CASE AUTH/3768/5/23

HEALTH PROFESSIONAL v SANDOZ

Alleged misleading promotion of natalizumab prior to receiving marketing authorisation

Since this complaint was received, Sandoz has confirmed that it will no longer accept the jurisdiction of the PMCPA. Following notification of the Panel's rulings, Sandoz stated that it did not accept the Panel's rulings of breaches of the Code but did not wish to appeal the Panel's rulings. Should Sandoz choose to re-join the PMCPA's jurisdiction, it would be required to settle the full balance of administrative charges and provide a full undertaking and assurance. The complainant and the Medicines and Healthcare products Regulatory Agency (MHRA) were informed of the position.

CASE SUMMARY

This case was in relation to an advance budgetary notification (ABN) slide deck and summary document for the introduction of a natalizumab biosimilar from Sandoz for the treatment of multiple sclerosis.

The Panel ruled a breach of the following Clauses of the 2021 Code because, on the balance of probabilities, the ABN materials had not met the requirements for advance notification and had amounted to the promotion of natalizumab before the grant of a marketing authorisation; specifically in relation to:

- **The inclusion of information about the cost and required expertise associated with biosimilar development in the full ABN slide deck and summary document**
- **The amount of information on the phase III study that was included in the full ABN slide deck**
- **Reference to 'Sandoz natalizumab' as 'an affordable option to expand patient access and enable reinvestment opportunities' and whether this could be substantiated.**

Breach of Clause 3.1 (x3)	**Promotion of a medicine prior to the grant of its marketing authorisation**
Breach of Clause 5.1	**Failing to maintain high standards**
Breach of Clause 6.2	**Making an unsubstantiated claim**

The Panel ruled no breach of the following Clauses of the 2021 Code in relation to:

- **The mention of similarity to the reference product**
- **The inclusion of information on the Phase III study that was included in the summarised ABN document**
- **Reference to the inclusion of JC Virus testing**
- **The timing of the ABN**
- **The requirements of Clause 11.1 having been adequately covered by the rulings on Clause 3.1**
- **The use of 'pricing corridors'**

- **The omission of information regarding the costs of administration methods**
- **Clause 2, which was a sign of particular censure and reserved for such use.**

No Breach of Clause 2	**Requirement that activities or materials must not bring discredit upon, or reduce confidence in, the pharmaceutical industry**
No Breach of Clause 3.1 (x4)	**Requirement that a medicine must not be promoted prior to the grant of its marketing authorisation**
No Breach of Clause 6.1	**Requirement that information/claims/comparisons must not be misleading**
No Breach of Clause 6.3	**Requirement that all artwork must conform to the letter and spirit of the Code**
No Breach of Clause 11.1 (x5)	**Requirement that a medicine must not be promoted prior to the grant of its marketing authorisation**
No Breach of Clause 14.1	**Requirement that comparisons must not be misleading**
No Breach of Clause 14.4	**Requirement that exaggerated or all-embracing claims must not be made**

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 from a contactable complainant who described themselves as a neurologist physician specialising in managing multiple sclerosis patients about Sandoz Limited.

COMPLAINT

The complainant described themself as a neurologist physician specialising in managing multiple sclerosis patients. The complainant stated they had been presented by their trust with a document produced by Sandoz which included an advance budgetary notification with regard to the introduction of natalizumab by Sandoz (a biosimilar) for treatment of multiple sclerosis.

The complainant alleged that the document aimed to sell the Sandoz natalizumab to pharmacists and physicians despite it not being licensed for use in the UK. Their concerns were:

1 'The document includes statements about the value of biosimilars in general such as that '*biosimilar manufacturing requires state-of-the-art technologies, and expertise*', '*Biosimilar development cost ranges* ***between 150 and 300 million USD or higher***' and describing the '*complex procedure*' and expertise required for developing biosimilars in general to sell the value of the biosimilar medicine against the reference medicine and assure clinicians that it is of similar quality' (emphasis added by complainant).

2 'In the summary section the company continues to sell its medicine proposition by stating in the first point that '*Biosimilar products demonstrate a high similarity to a reference medicine based on comprehensive comparability studies*'. It further continues by stating in the same summary section that '*Sandoz natalizumab*

provides HCPs and payers with an affordable option to expand patient access and enable reinvestment opportunities to ensure sustainability in healthcare systems', however no evidence is available to suggest how savings from Sandoz natalizumab, if any, can result in reinvestment opportunities and greater patient access.'

3 'The document describes in detail the clinical data for the biosimilar medicine including a detailed description of a phase III study to sell the medicine against the reference medicine. The heading on this section stated boldly '***Sandoz natalizumab matched the clinical efficacy of the reference natalizumab***'' (emphasis added by complainant).

4 'The document states boldly information regarding the '*final package on launch*' of Sandoz medicine stating '***JCV testing will be part of the final package on launch***' to sell the future package that Sandoz will be providing when introducing the medicine' (emphasis added by complainant)

5 'The cost savings presented in the document based on the list price of the biosimilar natalizumab compared to the reference medicine are negligible and don't represent any significant savings of the overall medicines' expenditure of the NHS. The NHS expenditure on drugs is currently estimated to be around £17 billion according to official NHS data. The price of Sandoz natalizumab and the reference medicine are not stated in the document to provide clinicians with an objective understanding.'

