

CASE AUTH/3635/4/22

COMPLAINANT v NOVARTIS

Concerns about an Entresto podcast

CASE SUMMARY

This case related to an Entresto podcast developed for heart failure specialist nurses (HFSN)

The Panel ruled breaches of the following Clauses of the 2021 Code on the basis that:

- a claim of an increase in energy in relation to the ability to get dressed was misleading as it was incapable of substantiation;
- use of 'best' was inextricably linked to the promotion of Entresto and implied that Entresto was the best in this context;
- reference to a 'slight but acceptable drop in renal function' without any qualification downplayed the importance of renal function and was misleading and incapable of substantiation and failure at the relevant point to qualify or provide further information about an important safety matter, was such that Novartis had reduced confidence in, and brought discredit upon, the industry in breach of Clause 2;
- the written briefing overall was not sufficiently clear and detailed such that the speaker would understand the relevant requirements of the Code and it considered that Novartis had failed to maintain high standards in that regard.

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| Breach of Clause 6.1 | Requirement that claims/information must be accurate, up-to-date and not misleading |
| Breach of Clause 6.2 | Requirement that claims must be capable of substantiation |
| Breach of Clause 14.4 | Requirement that claims should not imply that a medicine or an active ingredient has some special merit, quality or property unless this can be substantiated |
| Breach of Clause 5.1 | Requirement to maintain high standards |
| Breach of Clause 2 | Requirement that material must not bring discredit upon, or reduce confidence in, the pharmaceutical industry |

The Panel ruled no breach of the following Clauses of the 2021 Code on the basis that:

- 'new' was qualified in relation to the speaker's experience at the time the product came to market and not when the podcast was made and it was not a claim that Entresto was 'new';
- it was reasonably clear that Entresto was being broadly compared to patients' previous treatment options in heart failure and, therefore in the Panel's view, the statement in question was not a hanging comparison;

- the complainant's allegation, in relation to the claim 'it improves their quality of life and life expectancy', that none of the clinical trials had quality of life as an endpoint was incorrect;
- the complainant had not established his/her case in relation to substantiation that qualification of the status of trial endpoints in relation to two claims was required;
- it disagreed that the word 'great' was a superlative;
- the complainant had not established why differences in the parameters for initiation and monitoring meant that using Entresto was more complicated than ACE inhibitors or ARBs or his/her case as to the relevant differences between the monitoring requirements for patients on Entresto or ACE inhibitors;
- in the particular circumstances of this case, the briefing was adequately covered by the breach of Clause 5.1 ruling and an additional ruling of breach of Clause 2 would be disproportionate.

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| No Breach of Clause 6.1 | Requirement that claims/information must be accurate, up-to-date, unambiguous and not misleading |
| No Breach of Clause 6.2 | Requirement that claims must be capable of substantiation |
| No Breach of Clause 6.5 | Requirement that the word 'new' should not be used to describe any product which has been generally available for more than 12 months in the UK |
| No Breach of Clause 14.4 | Requirement that claims should not imply that a medicine or an active ingredient has some special merit, quality or property unless this can be substantiated. |
| No Breach of Clause 5.1 | Requirement to maintain high standards |
| No Breach of Clause 2 | Requirement that 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 complainant who described himself/herself as a cardiac specialist health professional complained about the promotion of Entresto (sacubitril/valsartan) by Novartis Pharmaceuticals UK Ltd.

The complainant provided a link to the material at issue, Episode 2 of the podcast series 'Heart to Heart', which was developed for heart failure specialist nurses (HFSN) and available as a podcast on a Novartis website for health professionals and relevant decision makers. The episode at issue was entitled 'Updating guidelines to empower HFSNs to initiate Entresto (sacubitril/valsartan) – why is it important and how can it be achieved?'

General comments by the complainant

The complainant stated that there were a number of issues with Episode 2 of the series. In the podcast a named HFSN speaker discussed why local guidelines had been changed to recognise HFSNs as specialists and to enable them to initiate Entresto. As well as discussing how this was possible, the speaker shared their experience of the impact of Entresto on patient

outcomes, and why it had led to earlier initiation for eligible symptomatic chronic HFrEF (heart failure reduced ejection fraction) patients.

When writing to Novartis, the Authority asked it to consider the requirements of Clauses 2, 5.1, 6.1, 6.2, 6.5 and 14.4 of the Code as cited by the complainant.

