Journal of Cardiology Volume 26 Supplement 1, dated July–September 2019- . The online version consisted of 5 supplements published online at the British Journal of Cardiology (BJC) website, available at https://bjcardio.co.uk/.

The allegations had been summarized by clause and Novartis' responses were given below:

Clause 4.9 of the 2019 Code:

- **The five supplements did not include adverse event reporting information.** All 5 promotional supplements included a link to the prescribing information. The prescribing information contained the adverse event reporting information for Entresto. This link was provided at the top of the page, so was very easily accessible for healthcare professionals reading the supplements. A screenshot of where the adverse event reporting could be found within the prescribing information was provided. Novartis aimed to have prominent adverse event reporting on all materials, as required by the Code. Novartis realized that not having it in the main body of the supplement was an oversight. Therefore, taking a cautious approach, Novartis had removed all the supplements from the BJC website, and accepted a breach of Clause 4.9 in this instance.

Clause 7.2 of the 2019 Code

- **Article not accurate, as Entresto was no longer a black triangle product.** Whilst Entresto was no longer a black triangle product now (2022), at the time that the promotional supplements were published in 2019 it was still a regulatory requirement to have the black triangle on Entresto. Therefore, the inclusion of the black triangle accurately represented the regulatory considerations at the time that the supplements were published.

- The date of the supplements being published was clearly shown at the top of the supplements so it would have been very clear to health professionals that these supplements were produced in 2019 and might no longer represent the latest information. It was not standard practice to retrospectively correct information in promotional supplements and articles. All articles/supplements in journals were, by their very nature, historic as science was constantly evolving.

  The supplements were accessed through the Supplement Archive Tab on the webpage, so it would be clear to the health professionals that the information was not current. The archive arranged the supplements year by year, as seen in the documentation provided, so the health professional would be aware that the information was from 2019.

- The BJC had supplied Novartis with a copy of the website terms and conditions. By using the website, the health professional would have implied acceptance of these terms and conditions. Below were some relevant statements:

> '[Named publisher] has taken all reasonable care to ensure the British Journal of Cardiology (BJC) website published pages were accurate on the stated date of publication or last modification.
>
> [Named publisher] takes no responsibility for the consequences of error or for any loss or damage suffered by users of any of the information published on any of these pages, and such information does not form any basis of a contract with readers or users of it.
>
> It is the nature of websites, many of which are constantly changing, that information published may be for test purposes only, may be out of date, or may be the personal opinion of the author. Users should verify information gained from the website with the appropriate original sources, including the British Medical Formulary, before relying on it. Material published is the copyright of [Named publisher] and may not be reproduced without permission. Copyright exists in all other original material published on the website by staff or may belong to the author depending on the circumstances of publication.'

BJC also had a clear disclaimer at the bottom of all their supplements, including the 5 online supplements:

[Named publisher] advises healthcare professionals to consult up-to-date Prescribing information and the full Summary of Product Characteristics available from the manufacturers before prescribing any product. [Named publisher] cannot accept responsibility for any errors in prescribing which may occur.'

- This disclaimer and the excerpt from the terms and conditions above made it very clear that the health professional would be aware that the information was from 2019. Therefore, Novartis did not believe that this was in breach of Clause 7.2.

Clause 14.1 of the 2019 Code:

- **The five supplements were not certified in their final forms (14.1).** This was treated as one item, as all articles were written and published at the same time in one journal. They were all thoroughly reviewed, and as one item, no article had ever been used as a seperate item on its own. This was, hence, certified by a medical signatory as one job, in accordance with this clause and its supplementary information on certifying dynamic content. The job (ENT19-C029) included both print and digital versions of the final supplements, .

Clauses 2 and 9.1 of the 2019 Code:

Novartis noted that the complainant alleged breaches of Clauses 2 and 5.1 (9.1 under 2019 Code which applied to the materials complained of). As well as drawing attention to the supplements addressed in the rest of this response, the complainant additionally added some comments regarding information that they stated they had received from 'a former peer who worked at Novartis'.

In this response, Novartis considered it appropriate to address the potential application of the requirements of Clauses 2 and 9.1 to the materials which formed the main subject matter of the complaint and then separately to the more general comments made.

Applicability to the materials mentioned in the complaint

Novartis stated that it had set out above why the company believed the supplements complained of did not breach Clauses 7.2 and 14.1 of the 2019 Code. To the extent that Novartis' position was accepted by the Panel, it followed that there could be no associated breach of Clauses 2 and 5.1.