6 'The document includes a graph illustrating the potential savings if a discount of 30% or 40% or 50% was offered by the company compared to the reference medicine. The savings according to the graph could vary widely from £14.5m to £24.3. The document doesn't state exactly which discount will be available for the NHS to help with calculating any possible budget savings, if any, and therefore leaves such key information open for interpretation by clinicians. The only objective of this document appears to be exaggerating any savings benefits resulting from selling the Sandoz medicine when compared with the reference medicine.'

7 'The document did not consider all the evidence available in regard to natalizumab, in particular the availability of natalizumab (Tysabri) prefilled syringe which is administered subcutaneously and therefore requires much less resource for administration in the hospital leading to significant amount of savings for the NHS. Therefore, the cost comparison of the biosimilar natalizumab to the reference medicine is inappropriate and not balanced in terms of budget comparison.'

The complainant had referred to page 12 of the ABPI Code of Practice for the Pharmaceutical Industry 2021 and understood that such information was allowed to be provided by pharmaceutical companies if a product:

- contained a new active substance or
- contained an active substance prepared in a new way, such as by the use of biotechnology or
- was to have a significant addition to the existing range of authorized indications or
- was to have a novel and innovative means of administration.

Considering the information in the document provided by Sandoz, the complainant alleged that none of these criteria were met and stated that they were therefore puzzled as to what other purpose this document served apart from selling a medicine in such an inappropriate way.

The complainant alleged that the document did not state if the medicine was or would be available in the UK for use. The complainant stated that Sandoz, however, had confirmed the introduction of the new medicine in a few months. As such, the complainant alleged that this document had no other purpose than inappropriately selling this medicine to the NHS. The complainant alleged that there was actually no time in their hospital trust to assess or adjust any budget implication, if any, given the limited time available until the introduction of this medicine.

The complainant alleged that the NHS medicine cost was estimated at about £17 billion and therefore such a document was not of any relevance for them in the trust and any savings provided by Sandoz did not provide any significant budget implications for the NHS.

When writing to Sandoz, the Authority asked it to consider the requirements of 2, 3.1, 5.1, 6.1, 6.2, 6.3, 11.1, 14.1 and 14.4 of the 2021 Code.

RESPONSE

Sandoz stated that it took its responsibility in following the Code very seriously and would provide a complete and frank response to the PMCPA.

Sandoz responded to the concerns raised by the complainant and the Authority in the segments below.

Background and context of the Advanced Budgetary Notification (ABN) for the Sandoz natalizumab biosimilar (the 'Sandoz ABN')

Sandoz submitted that, in line with the guidance in the supplementary information to Clause 3.1, the purpose of the Sandoz ABN was to enable NHS organisations and others involved in the purchase of medicines to receive information about the introduction of a new biosimilar medicine that could significantly affect their level of expenditure.

The supplementary information to Clause 3.1 made it clear that non-promotional material could be provided as an ABN where it related to a product which contained an active substance prepared in a new way, such as by use of biotechnology. Biosimilars were prepared using biotechnology. Sandoz did not have access to information on the production process for the natalizumab reference product (brand name Tysabri which was sold by Biogen) and so had (through a third party) developed its own method of preparing the product. Sandoz submitted that its biosimilar product therefore contained an active substance prepared in a new way. In addition, prior to preparation of the Sandoz ABN, Sandoz received informal advice from the PMCPA who confirmed that ABNs for biosimilar products were permitted under the Code (with the usual caveats of items/activities being non-promotional in nature).

In preparation for the launch of the Sandoz natalizumab, and as required by the supplementary information to Clause 3.1, Sandoz submitted the necessary information/documentation to the national horizon scanning databases ahead of its ABN activities.

Sandoz prepared the following items for Sandoz ABN. Copies were provided to the Panel and described by Sandoz as follows:

1 Full ABN slide deck

- A non-promotional document.
- Presented only to individuals responsible for making policy decisions on budgets.
- The deck was not left behind or sent to those individuals that it was presented to by Sandoz.

2 Summarised ABN

- A non-promotional document.
- Outlined the salient points from the full ABN slide deck.
- Provided reactively (upon request) only to individuals that had seen the full ABN slide deck and so were responsible for making policy decisions on budgets.

3 Briefing documents for Sandoz Trained Appropriate Personnel (STAPs)

- Provided clear guidance on:
  - the nature and associated activities of the ABN (non-promotional)
  - the provision of information to the appropriate stakeholders i.e. only those that were responsible for making policy decisions on budgets
  - the separation of promotional and non-promotional calls.

4 Advanced Notification Confirmation Form

- This was used to obtain confirmation from the relevant stakeholders that they were responsible for making policy decisions on budgets before the ABN was presented.
- Once a signed confirmation form was received by Sandoz from the individual in question, the ABN slide deck was presented to the individual. The summarised ABN was provided reactively if a summary was requested by the individual.