General comments by Novartis

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

Novartis stated that it maintained a website intended for a UK health professional audience containing information pages on Novartis medicines, each time a health professional accessed the website they were asked to confirm that they were a health professional or relevant decision-maker. There was a dedicated section on Entresto. In this subsection, Novartis maintained a page called 'Entresto resources' and on the Entresto resources page, there was a tab which allowed the user to access the 'Heart to Heart' Podcast series designed for HFSNs. There were five episodes in this podcast series.

In conclusion, Novartis submitted that none of the alleged Clauses had been breached. Novartis stated that it took safety extremely seriously and this and any other materials remained fully compliant with the Code and Novartis' internal policies regarding promotional material.

General comments by the Panel

The Panel noted that the podcast was one in a series designed by Novartis for Heart Failure nurses for inclusion in the Entresto resources and training section of the Novartis products promotional website. The interview in this particular episode was conducted by a Novartis employee. The Panel noted that whilst described as a podcast, the material was published in an audio-visual format.

The Panel noted that the podcast was an Entresto promotional item for which Novartis was responsible under the Code. The Panel noted that it was well-established that if companies' materials within the scope of the Code contained interviews with patients or health professionals, such published interviews should comply with the Code and the pharmaceutical company was responsible for their content. To permit otherwise would allow companies to circumvent the requirements of the Code. The Panel noted that Novartis had complete editorial control over the content of the podcast.

The Panel considered the case as presented by the complainant and responded to by Novartis as follows:

1 Use of 'new' in the context of Entresto

COMPLAINT

The complainant alleged that mention of the word 'new' in the context of Entresto was in breach of Clause 6.5.

RESPONSE

Novartis submitted that the health professional was sharing their own historical personal experience of using the product at the time when it was new to the market. This was clear in the way it was described and had been further reinforced with a written caption at this point of the video stating 'Entresto first received marketing authorisation in 2015. The speaker was referring to their historical experiences'. Therefore, no claims were made that Entresto was new and Novartis did not accept a breach of Clause 6.5.

PANEL RULING

The Panel noted the complaint regarding use of the word 'new' in the context of Entresto was contrary to Clause 6.5 which prohibited use of the word 'new' to describe any product or presentation which had been generally available, or any therapeutic indication which had been promoted for more than 12 months in the UK. The Panel noted that at the relevant point in the interview the visual accompanying the audio included a written pop-up box which read, 'Entresto first received marketing authorisation in 2015. The speaker is referring to their historical experiences'. The Panel considered that the location of the pop-up box towards the bottom of the screen was on the outer limits of acceptability, but that, on balance, it would be seen by viewers who would then understand that 'new' was used in relation to the speaker's experience at the time the product came to market and not when the podcast was made and that it was not a claim that Entresto was 'new'. Accordingly, the Panel ruled **no breach of Clause 6.5**.

2 Hanging comparison – 'majority of my patients have had an improved quality of life,'

COMPLAINT

The complainant alleged that a claim that the majority of patients have had improved quality of life, was a hanging comparison as it did not say vs what the improvement had been in was in breach of Clauses 6.1 and 5.1.

RESPONSE

Novartis submitted that the health professional was asked to share their personal experience of patients who had been on Entresto. In the health professional's response, he/she referred to the improved quality of life compared to the heart failure treatments that the patients had been on prior to the introduction of Entresto, specifically mentioning captopril where admission into hospital for initial dosing was required, which was not the case for Entresto. Therefore, there was no hanging comparison as no claim was made that would imply that the medicine improves quality of life without context.

Transcript excerpt:

'What's been your personal experience so far with Entresto?'

'Well, I'd say that it's made a huge difference to a huge amount of our patients. I think at first, like anything, you're a little bit wary about a new drug and the different side-effects and the big long list that came along with it of the dos and don'ts and watch out for and things. But then you look back to in the day when you used to have to do a captopril trial and a patient would have to come to a ward for four hours just to be checked, and you

realise how far we've come. So, I'd say the majority of my patients have had an improved quality of life definitely on Entresto.'

Novartis submitted that if the complaint related to a standalone claim of quality of life improvement, the pivotal PARADIGM-HF trial of 8399 patients measured of quality of life as determined by the Kansas City Cardiomyopathy Questionnaire (KCCQ) demonstrated significant improvements of sacubitril/valsartan vs ACE (angiotensin-converting enzyme) inhibitor comparator (enalapril) across domains (Chandra A, *et al.* 2018). This data substantiated a claim of improved quality of life (QoL) vs an ACE inhibitor.

