CASE AUTH/3649/5/22

ANONYMOUS HEALTH PROFESSIONAL v DAIICHI SANKYO

SMC Guidelines card for Nilemdo and Nustendi

CASE SUMMARY

This case was in relation to a Scottish Medicines Consortium (SMC) Guidelines summary card for Nilemdo (bempedoic acid) and Nustendi (bempedoic acid and ezetimibe), produced as promotional material by Daiichi Sankyo.

The Panel ruled a breach of the following Clauses of the 2021 Code for failing to make immediately apparent to health professionals in the body of promotional material, which referred to the therapeutic use of Nilemdo or Nustendi in combination with a statin, that there was a contraindication regarding concomitant use with simvastatin >40mg daily, and for failing to comply with an undertaking given in Case AUTH/3504/4/21:

Breach of Clause 3.3	**Failure to comply with an undertaking**
Breach of Clause 6.1	**Misleading impression provided**
Breach of Clause 5.1	**Failure to maintain high standards**
Breach of Clause 2	**Bringing discredit upon, and reducing confidence in, the pharmaceutical industry**

The Panel ruled no breach of the following Clauses of the 2021 Code as the complainant had not established that the material was incapable of substantiation nor that the omission in the body of the material of the contraindication for Nustendi when co-administered with a statin in patients with active liver disease or unexplained persistent elevations in serum transaminases meant the material was misleading, given the material did not imply there were no liver disease considerations:

No Breach of Clause 6.1	**Requirement that claims must not be misleading**
No Breach of Clause 6.2	**Requirement that claims must be capable of substantiation**

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 health professional complained about a Guidelines card which documented SMC guidance on Nilemdo (bempedoic acid) and Nustendi (bempedoic acid and ezetimibe) (BEM/21/0732, December 2021).

COMPLAINT

The complainant stated that the production and printing of this Guidelines summary card had been commissioned and funded by Daiichi Sankyo UK. Daiichi Sankyo UK had reviewed the card for technical accuracy and regulatory compliance. It was 4 pages in total with the first 2 pages discussing SMC recommendations for use of Nilemdo and Nustendi.

The complainant alleged the following text presented on the Nilemdo page 1 was misleading and not in line with licence:

> 'Indication under review: in adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet:
>
> - In combination with a statin, or a statin with other lipid-lowering therapies in patients unable to reach low-density lipoprotein cholesterol (LDL-C) goals with the maximum tolerated dose of a statin.'

The complainant further alleged the following text on the Nustendi page 2 was misleading and not in line with licensed indication:

> 'Indication under review: in adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet:
>
> - in combination with a statin in patients unable to reach LDL-C goals with the maximum tolerated dose of a statin in addition to ezetimibe.'

The complainant stated that both Nilemdo and Nustendi were contraindicated with simvastatin >40mg.

The complainant further stated that Nustendi was also contraindicated for the following: adult patients co-administered with a statin in patients with active liver disease or unexplained persistent elevations in serum transaminases. Even the summary of product characteristics (SPCs) for both products clearly referenced seeing Sections 4.2, 4.3, and 4.4 for information on contraindications within the licensed indication section so that information on simvastatin was clear. The complainant alleged these key points around contraindications were not mentioned anywhere on either page 1 or 2.

The complainant alleged that the impression that the guidelines card gave was a definitive risk to patient care and patient safety as it implied Nilemdo and Nustendi could be added to any statin therapy without any qualification around the challenges with simvastatin >40mg; the contraindication information should have been made clear directly next to the claims discussing combining Nilemdo and Nustendi with a statin.

The complainant alleged that this was also a breach of undertaking as in Case AUTH/3504/4/21, the Panel had found Daiichi Sankyo in breach for the same issue. The complainant cited Case AUTH/3504/4/21, point 4 as follows:

> 'In the Panel's view, given Nilemdo and Nustendi's therapeutic indications, the contraindication regarding concomitant use with simvastatin >40mg daily needed to be immediately apparent to health professionals in promotional material which referred to adding on to existing oral lipid-lowering treatments. The Panel considered the immediate and overall impression of the claim at issue to a busy health professional. The Panel considered that the claim was misleading; read in isolation it implied that Nilemdo and

> Nustendi could be added to any existing oral lipid lowering treatments which was not so; the medicines were contraindicated with simvastatin >40mg daily. The claim could not stand alone and the Panel therefore ruled a breach of the Code. The Panel noted that the misleading impression could not be substantiated and a breach of the Code was ruled.'