Although the item mentioned by the complainant was not attached to the complaint, Sandoz assumed it was the summarised ABN. As stated above, this document was described by Sandoz as a non-promotional item sent reactively by the STAPs upon request after the full ABN deck had been presented.

Sandoz submitted that it provided clear and extensive briefings to the STAPs including verbal and non-verbal briefings as part of a series of training on the use of ABN material. The verbal briefings included guidance from the Compliance Manager at the time. The additional written briefing provided to the STAPs highlighted the separation of promotional and non-promotional calls (copy provided) when having discussions with stakeholders on the ABN. STAPs were briefed to only discuss the ABN with individuals responsible for making policy decisions on budgets (copy provided). It was prohibited to provide the information to prescribers unless they had confirmed by signing the Advanced Notification Confirmation Form that they also had budgetary responsibility.

Sandoz stated that, upon receiving the signed confirmation, the STAPs went through the full ABN slide deck with the individual that had provided the confirmation. The ABN slide deck demonstrated the potential impact of the introduction of Sandoz natalizumab. The slide deck was not sent to the individual that it was presented to or left behind (in hard copy, or otherwise).

Sandoz stated that:

'- none of the documents aimed to sell natalizumab to pharmacists or physicians
- only individuals responsible for making policy decisions on budgets were approached and those individuals confirmed that they were responsible for making policy decisions on budgets to Sandoz in writing
- all the documents described above were certified by our final medical signatory.'

The summarised ABN

Sandoz stated that many individuals responsible for making policy decisions on budgets, upon being presented with the full ABN requested a summary of the ABN. That being the case, an abridged version of the ABN was created by Sandoz to aid these individuals during their budgetary planning. Sandoz submitted that the summarised ABN was only made available upon request from the appropriate stakeholders, as explained above. Sandoz personnel did not use the ABN documents (full or summary version) as promotional items or promotional leavepieces that were used to sell the merits of the medicine or against its competitors.

Sandoz stated that the summarised ABN contained the following information:

'• The economic burden of multiple sclerosis
- Familiarisation with the stringency required for an introduction of a biosimilar
- Outlining the topline results of the bioequivalence studies for the Sandoz natalizumab biosimilar
- Confirmation that JCV testing shall be part of the Sandoz offering upon launch (JCV testing is provided to support the early detection of progressive multifocal leukoencephalopathy, as advised by the Medicines and Healthcare products Regulatory Agency https://www.gov.uk/drug-safety-update/natalizumab-tysabri-progressive-multifocal-leukoencephalopathy-updated-advice-to-support-early-detection)
- The potential projected costs savings with the introduction of Sandoz natalizumab.

Erroneous recipient of the summarised ABN

Sandoz noted that the complainant stated in the complaint that the summarised ABN document was presented to them by their Trust. Sandoz submitted, therefore, it was clear that the complainant was not the intended recipient of the summarised ABN and did not sign the Advanced Notification Confirmation Form. This meant that the complainant did not have the full context in which the material was intended to be used. In order for Sandoz to be able to provide further information, if needed, Sandoz requested clarification on the context in which the complainant received the ABN from their Trust.

Marketing authorisation for the Sandoz natalizumab

Sandoz shared the earliest date by which it was expecting to receive marketing authorisation of the natalizumab biosimilar – to be treated as confidential by the PMCPA.

Sandoz responses to complainant's concerns

Sandoz adopted the same numbering as used in the complaint in its responses below.

Complainant's Concern 1

'…Biosimilar development cost ranges between 150 and 300 million USD or higher…'

Sandoz submitted that the development of biosimilars was highly regulated by the European Medicines Agency and the European Commission. Strict criteria needed to be met, prior to the granting of marketing authorisation. Sandoz had extensive experience and heritage in biosimilars, and so could confidently state that development costs of a biosimilar medicine ranged between 150 and 300 million USD or higher depending on the complexity of the molecule.

Sandoz submitted that, unlike for some other disease areas where multiple biosimilar products were available, the introduction of a biosimilar in neurology was new; Sandoz natalizumab would be the first biosimilar in this therapy area. It was therefore considered necessary to provide basic information on biosimilars in general in the Sandoz ABN since the stakeholders to whom the Sandoz ABN was to be presented would not be familiar with biosimilars in this therapy area. Sandoz submitted that the information provided was educational rather than promotional and Sandoz considered that its inclusion was necessary, in this context, to provide an adequate account of the properties of Sandoz natalizumab as permitted by the supplementary information to Clause 3.1 of the Code.

Complainant's Concern 2

'…Evidence to suggest that savings from Sandoz natalizumab can result in reinvestment opportunities and greater patient access…'

Sandoz submitted that its natalizumab biosimilar was expected to be x% (figure provided) cheaper (at the conservative end) than the list price of the reference medicine. Therefore, it was realistically expected that the NHS could make potentially significant savings with the introduction of this biosimilar. The relevant policies of the NHS and any Trusts where decisions on formulary inclusion or the reinvestment of savings were concerned, fell within the remit of the budget holders of the respective organisations.

The information provided was not promotional and was provided to help the recipient assess the budgetary implications that Sandoz natalizumab might have on their organisation's expenditure as permitted by the supplementary information to Clause 3.1 of the Code.