Novartis submitted that this was an accurate, balanced and unambiguous claim and therefore not in breach of Clause 6.1. High standards had been maintained therefore Clause 5.1 had not been breached.

PANEL RULING

The Panel noted that Clause 6.1 required, among other things, comparative statements to be balanced, fair, objective, unambiguous and not misleading. The supplementary information to Clause 6.1 stated that 'hanging comparisons whereby a medicine is described as being better or stronger or suchlike without stating that with which it is compared, must not be made'.

The Panel noted that the claim was made as part of a longer response to the question posed by the Novartis interviewer 'What's been your personal experience so far with Entresto?'. The speaker responded, 'Well, I'd say that it's made a huge difference to a huge amount of our patients. I think at first, like anything, you're a little bit wary about a new drug and the different side-effects and the big long list that came along with it of the dos and don'ts and watch out for and things. But then you look back to in the day when you used to have to do a captopril trial and a patient would have to come to a ward for four hours just to be checked, and you realise how far we've come. So, I'd say the majority of my patients have had an improved quality of life definitely on Entresto'.

The Panel considered that the full response referred to quality of life improvements in the context of the progress made over time in the treatment of heart failure; immediately prior to the statement in question the speaker had referred to treatments available historically, specifically captopril, and the additional complexity when initiating treatment at that time.

The Panel considered that it was reasonably clear from the speaker's full response that Entresto was being broadly compared to patients' previous treatment options in heart failure. Therefore, in the Panel's view, the statement in question was not a hanging comparison as alleged. The Panel ruled **no breach of Clause 6.1** and consequently **no breach of Clause 5.1**.

3 Increase in energy

COMPLAINT

The complainant referred to a mention of increase in energy for patients and alleged that as none of the clinical trials for Entresto had improvement in energy as a primary endpoint or even an endpoint there was no robust dataset to substantiate such a claim in breach of Clauses 6.1, 5.1 and 2.

RESPONSE

Novartis submitted that again, the health professional was sharing his/her experience of what patients on Entresto had said to him/her. Increase in energy for patients could be linked to a number of elements of QoL and correlated with demonstrated improvements in QoL. This had been demonstrated in the pivotal PARADIGM-HF trial where 7 out of 10 physical and social activities were significantly improved vs the enalapril group including elements such as 'ability to do chores' (Chandra A, *et al.* 2018). Therefore, there was no breach of Clause 6.1 and, as high standards had been maintained, there was no breach of Clauses 5.1 and 2.

PANEL RULING

The complainant alleged that the mention of an increase in energy for patients breached Clauses 6.1, 5.1 and 2 as none of the clinical trials for Entresto had improvement in energy as a primary endpoint or even an endpoint at all so there was no robust dataset to substantiate such a claim. The Panel noted that both the complainant and Novartis had commented on this matter in relation to Clause 6.1, rather than Clause 6.2 which referred to substantiation.

The Panel noted that the claim had been made in response to the question 'What do your patients say when they've been on Entresto for a little bit and then they come back and see you?'. The Panel noted that the speaker had stated 'The first thing they tell you is not so much their breathing. It's their energy.' but had immediately qualified the 'increase in energy' claim by referring to improved exercise tolerance and having more energy to do the everyday things, in particular, 'being able to get washed and dressed without feeling puffed and tired.'

Novartis submitted that an increase in energy for patients had been demonstrated in the pivotal PARADIGM-HF trial where 7 out of 10 physical and social activities were significantly improved vs the enalapril group including elements such as 'ability to do chores'. The Panel noted that Chandra *et al.* 2018, a secondary analysis of the PARADIGM-HF trial, stated that 'in longitudinal analyses during the entire study (36 months), sacubitril/valsartan was associated with significantly greater change score differences in all activities except dressing yourself'.

In the Panel's view, whilst Chandra *et al.* 2018 demonstrated statistically significant improvements in certain daily activities, such as walking 100 yards and jogging, it did not support the statement at issue in relation to energy levels within the context of being able to get dressed. The Panel therefore considered that the claim of an increase in energy in relation to the ability to get dressed, which was explicitly referred to by the speaker, was misleading contrary to the requirements of Clause 6.1 as it was incapable of substantiation and **ruled a breach of Clause 6.1**. The Panel considered that Novartis had not maintained high standards in this regard. It had editorial control over the published version of the podcast and was responsible for its content. The Panel therefore **ruled a breach of Clause 5.1** in this regard. The Panel noted its rulings above and considered that the matter was adequately covered by the ruling of a breach of Clause 5.1. The Panel considered that, in the particular circumstances of this case, a ruling of breach of Clause 2 would be disproportionate. Clause 2 was used to indicate particular censure and reserved for such use and the Panel, therefore, ruled **no breach of Clause 2**.