The complainant alleged that in relation to this SMC card, the misleading claims were identical to the previous case and in breach of Clauses 6.1, 6.2, 3.3, 5.1 and 2.

When writing to Daiichi Sankyo, the Authority asked it to consider the requirements of Clauses 6.1, 6.2, 3.3, 5.1 and 2 of the Code.

RESPONSE

Daiichi Sankyo UK stated that it took its obligations under the Code seriously and strove to maintain high standards and to behave responsibly and ethically at all times. Daiichi Sankyo submitted it denied the allegations made by the complainant, as outlined below.

For background information, Daiichi Sankyo confirmed that 'a Guidelines card' which the complainant referred to, was a SMC summary card entitled 'MGP SMC summary card – electronic' (Job code: BEM/21/0732, Date of prep: December 2021) and was launched in December 2021. The summary card was available for General Practitioners (GPs), Payors and Policy makers who were registered to the Guidelines website which was intended for UK health professionals. The SMC summary card was scheduled to be removed in July 2022. The intention of the material was to provide a summary of the guidance as outlined by SMC2363 and SMC2406 on the use of bempedoic acid (alone) and bempedoic acid with ezetimibe (fixed-dose combination) for treating primary hypercholesterolemia or mixed dyslipidaemia. The information provided in the summary card was cited directly from the recommendations outlined in the relevant sections within SMC2363 and SMC2406. It did not include any further information, claims or comparisons that would require additional substantiation other than what was provided on the piece.

Daiichi Sankyo addressed each of the allegations in sequential order in the format as presented by the complainant.

Allegation 1:

> 'The following text presented on the Nilemdo page 1 was misleading and not in line with licence: Indication under review: in adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet: • In combination with a statin, or a statin with other lipid-lowering therapies in patients unable to reach low-density lipoprotein cholesterol (LDL-C) goals with the maximum tolerated dose of a statin. The following text on the Nustendi page 2 was misleading and not in line with licensed indication: Indication under review: in adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet: • in combination with a statin in patients unable to reach LDL-C goals with the maximum tolerated dose of a statin in addition to ezetimibe.'

Daiichi Sankyo refuted the allegation that the indication under review was misleading and not in line with licence. Daiichi Sankyo submitted that the guidelines card cited the licensed indications stated within the advice published in SMC2363 and SMC2406 and reflected the

licensed indications stated within the respective SPCs for both Nilemdo and Nustendi, therefore it did not mislead.

Allegation 2:

> 'Both Nilemdo and Nustendi were contraindicated with Simvastatin >40mg. Furthermore, Nustendi was also contraindicated for the following: adult patients co-administered with a statin in patients with active liver disease or unexplained persistent elevations in serum transaminases. Even the SPCs for both products clearly referenced seeing see sections 4.2, 4.3, and 4.4 for information on contra-indications within the licensed indication section so that information on Simvastatin was clear. These key points around contra-indications were not mentioned anywhere on either page 1 or 2.'

Daiichi Sankyo submitted that the information within the advice section of the 'SMC Summary Card' was a direct extrapolation from the SMC advice published for both products. It adhered to the request from the SMC that 'No part of this advice may be used without the whole of the advice being quoted in full' (SMC2363 & SMC 2406) copy provided. The language therefore had not been adapted and was specific to the advice for each product and this information formed the basis of the content included on pages 1 and 2 of the SMC summary Card.

Daiichi Sankyo submitted that the information pertaining to 'sections 4.2, 4.3, and 4.4' that the complainant referred to, formed part of the wording within the SPC for both Nilemdo and Nustendi. The purpose of this information was to refer those readers of the SPC to additional information within these subsections in its entirety.

Daiichi Sankyo submitted that the sections to which the complainant referred were listed as: 4.1 Therapeutic indications, 4.2 Posology and method of administration, 4.3 Contraindications and section 4.4 Special warnings and precautions for use within both the SPC for Nilemdo and Nustendi. Daiichi Sankyo believed that it was not a Code requirement to include the entire information contained within these sections of the SPC within promotional materials when stating the licensed indication. Instead, Daiichi Sankyo believed it was required to include the pertinent sections as a summary in the prescribing information.