Complainant's Concern 3

'…A detailed description of a phase III study to sell the medicine against the reference medicine…'

Sandoz submitted that the summarised ABN provided an objective summary of the efficacy and safety results (copies provided) of the Sandoz biosimilar demonstrating bioequivalence to the reference medicine. Sandoz submitted that the data was presented scientifically, and no promotional claims were made. The information presented made up a quarter of the second page of the summarised ABN and so Sandoz disagreed with the complainant's characterisation of this summary as a '*detailed description*' of the study. Sandoz stated that the demonstration of equivalence to the reference product was a legal requirement that must be met in order for a licence for a biosimilar product to be granted by a regulatory agency. The purpose of the study

was to compare the biosimilar against the reference medicine to show that it was equivalent, not to sell it against the reference medicine.

Sandoz submitted that, in line with the supplementary information to Clause 3.1, it had kept the information in the summarised ABN factual and limited to that sufficient to provide an adequate but succinct account of the biosimilar's properties. Since the product was a biosimilar, it was not possible to provide an account of its properties without mentioning the reference product.

Complainant's Concern 4

'…The document states boldly information regarding the final package….JVC testing will be part of the final package on launch to sell the future package that Sandoz will be providing when introducing the medicine.'

Sandoz submitted that, as explained above, JCV testing was provided to support the early detection of progressive multifocal leukoencephalopathy. JCV testing was currently provided free of charge by the manufacturer of the natalizumab reference product. Therefore, to ensure that Sandoz enabled stakeholders to prepare financially for the introduction of the natalizumab biosimilar, it was important to confirm that JCV testing would be part of the final package offered when the medicine was launched. The certainty on this point allowed the recipient of the information to understand what would be provided by Sandoz on launch, it served to aid the NHS budget holders in their planning and allowed them to understand their likely expenditure as permitted by the supplementary information to Clause 3.1 of the Code. Sandoz submitted that the information was not promotional and so disagreed with the complainant that its purpose was to sell the biosimilar.

Complainant's Concern 5

'…The price of the Sandoz natalizumab and the refence medicine are not stated in the document to provide clinicians with an objective understanding…'

Sandoz submitted that the list price of the biosimilar was not set at the point of commencement of the ABN activities; the pricing discussions with NHS England were confidential in nature. Thus, to provide a realistic picture of costs to the relevant stakeholders, Sandoz provided a pricing corridor with savings of 30%, 40% and 50% (reference provided). Sandoz believed this provided appropriate stakeholders with an illustrative view of the potential savings over the reference medicine within the pricing corridor.

Sandoz submitted that the information provided was appropriate to aid the recipient to understand the likely cost or savings and budgetary implications that the introduction of Sandoz natalizumab could provide as permitted by the supplementary information to Clause 3.1 of the Code.

Complainant's Concern 6

'…The only objective of this document appears to be exaggerating any savings benefits resulting from selling the Sandoz medicine when compared to the reference medicine…'

Sandoz submitted that the objective of the document (the summarised ABN), as stated above, was to allow individuals responsible for making policy decisions on budgets within the NHS to

plan adequately for the launch of the natalizumab biosimilar. The section on potential savings consisted of a quarter of page 2 of the summarised ABN. Sandoz submitted that it had not exaggerated the potential costs savings of the biosimilar; Sandoz provided the following within the summarised ABN (reference provided):

- Cost savings vs reference medicine, within 30%, 40% and 50% pricing corridor.
- Cost savings if the biosimilar was prescribed for 50 patients at the 30%, 40% and 50% pricing corridor.

Sandoz submitted that it provided an objective view of the potential cost savings, with a sample population (n=50). The final potential savings were clear and not misleading, readers could ascertain for themselves if the savings were meaningful or not. Therefore, Sandoz disagreed with the complainant that the objective of the ABN was to exaggerate the savings of the biosimilar. Moreover, Sandoz submitted that NHS and Trusts budget holders were familiar with similar representations of potential savings when discussing medicines that had yet to receive their marketing authorisation or a set list price. The information provided was therefore appropriate to aid the recipient to understand the likely cost or savings and budgetary implications that the introduction of Sandoz natalizumab could provide as permitted by the supplementary information to Clause 3.1 of the Code.

Complainant's Concern 7

'…The document did not consider all the evidence available in regard to natalizumab, in particular the availability of natalizumab (Tysabri) prefilled syringe which is administered subcutaneously…'

Sandoz submitted that the summarised ABN was not a promotional item. The reference product was only mentioned to put the new biosimilar into context in the therapy area and to confirm that the legal requirement to demonstrate equivalence to the reference product had been met.

Sandoz considered that including information about the availability of a competitor natalizumab product available as a pre-filled syringe would be inappropriate for an ABN. Such information would be relevant when looking to promote against competitor products, in the appropriate manner – i.e. through promotional material post granting of marketing authorisation.

Sandoz's comments on requirements of the clauses specified in the PMCPA letter

Sandoz had considered the clauses mentioned in the letter from the PMCPA and set out its response on each specific clause below.