4 Quality of life

First claim: 'It improves their quality of life and their life expectancy' and second claim: 'can improve their life expectancy, their quality of life'

COMPLAINT

The complainant referred to the claim 'It improves their quality of life and their life expectancy' and stated that as none of the clinical trials for Entresto had quality of life as an endpoint, and life expectancy was only a secondary endpoint and not a primary endpoint, which should have been qualified during the video. Breaches of Clauses 6.1, 5.1 and 2 were alleged.

The complainant alleged that in relation to the claim 'can improve their life expectancy, their quality of life', it was not qualified which were secondary endpoints, in breach of Clauses 6.1, 6.2, 5.1 and 2.

RESPONSE

Quality of Life

Novartis submitted that with regard to the QoL, this was a claim supported by formal QoL assessment in the PARADIGM-HF trial as highlighted above. Qualification that the QoL measure was a secondary endpoint was not required under the Code. Endpoints were assessed using a sequentially rejective procedure with the first two secondary endpoints at the highest level of the testing sequence (including overall QoL assessed by the effect on KCCQ clinical summary score) the primary and both of these secondary endpoints were met.

Life Expectancy

Novartis submitted that with regard to life expectancy, the primary endpoint of the pivotal PARADIGM-HF trial showed that Entresto was superior to enalapril in reducing the rates of death from cardiovascular causes or hospitalization for heart failure (the composite primary endpoint) and death from any cause among patients with heart failure and a reduced ejection fraction (McMurray J *et al*, 2014). As this trial supported the improved life expectancy claim, and as it was the primary endpoint, qualification of the statement was not required.

Therefore, Novartis submitted that these claims were adequately supported and there was no breach of Clause 6.1 or 6.2. High standards had been maintained therefore there was no breach of Clauses 5.1 and 2.

PANEL RULING

The Panel noted that Novartis had responded to these claims together. The Panel, noting that there were some differences between the claims and allegations, ruled upon each separately.

The Panel noted that these claims were made by the speaker as part of longer answers to a question posed by the Novartis employee as follows:

'our patients now have the ability to start this medication [Entresto] knowing the benefit it gives far sooner, so when you look at it, it improves their quality of life and their life expectancy'

and

'I think the biggest change for me was why would I not give someone the opportunity to be on a medication [Entresto] we know can improve their life expectancy, their quality of life, their symptoms, improve their cardiac output, their ejection fraction.'

Quality of Life endpoint

The Panel noted Novartis' submission that the 'PARADIGM-HF trial had assessed health-related quality of life measures and that the Code did not require qualification that the QoL measure was a secondary endpoint'. The Panel also noted its comments above at point 3 in relation to the PARADIGM-HF trial and Chandra *et al* and considered that they were relevant here. The change in the KCCQ, a widely used disease-specific HRQL instrument that has been validated for heart failure at 8 months was a secondary endpoint in the PARADIGM HF trial and showed a statistically significant improvement vs enalapril.

The Panel considered that the PARADIGM-HF trial and Chandra *et al* had assessed HQRL measures and therefore the complainant's allegation, in relation to the claim 'it improves their quality of life and life expectancy', that none of the clinical trials had quality of life as an endpoint was incorrect. Accordingly, and based on the narrow allegation, the Panel ruled **no breach of Clauses 6.1, 5.1 and 2**.

Status of trial endpoint

The Panel noted that the complainant's concerns about making it clear whether a matter was a secondary endpoint, applied to the first claim in relation to life expectancy and the second claim in relation to both life expectancy and quality of life. The Panel noted the narrow nature of the allegations.

The Panel noted that it was not unacceptable to use secondary endpoints without qualification to substantiate claims, whether such use was acceptable would be decided on a case-by-case basis bearing in mind amongst other things the quality standards in Clause 6.

The Panel noted that a claim of increasing life expectancy might be defined as the mean number of years a cohort of people might expect to live according to the current age-specific mortality rates and an estimate of a long-term treatment effect. The Panel noted the differences between this and the primary composite endpoint in the PARADIGM-HF trial. Nonetheless, the Panel noted the narrow nature of the allegation.