Novartis supported the establishment of robust Adverse Event reporting information requirements and procedures. Novartis' internal SOP entitled 'The Promotional and Non-Promotional Materials Including Items of Medical Utility Local P3 SOP' (copy provided) stated the importance of having the Adverse Event reporting information on materials and the final signatories had all been trained on this requirement. No evidence was presented that the error that had been made in this instance was attributable to anything other than a one-off instance of individual oversight during the review process. There was no evidence presented in the complaint that it was representative of any kind of pattern. The material had been removed from the website promptly upon it being brought to Novartis' attention.

Therefore, while accepting a breach of Clause 4.9, it was Novartis' view that such a finding would not, in these particular circumstances, constitute a failure to maintain high standards or bring discredit on the industry.

Applicability to complainant's general comments

The complainant had lodged this complaint as a health professional, but it was clear that they also had an understanding of how pharmaceutical companies undertook reviews of materials and had a strong opinion on how this should work. Further, the comments made vague allegations about the working practices and culture within Novartis, based on hearsay of what someone had been told by another person who worked there.

Novartis' view was that this element of the complaint was completely unevidenced and appeared to amount to no more than passing on gossip with the intention of creating prejudice in how the Panel considered Novartis' response to alleged breaches of Clauses 9.1 and 2 (2019 Code) by the actual materials cited.

Outside of the 2019 journal supplements referred to in the main complaint, the complainant offered no evidence that Novartis' compliance had been substandard. The supplements referred to were just one example from many thousands of items Novartis had prepared and released which had not attracted any assertions of being anything other than in full compliance with the requirements of the Code. Novartis strongly refuted the notion that Novartis' compliance culture was of concern or below industry standard as the complaint seemed to suggest.

Even with robust oversight, human errors would inevitably occur over the course of many thousands of items being reviewed and Novartis welcomed the opportunity for these to be highlighted to us so that the company might correct these promptly and review and further refine its processes as a result. Typically, such errors were bought to Novartis' attention during the

signatory process or later via inter-company dialogue. Here though, the complainant clearly had some level of understanding of compliance requirements but had, nevertheless, chosen to make an anonymous complaint rather than seek to engage with Novartis directly or setting out their level of expertise and/or how this qualified them to criticise how Novartis organised itself.

Novartis' view was that its internal policies procedures and training in this regard exceeded industry standard. Beyond the passed-on word of 'a peer who worked at Novartis' (it was not made clear when this person worked at Novartis, or in what role), no evidence was offered in support of vague assertions relating to how teams were organised and staffed within Novartis. As such, this aspect of the complaint was completely without merit with regard to Clauses 9.1 and 2.

While preparing this response, Novartis had received another complaint relating to material in the same therapeutic area (Case AUTH/3648/5/22). Novartis would, of course, be responding to the detail of that complaint in due course. However, Novartis believed that it was worth noting that this more recent complaint displayed distinct similarities to the complaint in how it was structured. While focused on the content of historical materials (from 2020), this more recent complaint ended similarly to this one, setting out generalised and vague attacks on how Novartis was organised internally with very similar language. Given the complainant had self-declared themselves to be a health professional, Novartis suspected that the complainant worked with, or had previously worked with, Novartis in a role supporting approval of materials.

This followed a spate of recent complaints against Novartis across the last couple of months (currently 7 complaints had been received and addressed or were currently being addressed). These complaints were largely similar in structure and similarities had been noted by the teams working on Novartis' responses.

Based on these similarities, Novartis urged the Panel to establish whether any, or all, of the recent complaints against Novartis had originated from the same (or closely connected) source(s).

Novartis stated that it further encouraged the Panel to undertake further engagement with the complainant health professional, to satisfy itself that the complainant was acting within the spirit of the Code and their own professional obligations.

PANEL RULING

The Panel noted Novartis' comments with regards to the similarities in relation to complaints it had received recently and that it suspected that the complainant worked with, or had previously worked with, Novartis in a role supporting approval of materials. This information had not been provided to the PMCPA by the complainant when asked about conflicts of interest. The PMCPA strongly encouraged employees and others to raise concerns directly with the company prior to making complaints to the PMCPA. The Panel noted that the Constitution and Procedure stated that the complainant had the burden of proving his/her complaint on the balance of probabilities. The intent in or who was raising the complaint was not a relevant factor as to whether or not there was a breach of the Code.