Clause 3.1

(Advance Notification of New Products or Product Changes Which May Significantly Affect Expenditure)

Sandoz stated it believed that the Sandoz ABN met the requirements of Clause 3.1, for advanced budgetary notification as described in the supplementary information to Clause 3.1 as:

- the introduction of Sandoz natalizumab may significantly affect the expenditure of NHS organisations

- the information was directed only to individuals that met the specific criteria set out in the supplementary information to Clause 3.1. Sandoz took steps to ensure that the individuals that the Sandoz ABN was presented to had confirmed in writing that they met the criteria
- non-promotional information that was provided:
    - related to the biosimilar
    - contains an active substance prepared in a new way, by the use of biotechnology.'

Therefore, Sandoz denied any breach of Clause 3.1.

Clause 6.1

(*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 recipients to form their own opinion of the therapeutic value of the medicine.)*

Sandoz submitted that, as explained in greater detail above, the ABN documents presented data in a non-promotional, balanced and objective manner. Sandoz did not exaggerate the merits of the natalizumab biosimilar.

Sandoz submitted that, unlike for some other disease areas where multiple biosimilar products were available, the introduction of a biosimilar in neurology was new; Sandoz natalizumab would be the first biosimilar in this therapy area. It was therefore considered necessary to provide basic information on biosimilars in general in the Sandoz ABN since the stakeholders to whom the Sandoz ABN was to be presented would not be familiar with biosimilars in this therapy area. The information provided was educational rather than promotional and Sandoz considered that its inclusion was necessary, in this context, to provide an adequate account of the properties of Sandoz natalizumab as permitted by the supplementary information to Clause 3.1 of the Code.

Sandoz submitted that the bioequivalence study was clearly presented without the addition of promotional claims. In line with the supplementary information to Clause 3.1, Sandoz stated it had kept the information in the summarised ABN factual and limited to that sufficient to provide an adequate but succinct account of the biosimilar's properties.

Thus, Sandoz denied any breach of Clause 6.1.

Clause 6.2

(Any information, claim or comparison must be capable of substantiation)

Sandoz submitted it had provided substantiation for all the information available within the summarised ABN. Sandoz included the necessary references in the Annexes to its response. Sandoz denied any breach of Clause 6.2.

Clause 6.3

(All artwork, including illustrations, graphs and tables, must conform to the letter and spirit of the Code and, when taken from published studies, a reference must be given.
Graphs and tables must be presented in such a way as to give a clear, fair, balanced view of the matters with which they deal and must not be included unless they are relevant to the claims or comparisons being made.)

Sandoz submitted that the pertinent information from the bioequivalence studies was provided in summarised ABN to aid the recollection of the reader. The information was presented in a clear, fair and balanced manner. The associated artwork and graphs in the summarised ABN were representative of the data of the bioequivalence trials; therefore, Sandoz denied any breach of Clause 6.3.

Clause 11.1

(A medicine must not be promoted prior to the grant of the marketing authorisation which permits its sale or supply)

Sandoz submitted that both the full and summarised ABN materials were non-promotional, and the processes and guidance put in place by Sandoz demonstrated that they were not used for promotion, therefore they were out of the scope of Clause 11.1. The materials were created to facilitate budgetary discussions with appropriate individuals responsible for making policy decisions on budgets. Sandoz strongly believed that it had met the requirements of Clause 3.1 and had delivered the ABN in the appropriate manner. Sandoz submitted that no promotional claims were made on the materials, only factual data was presented to the reader. Sandoz, therefore, believed that it had not breached Clause 11.1.

Clause 14.1

(A comparison is only permitted in promotional material if:

- it is not misleading
- medicines or services for the same needs or intended for the same purpose are compared
- one or more material, relevant, substantiable and representative features are compared
- no confusion is created between the medicine advertised and that of a competitor or between the advertiser's trademarks, brand names, other distinguishing marks and those of a competitor
- the trademarks, brand names, other distinguishing marks, medicines, services, activities or circumstances of a competitor are not discredited or denigrated
- no unfair advantage is taken of the reputation of a trademark, brand name or other distinguishing marks of a competitor
- medicines or services are not presented as imitations or replicas of goods or services bearing a competitor's *trademark or brand name)*

Sandoz believed that the ABN material did not fall under the category of promotional material, and therefore was out of scope for Clause 14.1. Sandoz submitted that the materials were created to facilitate budgetary discussions with appropriate individuals responsible for making policy decisions on budgets. Sandoz strongly believed that it had met the requirements of Clause 3.1 and had delivered the ABN in the appropriate manner. Sandoz submitted that a

comparison to another product was made purely to demonstrate that the biosimilar was equivalent to the reference product which was a legal requirement for obtaining a biosimilar licence. Sandoz stated that it had provided clear, objective information and had not disparaged a competitor. Thus, Sandoz denied any breach of Clause 14.1.

Clause 14.4

(Promotion must encourage the rational use of a medicine by presenting it objectively and without exaggerating its properties. Exaggerated or all-embracing claims must not be made and superlatives must not be used except for those limited circumstances where they relate to a clear fact about a medicine. Claims should not imply that a medicine or an active ingredient has some special merit, quality or property unless this can be substantiated.)