The Panel noted that the complainant's statement that life expectancy was a secondary and not a primary endpoint was incorrect. It appeared that life expectancy was not a discrete primary or secondary endpoint. Some relevant data was part of the primary endpoint (reduction in rates of death), and death from any cause was a secondary endpoint. The Panel had some concerns about the life expectancy claim, however, it noted that the complainant's sole allegation on this point was that the status of the endpoint should be clarified. The Panel, noting its comments above, considered that the complainant had not established his/her case on the balance of probabilities and ruled **no breach of Clauses 6.1, 5.1 and 2** on this narrow point. This ruling applied to the reference to life expectancy in the first and second claim above.

In relation to the reference to quality of life in the second claim at issue 'can improve their life expectancy, their quality of life.', the Panel noted that the complainant's sole concern was that the status of the endpoint should be clarified. The Panel noted its general comments above

about the use of secondary endpoints without qualification to substantiate claims and its comments at Point 3 and immediately above about the quality of life trial data. The Panel considered that the complainant had not established why the reference to quality of life in the second claim in question required qualification of its trial endpoint status as alleged and thus ruled **no breach of Clauses 6.1, 5.1 and 2.**

The Panel noted that the complainant had also raised Clause 6.2 but had not made any specific allegation about substantiation. The Panel noted that the complainant bore the burden of proof and considered that he/she had not established his/her case in relation to substantiation and ruled **no breach of Clause 6.2.**

5 Reference to best possible treatments

COMPLAINT

The complainant alleged that wanting people on best possible treatment, best was a superlative and should not be used to describe Entresto in breach of Clause 14.4.

RESPONSE

Novartis submitted that 'best' was used in reference to management of heart failure according to guidelines. The Novartis employee was referring to the fact that health professionals had a duty of care to their patients, and this required them to prescribe the best treatments available and was not being used to describe Entresto.

Transcript excerpt:

'It really drives home the importance. You're obviously passionate about getting the best for your patients. It clearly comes across. And looking at changing guidelines and driving that change amplifies that because you want your people on the best possible medications to give them the best opportunity in life, don't you? How did you go about identifying or driving that change?'

Therefore, Novartis did not believe that a superlative was claimed for Entresto. Instead, the employee was encouraging use of all 'best possible treatments' following professional society guidelines. There had been no breach of Clause 14.4 on this point.

PANEL RULING

The Panel noted the allegation that 'best' was a superlative and should not be used to describe Entresto. Clause 14.4 of the Code and its supplementary information stated that superlatives must not be used except for those limited circumstances where they relate to a clear fact about a medicine.

The Panel noted that the complainant referred to the phrase 'want people on the best possible treatments' and identified the time point at which the phrase in question occurred. The Panel noted that at this point in the podcast the Novartis employee was introducing a section where the speaker was invited to describe how they drove a change in guidelines. The Novartis employee said; 'You're obviously passionate about getting the best for your patients. It clearly comes across. And looking at changing guidelines and driving that change amplifies that because you want your people on the best possible medications to give them the best

opportunity in life, don't you? How did you go about identifying or driving that change? What were the important things that you thought about?'. The Panel noted that the relevant time point did not contain the exact phrase identified by the complainant. The Panel ruled on the closely similar phrase 'want your people on the best possible medications' which fell within the relevant part of the transcript responded to by Novartis.

The Panel noted that the Novartis employee had repeatedly used 'best' in his/her introduction. It noted that no named medications were referred to in this introduction but, nonetheless, the podcast was promotional for Entresto which was the only product referred to by brand name, although there was reference to generic captopril elsewhere. The Panel considered that use of the word 'best' in relation to 'want your people on the best possible medications to give them the best opportunity in life' was inextricably linked to the promotion of Entresto and thereby implied that Entresto was the best in this context. Accordingly, the Panel ruled **a breach of Clause 14.4**.

6 Claim – 'we know the treatments are great'

COMPLAINT

The complainant referred to the claim that 'we know the treatments were great', stating that 'great' was a superlative and should not be referred to in the context of a product presentation about Entresto especially by a Novartis employee. A breach of Clause 14.4 was alleged.

RESPONSE

Novartis submitted that this statement was made by the speaker, rather than the Novartis employee, as he/she explained how he/she viewed current heart failure management vs historical management rather than Entresto specifically.