Daiichi Sankyo submitted the information that was contained within Sections 4.2, 4.3 and 4.4 of the SPC had been provided as part of the prescribing information for both Nilemdo and Nustendi and this could be found on pages 3 and 4 of this SMC Summary Card. The indications and information outlined in the prescribing information provided within the material, within the body of the SMC summary card and SMC2363 and SMC2406, were all in line and consistent with the SPC for both products.

Daiichi Sankyo submitted that the prescribing information, which had been clearly signposted at the bottom of pages 1 and 2 (figure 1 below) and was available on pages 3 and 4 of the document, provided information in line with the requirements of the Code, including 'Contraindications' for use of both Nilemdo and Nustendi, respectively. Under the heading 'Contraindications' for both products, the statement 'concomitant use with simvastatin >40mg daily' could be found. Under the heading 'Contraindications' for Nustendi the statement 'coadministration with statin in patients with active liver disease or unexplained persistent elevations in serum transaminases; when Nustendi is coadministered with a statin, consult the SmPC for that particular statin therapy' was included.

Daiichi Sankyo submitted that the 'Contraindications' heading, as well as all relevant information headings in the prescribing information, were emphasised prominently in bold font, so that the audience could easily locate the information they might require. In addition, there was a statement at the top of the prescribing information directing the reader to 'Refer to the Summary of product of characteristics (SmPC) prior to prescribing'.

Daiichi Sankyo submitted that clear instructions on the location of the prescribing information was provided with a clear and prominent statement on the bottom of page 1 and 2 of the SMC summary card directing readers to the prescribing information on pages 3 and 4. Therefore, Daiichi Sankyo also disagreed with the complainant's allegation suggesting that text on page 1 and 2 was misleading.

Daiichi Sankyo stated that, furthermore, in recognition that this was a 'SMC Summary Card', there was a clear, prominent box highlighted in purple, underneath the SMC2363 and SMC2406 guidance advising the audience to refer to the full guidance: 'This summary card only displays the concise guidance; readers are strongly advised to refer to the full guidance for both products at https://www.scottishmedicines.org.uk/medicines-advice/bempedoic-acid-nilemdo-resub-smc2363/ https://www.scottishmedicines.org.uk/medicines-advice/bempedoic-acidezetimibe-nustendi-abb-smc2406/'.

Allegation 3:

> 'The impression that the guidelines card gave were a definitive risk to patient care and patient safety as it implied Nilemdo and Nustendi could be added to any statin therapy without any qualification around the challenges with Simvastain at >40mg.'

Daiichi Sankyo stated that, as outlined previously in its response, the information contained within the 'SMC Summary Card' was taken directly from the SMC2363 and SMC2406 published advice, which in turn had been based on the licensed indication for both Nilemdo and Nustendi. The section to which the complainant referred 'indication under review' was reflective of the licensed indications for both Nilemdo and Nustendi. This was factual information referenceable to the licensed indications for both products and reflected the published SMC advice for both products.

Daiichi Sankyo submitted that prescribing Information had been provided as part of this promotional material which contained information under 'Contraindications' listed for both Nilemdo and Nustendi and included a clear statement on concomitant use with Simvastatin >40mg daily.

Daiichi Sankyo disagreed with the complainant's allegation that this represented a definitive risk to patient care and patient safety as the company had provided supplementary information contained within the prescribing information to complement and further support the information available on the SMC website. In addition, Daiichi Sankyo had included a statement for health professionals to 'Refer to the Summary of product of characteristics (SmPC) prior to prescribing'.

Allegation 4:

> 'The contraindication information should have been made clear directly next to the claims discussing combining Nilemdo and Nustendi with a statin. This was also a breach of undertaking as in case AUTH/3504/4/21, the panel had found Daiichi Sankyo in breach for

> the same issue. In case AUTH/3504/4/21, point 4 commentary was as follows: In the Panel's view, given Nilemdo and Nustendi's therapeutic indications, the contraindication regarding concomitant use with simvastatin >40mg daily needed to be immediately apparent to health professionals in promotional material which referred to adding on to existing oral lipid-lowering treatments. The Panel considered the immediate and overall impression of the claim at issue to a busy health professional. The Panel considered that the claim was misleading; read in isolation it implied that Nilemdo and Nustendi could be added to any existing oral lipid lowering treatments which was not so; the medicines were contraindicated with simvastatin >40mg daily. The claim could not stand alone and the Panel therefore ruled a breach of the Code. The Panel noted that the misleading impression could not be substantiated and a breach of the Code was ruled.'