The Panel noted that the five articles in question appeared to be part of The British Journal of Cardiology Supplement 1 Volume 26, Supplement 1 July-September 2019 titled 'Advances in the treatment of chronic heart failure with reduced ejection fraction on real-world settings' (ref

ENT19-CO29, July 2019). The Panel noted Novartis' submission that the print version consisted of a total of 5 supplements published together and the online version consisted of 5 supplements published online at the British Journal of Cardiology (BJC) website.

The Panel noted that the complaint appeared to be in relation to the five articles of the supplement as they appeared online on the BJC website and the Panel made its rulings in this regard.

The Panel noted that in the online version, each article stated at the top of the front page 'This sponsored supplement was initiated and funded by Novartis Pharmaceuticals UK Ltd. Editorial control, however, was retained by the authors and editors but Novartis reviewed the supplement for technical accuracy and compliance with the relevant regulatory requirements before publication. Prescribing information for Entresto ▼(sacubitril/valsartan) in adult patients for treatment of symptomatic chronic heart failure with reduced ejection fraction is available here' which appeared to be a link to the relevant prescribing information.

The Panel noted the complainant's allegation that all the articles had an identical code and date which would highly indicate an error in approvals process and that the five articles had not been certified. The Panel noted Novartis' submission that the supplement, which contained all five of the articles, was treated as one item as all five were written and published at the same time in one journal and no article had ever been used as a seperate item. The Panel noted that all five articles were therefore reviewed as one item and the supplement was certified by a medical signatory as one job. The Panel did not consider that the complainant had established that the there was an error in the approval process or that the articles had not been certified as alleged and therefore ruled **no breach of Clause 14.1 of the 2019 Code** in relation to each of the five articles.

Clause 7.2 of the 2019 Code stated that information, claims and comparisons must be accurate, balanced, fair, objective and unambiguous and must be based on an up-to-date evaluation of all the evidence and reflect that evidence clearly. They must not mislead either directly or by implication, by distortion, exaggeration or undue emphasis. Material must be sufficiently complete to enable the recipient to form their own opinion of the therapeutic value of the medicine. The Panel noted Novartis' submission that whilst Entresto was no longer a black triangle product at the time of the complaint (2022), at the time that the promotional supplements were published in 2019 it was a regulatory requirement to have the black triangle on Entresto. In this regard, the Panel noted Novartis' submission that the date of the supplements being published was clearly shown at the top of the supplements and the supplements were accessed through the Supplement Archive Tab on the webpage where the supplements were arranged year by year so it would have been clear to health professionals that these supplements were produced in 2019 and that the information was not current. Whilst the Panel noted that the material was still in the public domain, in the particular circumstances of this case, the Panel did not consider that the complainant had established that the inclusion of the black triangle for Entresto on the 2019 articles, as they appeared on the BJC website, were inaccurate or misleading with regard to the presence of the black triangle as alleged and **no breach of Clause 7.2 of the 2019 Code** was ruled in relation to each of the five articles.

The Panel noted that the complainant bore the burden of proof and did not consider that he/she had established that Novartis did not have a dedicated signatory team or that compliance at Novartis had been substandard as alleged. The Panel therefore ruled **no breach of Clause 9.1 of the 2019 Code** in this regard.

The Panel noted that whilst the adverse event reporting statement was included within the prescribing information which was available via a link on each of the articles in question, it was not included within the body of the supplement or the articles themselves in line with the requirement of Clause 4.9. The Panel therefore ruled a **breach of Clause 4.9 of the 2019 Code** as acknowledged by Novartis in relation to each of the five articles.

The Panel noted its rulings above and although it considered that it was unacceptable to omit the adverse event reporting statement within the articles in question, it could, nonetheless, be viewed on the prescribing information when accessed from the link within each of the five articles in question. The Panel further noted Novartis' submission that the supplement had since been removed from the website. The Panel, noting its comments and rulings above, did not consider that in relation to the allegations overall, that Novartis had failed to maintain high standards and therefore **no breach of Clause 9.1 of the 2019 Cod**e was ruled.

The Panel did not consider that the particular circumstances of this case warranted a ruling of a breach of Clause 2 which was a sign of particular censure and was reserved for such use and **no breach of Clause 2 of the 2019** Code was ruled. "

Complaint received **5 May 2022**

Case completed **4 April 2023**