Transcript excerpt:

'So, in the worst scenario that I developed heart failure myself, I wouldn't look at it like a lot of patients used to, as in this is a death sentence because that is not necessarily the case anymore. We know that the treatments are great, the overlying care is good, the patients are really well-educated and supported, so it's a long-term condition and you manage it as you go along.'

Novartis submitted as the word 'great' was not used in relation to Entresto there was no breach of Clause 14.4.

PANEL RULING

The Panel noted the allegation that great was a superlative and should not be referred to in the context of a product presentation about Entresto especially by a Novartis employee. The Panel had some concerns about the use of the term 'great', however, it disagreed with the complainant that 'great' was a superlative, a term that denoted the highest quality or degree and therefore, based on the very narrow allegation, the Panel ruled **no breach of Clause 14.4**.

7 First claim – no more complicated than ARB or ACE inhibitor and Second claim – it is no different than using an ACE inhibitor

The Panel noted that Novartis had responded to these allegations together. The Panel noted that there were some differences between the claims and allegations and ruled upon each separately.

A First claim: 'no more complicated than ARB or ACE inhibitor'

COMPLAINT

The complainant referred to the fact that [Entresto] was no more complicated than ARB (angiotensin II receptor blocker) or ACEi (angiotensin-converting enzyme inhibitor) and alleged breaches of Clauses 6.1, 6.2 and 5.1 as this could not be substantiated. There were far more parameters around initiating and monitoring Entresto vs ARB or ACEi (considering there were many different ARBs and ACE inhibitor products). The complainant pointed out that the summary of product characteristics (SPC) for Entresto stated that:

'Treatment should not be initiated in patients with serum potassium level >5.4 mmol/l or with SBP <100 mmHg (see section 4.4). A starting dose of 24 mg/26 mg twice daily should be considered for patients with SBP ≥100 to 110 mmHg. Entresto should not be co-administered with an ACE inhibitor or an ARB. Due to the potential risk of angioedema when used concomitantly with an ACE inhibitor, it must not be started for at least 36 hours after discontinuing ACE inhibitor therapy (see sections 4.3, 4.4 and 4.5).'

RESPONSE

Novartis submitted that the speaker was referring to his/her personal experience of using and administering the different heart failure treatments. Entresto had similar initiation and monitoring requirements to ACE inhibitors/ARBs (SPCs of Entresto and enalapril provided) therefore it was reasonable in his/her view for these requirements to be similar. Therefore, the speaker statements were adequately supported.

Novartis submitted that health professionals trained in the management of heart failure would be familiar that there were requirements for initiating and monitoring most heart failure treatments. This video was not positioned to provide all considerations on initiating therapy. Prescribing information was included in the video and on the site where it was accessed which provided full information about initiation and monitoring of Entresto. There were clear links on the same page as the video that provide additional guidance on initiating Entresto including all the points referred to in the complaint.

Novartis submitted that, on that basis, the statements were substantiable and further information easily accessible such that there was no breach of Clauses 6.1 and 6.2. High standards had been maintained therefore no breach of Clause 5.1.

PANEL RULING

The Panel noted that the claim in question was part of a longer statement:

'So, as a team we were very comfortable using Entresto. We treated just like we do the ACE inhibitors or the ARBs in the fact that it is no more complicated. The only issue that we sometimes see is because it's a combination drug. Yes, it may have a slightly more effect on blood pressure, so just to be aware of that with your patients or your more vulnerable group of patients that may suffer with that.'

The Panel noted that the complainant's allegation specifically referred to the substantiation of the claim. He/she alleged that as there were differences in the parameters for initiation and monitoring between the classes of medicines, the claim could not be substantiated.

The Panel noted that the complainant had provided an extract from the SPC relating to circumstances when treatment with Entresto should not be initiated or should be initiated at a lower dose, however, the complainant had not established how this was more complex in comparison to ACE inhibitors and/or ARBs and the Panel recognised that complexity was a subjective term.

While noting that there were differences between the different classes of treatment, the Panel considered that, on the balance of probabilities and the very narrow allegation, the complainant had not established why differences in the parameters for initiation and monitoring meant that using Entresto was more complicated than ACE inhibitors or ARBs and therefore why the claim was misleading and could not be substantiated. Accordingly, the Panel ruled **no breach of Clauses 6.1 and 6.2** and therefore **no breach of Clause 5.1**.