Daiichi Sankyo stated the breach highlighted in Case AUTH/3504/4/21 and associated undertakings, related to the use of a promotional claim, which referred to 'adding on Nilemdo or Nustendi to existing oral lipid-lowering treatments' and the need for clarity around concomitant use with simvastatin >40mg when appropriate.

As a result of Case AUTH/3504/4/21, Daiichi Sankyo had implemented the following steps and processes below:

i) Immediately withdrew the website that was the subject of the original complaint
ii) Conducted a full review of Nilemdo/Nustendi promotional materials to ensure other materials potentially affected were identified
iii) Conducted a recall of all materials impacted and replaced them with revised content making the simvastatin contraindication disclaimer clear where required
iv) Briefed relevant Daiichi Sankyo staff on the case findings, implications and learnings
v) Updated all internal documents to reflect the changes and requirements for promotional materials as a result of the case findings.

Daiichi Sankyo submitted that the content of the SMC Summary Card did not apply to this undertaking. The information on the SMC summary card had been cited directly from the SMC2363 and SMC2406 advice and did not include any claims or comparisons which might require additional information for substantiation. Daiichi Sankyo submitted it was not a Code requirement to list the contraindications of the said products when stating the licensed indication. Prescribing information had been included as part of this promotional material and contained the contraindications as required. Daiichi Sankyo submitted it had taken all necessary steps to comply with the undertakings as a result of Case AUTH/3504/4/21 as described above.

Allegation 5:

> 'The following clauses had been breached, 6.1, 6.2, 3.3, 5.1 and 2.'

Daiichi Sankyo refuted the allegation that this item breached Clauses 6.1 or 6.2. The item was balanced, fair, objective, unambiguous and based on the most up-to-date advice from the SMC (SMC2363 and SMC2406) on Daiichi Sankyo's products. The item had sufficient information to enable the reader to form their own opinion of the therapeutic value of the medicines and did not mislead. The information on the SMC Summary Card had been cited directly from the SMC2363 and SMC2406 advice, which were readily accessible and did not include any claims or comparisons which might require additional information for substantiation. The SMC

Summary Card had been reviewed and certified to ensure consistency with both the Nilemdo and Nustendi licence indications.

Daiichi Sankyo stated that it disagreed with the allegation of a breach of Clause 3.3 as Daiichi Sankyo UK had taken all the necessary steps to ensure that compliance with the undertakings related to Case AUTH/3504/4/21 had occurred. As communicated earlier in its response, Daiichi Sankyo submitted this material did not contain any promotional claims or comparisons and therefore the undertakings referenced above did not apply. As there had been no breach of Clauses 6.1, 6.2 and 3.3, there was no evidence that high standards had not been maintained and no breach of Clause 5.1. Consequently, Daiichi Sankyo submitted there was no evidence it had prejudiced patient safety and thus no breach of Clause 2.

Conclusion

Daiichi Sankyo stated that the company had acted in line with the requirements of the Code, maintained high standards, and had not brought discredit upon, or reduced confidence in, the industry.

PANEL RULING

The Panel noted the material at issue was an electronic Scottish Medicines Consortium (SMC) summary Guidelines card, which consisted of four pages and had been commissioned and funded by Daiichi Sankyo UK. The first page discussed Nilemdo (bempedoic acid), the second page discussed Nustendi (bempedoic acid and ezetimibe) and the last two pages contained prescribing information for Nilemdo and Nustendi, respectively.

The Panel noted that each summary guidelines page for Nilemdo and Nustendi had the sub-heading 'Advice: following a resubmission' and 'Advice: following an abbreviated submission', respectively. Beneath each subheading was the statement that both medicines were accepted for restricted use within NHS Scotland, along with two further subheadings 'Indication under review' and 'SMC restriction'. The 'Indication under review' section included the full indications for Nilemdo and Nustendi, whereas the 'SMC restriction' was narrower than the full indications.