Sandoz submitted that the ABN materials were non-promotional, therefore were out of the scope of Clause 14.4. The materials were created to facilitate budgetary discussions with appropriate individuals responsible for making policy decisions on budgets. Sandoz strongly believed that it had met the requirements of Clause 3.1 and had delivered the ABN in the appropriate manner. No promotional claims were made in the ABN materials and therefore Sandoz did not believe they had breached Clause 14.4.

Clause 5.1

(High standards must be maintained at all times)

Given the evidence and explanations provided by Sandoz, they strongly believed that they had maintained high standards during the course of delivering the ABN information to appropriate stakeholders – therefore no breach of Clause 5.1 according to Sandoz.

Clause 2

(Upholding Confidence in the Industry)

Sandoz stated that it took its responsibility in upholding the Code extremely seriously. Sandoz stated that it had met the requirements for ABN activities and had taken precautionary measures to ensure that only the appropriate individuals received the correct information to aid with budgetary planning and forecasting. Sandoz submitted it believed this was a particular censure and strongly believed that it had not breached Clause 2.

Summary

Sandoz stated that it took its obligations under the Code very seriously and strove to hold its activities to the highest standards. Sandoz stated that it had ensured that its ABN activities were in line with Clause 3.1 of the Code. The complainant was never the intended recipient of the full or summarised ABN, as they did not meet the pre-requisite requirements to receive such material. Sandoz petitioned that the complaint be taken no further, given the above rationale.

PANEL RULING

The Panel noted the complainant, who described themselves as a neurology physician, alleged that their Trust had presented them with an advance budgetary notification (ABN) document for

the introduction of a natalizumab biosimilar from Sandoz for the treatment of multiple sclerosis. The Panel noted Sandoz's query about how the complainant had received the document, as they were not the intended recipient.

It appeared to the Panel that Sandoz personnel were briefed to ensure that individuals initially verified they had budgetary responsibility by signing an 'advanced notification confirmation form', following which they could be presented with ABN information in the form of a slide deck. The Panel noted from the briefing information that Sandoz personnel could offer to email a two-page summarised ABN document or could email the full ABN slide deck presented if it was explicitly requested.

While the Panel noted Sandoz based its submission on the summary document and that the majority of the description and cited wording in the complaint matched the summary document, the Panel noted one phrase cited by the complainant only appeared in the full slide deck and not in the summary document ('Biosimilar manufacturing requires state-of-the-art technologies, and expertise'). Another phrase cited by the complainant only appeared in the summary document and not in the full slide deck ('Biosimilar products demonstrate a high similarity to a reference medicine based on comprehensive comparability studies'). It appeared to the Panel, therefore, that the complainant had access to both materials. Noting that the intended audience could have been sent either or both documents, as outlined above, the Panel based its rulings on the two documents accordingly.

The full ABN slide deck comprised 13 slides, excluding the title slide and thank you slide. The first four slides provided background on multiple sclerosis, covering the economic burden, unmet needs and the treatment algorithm for disease-modifying therapies. There was one slide on biosimilar development. The Sandoz natalizumab biosimilar was introduced on slide 7, followed by three slides of clinical efficacy and safety data from a Phase III study. There were two slides with graphs illustrating potential cost savings from the biosimilar, a slide listing potential benefits, and a summary slide.

The summary document, entitled 'Natalizumab – Advance Budgetary Notification' was a two-page document. The first page included two sections: 'Multiple sclerosis economic burden' and 'Proposed natalizumab biosimilar'. The second page included information on the clinical efficacy of the biosimilar compared to the reference natalizumab, information on the indication of the reference natalizumab, graphs illustrating potential cost savings from the biosimilar, and a bullet-pointed summary.

The complainant alleged that 'the document' was promotional in nature and that the information in it did not fulfil the criteria for advance notification as set out in the Code.

The supplementary information to Clause 3.1, Advance Notification of New Products or Product Changes Which May Significantly Affect Expenditure, stated NHS organisations and others involved in the purchase of medicines need to estimate their likely budgets in advance, so there is a need for them to receive advance information about the introduction of new medicines or changes to existing medicines which may significantly affect their level of expenditure, including that which might arise from changes in the patient pathway and/or service delivery.

The Panel noted the list of points in the supplementary information to Clause 3.1 cited by the complainant (that an ABN must relate to a product which contains a new active substance, or; contains an active substance prepared in a new way, such as by the use of biotechnology, or; is

to have a significant addition to the existing range of authorised indications, or; is to have a novel and innovative means of administration).

The Panel considered from Sandoz's submission that its advance notification related to a biosimilar product that contained an active substance prepared in a new way; the product had not yet been granted a marketing authorisation and Sandoz had made efforts to ensure that the document was received only by individuals responsible for making policy decisions on budgets.

In the Panel's view, the advance notification of a biosimilar product was, in principle, appropriate. The Panel had to consider whether the circumstances of this case meant that the information provided went beyond the provisions for advance budgetary information set out in the supplementary information to Clause 3.1, as alleged. If any of the conditions were not met, then the proactive provision of information of the unauthorised medicine or indication was likely to be seen as promotion contrary to the requirements of Clause 3.

Complainant's point 1

The Panel noted the sections at issue were page 1 of the summary document beneath the title 'Proposed natalizumab biosimilar' and on slide 6 of the full ABN titled 'The high upfront investments and production costs are raising the bar for biosimilar development'.

The relevant sections of each document each included the statement 'Biosimilar development cost ranges **between 150 and 300 million USD or higher**, depending on the nature/complexity of the molecule. The research and manufacturing is a complex procedure as it is based on living organisms, tissues, or cells' (emphasis in the material). Each document also included the same graphic with text outlining the process steps involved in biosimilar development, from physicochemical characterisation to manufacturing and delivery; within the manufacturing and delivery section were additional graphics beneath the title 'expertise needed during biosimilar manufacturing'.

The Panel noted the complainant raised allegations regarding the inclusion of statements about the value of biosimilars in general and the expertise required for developing biosimilars and the allegation that this information was presented 'to sell the value of the biosimilar medicine against the reference medicine'.

The Panel noted Sandoz's submission that it was necessary to provide basic information on biosimilars in general because the introduction of a biosimilar in neurology was new and stakeholders would not be familiar with biosimilars. While the Panel considered the provision of limited information regarding biosimilars was not necessarily unacceptable, the Panel noted the requirements of Clause 3.1 that information provided was 'limited to that sufficient to provide an adequate but succinct account of the product's properties' and 'to put the new product or indication into context in the therapeutic area concerned'.

The Panel queried the suitability of the use of the language in the phrases cited by the complainant: 'Biosimilar manufacturing requires state-of-the-art technologies, and expertise', 'complex procedure' and 'Biosimilar development cost ranges **between 150 and 300 million USD or higher**'. In particular, the latter statement was highlighted in bold which, in the Panel's view, could not be seen as anything as other than drawing the reader's attention to the costs incurred by Sandoz.

In this regard, the Panel did not consider the inclusion of the cost and required expertise associated with biosimilar development in each material was necessary to enable the reader to assess the likely impact on their budget. The Panel therefore ruled **a breach of Clause 3.1**, in relation to the full ABN slide deck and summarised ABN document. The Panel considered the requirements of Clause 11.1 were adequately covered by the breach of Clause 3.1 and therefore ruled **no breach of Clause 11.1**.

Complainant's point 2

The Panel noted the complainant raised allegations about two bullet points that were present within the 'summary' section of the summary ABN document and ruled on this document accordingly. The complainant alleged that the summary point 'Biosimilar products demonstrate a high similarity to a reference medicine based on comprehensive comparability studies' continued to sell Sandoz's medicine, and that there was no evidence for the point 'Sandoz natalizumab provides HCPs and payers with an affordable option to expand patient access and enable reinvestment opportunities to ensure sustainability in healthcare systems'.

In relation to the first point, the Panel considered mention of similarity to the reference product provided contextual information to the rationale for using a biosimilar. In this regard, the Panel ruled **no breach of Clauses 3.1 and 11.1**.

In relation to the second point, the Panel noted that the statement appeared directly above the graphical representations of the anticipated cost savings. It further noted the specific wording used in the summary ABN document ('Sandoz natalizumab provides …') and that Sandoz's medicine was awaiting marketing authorisation. In the Panel's view, reference to 'Sandoz natalizumab', rather than biosimilars broadly, implied there was evidence that Sandoz's medicine specifically had demonstrated it would provide HCPs and payers with an affordable option to expand patient access and enable reinvestment opportunities, which was unlikely to be so. The Panel queried the use of the term 'affordable', which it noted was subjective and queried whether this could be substantiated. The Panel considered that the summary point at issue was, on the evidence available, incapable of substantiation and, on balance, ruled **a breach of Clause 6.2** for the summary ABN document.

Complainant's point 3

The Panel noted the allegation that 'a detailed description of a phase III study' had been provided 'to sell the medicine against the reference medicine'. According to Sandoz's submission, this was provided as 'an objective summary' to demonstrate bioequivalence to the reference medicine and no promotional claims were made. In relation to the summary document, the Panel noted there were graphics utilised to explain the study design and results of the study, with two bullet points each for results and safety demonstrating comparable results with the reference product. The Panel considered that the information presented in the relevant section of the summary document was, on balance, limited to that sufficient to provide a succinct account of the biosimilar's equivalence to the reference product. The Panel therefore ruled **no breach of Clauses 3.1 and 11.1** in relation to the summary document.

The Panel noted the slides in the full ABN included more information on the phase III study than was included in the summary document. There were three detailed slides covering the study design, clinical efficacy data, and safety data. In the Panel's view, the detailed provision of clinical data went beyond a succinct account of the product's properties and could not be seen

as anything other than promotion. Noting that the product did not have a marketing authorisation, the Panel ruled **a breach of Clause 3.1**, in relation to the full ABN slide deck. The Panel considered the requirements of Clause 11.1 were sufficiently covered by the breach of Clause 3.1 and therefore ruled **no breach of Clause 11.1**.