For example, the summary card for Nilemdo stated:

> *'**Indication under review:** in adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet:*
>
> - *In combination with a statin, or a statin with other lipid-lowering therapies in patients unable to reach low-density lipoprotein cholesterol (LDL-C) goals with the maximum tolerated dose of a statin or*
> - *Alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contra-indicated.*
>
> *SMC restriction: for use in combination with ezetimibe in patients who are:*
>
> - *statin intolerant or for whom a statin is contra-indicated and*
> - *where ezetimibe alone does not appropriately control LDL-C and*
> - *where proprotein convertase subtilisin/ kexin type 9 (PCSK9) inhibitors are not appropriate.'*

The Panel noted that the complainant referred to Nilemdo and Nustendi being contraindicated with concomitant simvastatin > 40mg and Nustendi also being contraindicated when co-administered with a statin in patients with active liver disease or unexplained persistent elevations in serum transaminases. The complainant stated that the SPCs for both products clearly referenced seeing sections 4.2, 4.3 and 4.4 for information on contraindications within the licensed indication section so that information on simvastatin was clear and that the key points around contraindications were not mentioned anywhere on page 1 or 2.

The Panel noted Daiichi Sankyo's submission that the advice section of the summary card was a direct extrapolation from the SMC advice published for both products. The Panel further noted Daiichi Sankyo's submission that the prescribing information was clearly signposted at the bottom of pages 1 and 2, and was available on pages 3 and 4 of the document; the prescribing information, under the heading 'Contraindications' included 'concomitant use with simvastatin >40mg daily' for both products, and the statement 'coadministration with statin in patients with active liver disease or unexplained persistent elevations in serum transaminases; when Nustendi is coadministered with a statin, consult the SmPC for that particular statin therapy' for Nustendi.

The Panel noted that Section 4.1, Therapeutic indications, of the Nilemdo and Nustendi SPCs each referred the reader to Sections 4.2 (posology and method of administration), 4.3 (contraindications) and 4.4 (special warnings and precautions for use) when referring to the use of each medicine in combination with a statin (emphasis added by the Panel below):

> 'Nilemdo is indicated in adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet:
>
> - **in combination with a statin** or statin with other lipid-lowering therapies in patients unable to reach LDL-C goals with the maximum tolerated dose of a statin **(see sections 4.2, 4.3, and 4.4)** or,
> - alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated.'
>
> 'Nustendi is indicated in adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet:
>
> - **in combination with a statin** in patients unable to reach LDL-C goals with the maximum tolerated dose of a statin in addition to ezetimibe **(see sections 4.2, 4.3, and 4.4),**
> - alone in patients who are either statin-intolerant or for whom a statin is contraindicated, and are unable to reach LDL-C goals with ezetimibe alone,
> - in patients already being treated with the combination of bempedoic acid and ezetimibe as separate tablets with or without statin.'

The Panel considered that Sections 4.2, 4.3 and 4.4 of the SPC gave important safety information in relation to concomitant use with simvastatin including that both Nilemdo and Nustendi were contraindicated in patients taking simvastatin >40mg daily. Section 4.3 of the Nustendi SPC also listed 'Nustendi coadministered with a statin is contraindicated in patients with active liver disease or unexplained persistent elevations in serum transaminases' as a contraindication.

The Panel considered that whether a contraindication needed to be highlighted within a particular section of promotional material, in addition to its requirement to be included within the prescribing information that was required on all promotional material, depended on a consideration of all of the circumstances including the nature of the contraindication and the content, layout, audience and intended use of the material.

The Panel noted that the material at issue was commissioned and funded by Daiichi Sankyo and was promotional material; it thus needed to comply with the requirements of the Code including that the material must be sufficiently complete to enable recipients to form their own opinion of the therapeutic value of the medicine and must not be misleading. It was an established principle that companies could not rely on prescribing information to qualify a claim or negate a misleading impression.

The Panel noted the intention of the material at issue was to provide a summary of SMC guidance and that the information was cited directly from the recommendations. However, the Panel noted the 'Indication under review' section for both Nilemdo and Nustendi specifically referred to therapeutic use in combination with a statin; in the Panel's view, this was far broader than the SMC restriction, positioned later in chronology and to the right of each page, which stated Nilemdo and Nustendi were 'for use in patients who are statin intolerant or for whom a statin is contraindicated'.

The Panel considered the immediate and overall impression of the material to a busy health professional. In the Panel's view, given that simvastatin was a commonly prescribed lipid lowering treatment, the contraindication regarding concomitant use with simvastatin >40mg daily needed to be immediately apparent to health professionals in promotional material which referred to therapeutic use of Nilemdo or Nustendi in combination with a statin. The Panel, noting the body of the material specifically made reference to therapeutic use of Nilemdo and Nustendi in combination with a statin, considered that the material should have made the contraindication in patients taking simvastatin >40mg daily immediately apparent to readers. Whilst noting Daiichi Sankyo's submission that it adhered to the SMC's request that 'No part of this advice may be used without the whole of the advice being quoted in full', the Panel considered that this did not preclude Daiichi Sankyo providing important safety information in the body of its promotional material. The Panel considered that the sole inclusion of the contraindication regarding concomitant use with simvastatin >40mg in the prescribing information, did not negate the misleading immediate impression given in the body of the material that Nilemdo and Nustendi could be used therapeutically in combination with any dose of any statin, which was not so. Therefore, **a breach of Clause 6.1** was ruled.

In relation to the contraindication for Nustendi when coadministered with a statin in patients with active liver disease or unexplained persistent elevations in serum transaminases, the Panel considered that the body of the material did not imply that there would be no considerations in relation to patients with liver disease; health professionals would likely be cautious when prescribing to such patients and the contraindication was stated in the prescribing information. Noting the content and intended purpose of the SMC guidelines summary, in the Panel's view, the complainant had not established that the omission of this contraindication in the body of the material meant that it was misleading. **No Breach of Clause 6.1** was ruled in this regard.

The Panel noted the complainant bore the burden of proof. The Panel considered that the complainant had not established that the material was not capable of substantiation and **no breach of Clause 6.2** was ruled.

The Panel noted its comments and rulings in Case AUTH/3504/4/21, including that the contraindication with simvastatin >40mg daily needed to be immediately apparent to health professionals in promotional material, which referred to adding on to existing oral lipid lowering treatments. The Panel noted the undertaking in this regard was signed on 6 December 2021 by Daiichi Sankyo.

The Panel disagreed with Daiichi Sankyo's submission that the material did not contain promotional claims that would apply to the undertaking given in Case AUTH/3504/4/21. The Panel considered that stating the indications of Nilemdo and Nustendi in promotional material, which specifically made reference to therapeutic use in combination with a statin, was in effect making a claim about use in combination with a statin and therefore would be covered by the undertaking provided in Case AUTH/3504/4/21. The Panel noted that the SMC summary card in question (BEM/21/0732) had been certified on 10 December 2021, after the undertaking in Case AUTH/3504/4/21 had been signed, and considered that by not including that Nilemdo and Nustendi were contraindicated in patients taking simvastatin >40mg daily in the body of the promotional material in question, which referred to therapeutic use in combination with a statin, meant that Daiichi Sankyo had breached the undertaking given in Case AUTH/3504/4/21. The Panel ruled **a breach of Clause 3.3**.

The Panel noted its comments and rulings above and considered that Daiichi Sankyo had failed to maintain high standards and **a breach of Clause 5.1** was ruled.

The Panel noted the importance of undertakings and that inadequate action leading to a breach of undertaking was an example of an activity likely to be in breach of Clause 2. The Panel considered that failure to comply with the undertaking and assurance previously given in Case AUTH/3504/2/21 had brought discredit upon, and reduced confidence in, the pharmaceutical industry. The supplementary information to Clause 2 additionally listed prejudicing patient safety as an activity likely to lead to a breach of that clause. The Panel was concerned that in referring to therapeutic use in combination with a statin in the body of the material, without mentioning that Nilemdo and Nustendi were contraindicated with simvastatin>40mg daily except in the prescribing information, which was in smaller text and on a different page, particularly given that simvastatin was a commonly prescribed statin, meant that there was a risk that some patients on simvastatin >40mg daily might be inappropriately treated with Nilemdo or Nustendi. Patient safety was of the utmost importance and the Panel considered that the contraindication with simvastatin >40mg daily was not immediately apparent when reference to therapeutic use with a statin was referred to which might prejudice patient safety and was such as to reduce confidence in, and bring discredit upon, the pharmaceutical industry. **A breach of Clause 2** was ruled.

Complaint received **14 February 2022**

Case completed **23 February 2023**