Complainant's point 4

The Panel noted both materials stated that JC Virus (JCV) testing would be part of the final package; the complainant alleged this to be promotional. In the Panel's view, it was important for readers involved in making budgetary decisions to understand whether to factor in additional costs for testing when adopting the biosimilar product, noting Sandoz's submission that the manufacturer of the reference product also provided JCV testing free of charge and that the MHRA had advised Sandoz to provide JCV testing to support the early detection of progressive multifocal leukoencephalopathy. The Panel did not consider that reference to the inclusion of testing in the final package was promotional in itself, in this context, and the Panel therefore **no breach of Clauses 3.1 and 11.1** in relation to both documents.

Complainant's points 5 and 6

The Panel noted the complainant's allegations that the prices of the Sandoz biosimilar and reference medicine were not stated to provide clinicians with an objective understanding and that the cost savings were negligible and did not represent any significant savings against the overall NHS expenditure on medicines of around £17 billion. The complainant further highlighted a graph illustrating potential savings of £14.5m to £24.3m based on discounts of 30%, 40% or 50% compared to the reference medicine. The complainant alleged the lack of exact discount to help with calculating any possible budget savings, if any, meant that such key information was open for interpretation and exaggerated any savings.

The Panel noted Sandoz's submission that the list price of the biosimilar was not set at the point of commencement of ABN activities and that pricing discussions with NHS England were confidential. The Panel noted Sandoz's submission that the ABN included a 'pricing corridor' with savings of 30%, 40% and 50% to provide an illustrative view of the potential savings compared to the reference medicine and aid understanding of the likely budgetary implications, as permitted by the supplementary information to Clause 3.1. Both the full ABN and the summary version included illustrations of the projected cost savings for Trusts and nationally. Noting the impact of each percentage saving was nonetheless presented, the Panel considered it was not unreasonable to present likely budgetary implications based on such sensitivity analyses when the list price of the new product was not yet available. The Panel therefore ruled **no breach of Clauses 6.1, 6.3 and 14.4** of the Code in relation to each document.

Complainant's point 7

The Panel noted the complainant's allegation that the cost comparison was unbalanced as it did not include all the evidence available, particularly the impact of the availability of a prefilled syringe for the reference natalizumab which allegedly required less resource for administration leading to significant amount of savings for the NHS. The Panel noted Sandoz submitted that such information about the reference product would be inappropriate for an ABN; Sandoz made no comment in relation to the cost differences between the methods of administration.

Nonetheless, the Panel noted that the complainant bore the burden of proof and considered the complainant had not established their case that the omission of information regarding the costs of administration methods meant the cost comparison was unbalanced. The Panel therefore ruled **no breach of Clause 14.1** in relation to both documents.

Comments about the timing of the ABN in the complainant's closing comments

The Panel noted the complainant stated that there was insufficient time for the hospital trust to assess or adjust any budget implication, given the limited time available between the receipt of this ABN and the anticipated introduction of the medicine.

The Panel noted that the supplementary information to Clause 3.1 stated, among other things, when advance notification information was required, the medicines concerned would not be the subject of marketing authorisations although applications will often have been made; in this regard, the Panel noted there was no explicit period of time for the advance notification to be given.

The Panel noted Sandoz's submission that the necessary information was submitted to the national horizon scanning databases in March 2022, ahead of its ABN activities. While Sandoz provided the anticipated date of marketing authorisation, the Panel was not aware of a likely launch date. Noting that the complainant bore the burden of proof, the Panel considered it had not been established that the timing of the ABN was inappropriate such that it was contrary to the requirements for advance notification as listed in the supplementary information of Clause 3.1. The Panel therefore ruled **no breach of Clause 3.1**.

High standards

Bearing in mind all of the points above, the Panel considered that, on the balance of probabilities, the materials had not met the requirements for advance notification and had amounted to the promotion of natalizumab before the grant of a marketing authorisation. In that regard, the Panel considered that Sandoz had failed to maintain high standards and **a breach of Clause 5.1** was ruled.

The panel noted that the supplementary information to Clause 2 stated that one of the activities likely to be in breach of that clause was the promotion of a medicine prior to the grant of a marketing authorisation. The Panel considered each case on its own merits. In this instance, it noted that the notification of a biosimilar product was, in principle, appropriate and that the circumstances of this case, on the balance of probabilities, did not warrant a ruling of Clause 2, which was a sign of particular censure and reserved for such use. The Panel therefore, on balance, ruled **no breach of Clause 2**.

* * * * *

Since this complaint was received, Sandoz has confirmed that it will no longer accept the jurisdiction of the PMCPA. Following notification of the Panel's rulings, Sandoz stated that it did not accept the Panel's rulings of breaches of the Code but did not wish to appeal the Panel's rulings. Should Sandoz choose to re-join the PMCPA's jurisdiction, it would be required to settle the full balance of administrative charges and provide a full undertaking and assurance. The complainant and the Medicines and Healthcare products Regulatory Agency (MHRA) were informed of the position.

Complaint received	**11 May 2023**
Sandoz withdrew its agreement to comply with the Code and accept the jurisdiction of the PMCPA	**18 October 2023**
Case completed	**23 February 2024**