B Second claim: 'it is no different than using an ACE inhibitor'

COMPLAINT

The complainant alleged that the claim that 'it was not different than using an ACE inhibitor' was not qualified as Entresto was a combination product with different monitoring requirements to an ACE inhibitor so this claim could not be qualified. Breaches of Clauses 6.1, 6.2 and 5.1 were alleged.

RESPONSE

Novartis submitted that the speaker was referring to his/her personal experience of using and administering the different heart failure treatments. Entresto had similar initiation and monitoring requirements to ACE inhibitors/ARBs (SPCs of Entresto and enalapril provided) therefore it was reasonable in his/her view for these requirements to be similar. Therefore, the speaker statements were adequately supported.

Novartis submitted that health professionals trained in the management of heart failure would be familiar that there were requirements for initiating and monitoring most heart failure treatments. This video was not positioned to provide all considerations on initiating therapy. Prescribing information was included in the video and on the website where it was accessed which provided full information about initiation and monitoring of Entresto. There were clear links on the same page as the video that provided additional guidance on initiating Entresto including all the points referred to in the complaint.

Novartis submitted that on that basis, the statements were substantiable and further information easily accessible such that there was no breach of Clauses 6.1 and 6.2. High standards had been maintained and therefore there was no breach of Clause 5.1.

PANEL RULING

The Panel noted that the claim in question was part of a longer statement:

‘as long as they’re stable and their blood pressure allows and their renal function is stable, it is no different than using an ACE inhibitor.’

The Panel noted the allegation related to the lack of qualification of the above claim as Entresto was a combination product with different monitoring requirements to an ACE inhibitor, this claim could not be qualified. The Panel queried whether the complaint was sufficiently clear; it referred to a lack of qualification then stated that the claim could not be qualified. The Panel also considered the extract of the Entresto SPC as provided by the complainant at point 7A above:

‘Treatment should not be initiated in patients with serum potassium level >5.4 mmol/l or with SBP <100 mmHg (see section 4.4). A starting dose of 24 mg/26 mg twice daily should be considered for patients with SBP ≥100 to 110 mmHg. Entresto should not be co-administered with an ACE inhibitor or an ARB. Due to the potential risk of angioedema when used concomitantly with an ACE inhibitor, it must not be started for at least 36 hours after discontinuing ACE inhibitor therapy (see sections 4.3, 4.4 and 4.5).’

The Panel considered that the preceding comments from the speaker reproduced above provided some additional context to the claim and that the complainant had not established his/her case as to the relevant differences between the monitoring requirements for patients on Entresto or ACE inhibitors. On the narrow point alleged the Panel ruled **no breaches of Clauses 6.1 and 6.2** and therefore **no breach of Clause 5.1**.

8 Claim: ‘Slight but acceptable drop in renal function’

COMPLAINT

The complainant referred to the mention of understanding there might be a slight drop with renal function but it was an acceptable drop. The complainant alleged that it was inappropriate to play down renal function and say it was acceptable for a renal function drop without any qualification, considering the SPC contraindication was concomitant use with aliskiren-containing medicinal products in patients with diabetes mellitus or in patients with renal impairment (eGFR <60 ml/min/1.73 m²) (see sections 4.4 and 4.5). The complainant alleged a breach of Clauses 6.1, 6.2, 5.1 and 2.

RESPONSE

Novartis submitted that a drop in eGFR on initiation of ACE inhibitors and ARBs, as well as Entresto, was well-recognised among the clinical community and was an accepted clinical opinion. The Renal Association and British Society for Heart Failure guidance was that during initiation and titration of RAAS (renin-angiotensin-aldosterone system) inhibitors, testing renal function was mandatory and a decline in renal function of 30% or more could be acceptable for HfrEF patients (Clark *et al.* 2019).

Given the target audience of health professionals trained in the management of heart failure, Novartis submitted that it was reasonable to expect that this would be understood in the context of this guidance. Given the point raised by the complainant suggested this might not be universally appreciated, Novartis would take the action to add text to the video, summarising the statement and source provided above, to ensure this was further qualified.

With specific reference to the complainant's point on concomitant use with aliskiren, Novartis submitted that this was out with the context of the point covered. This was because aliskiren, which had limited use in the UK, was a specific contraindication to initiation of sacubitril/valsartan. This, and other cautions related to concomitant RAAS therapies, was provided in the prescribing information, was included in the video and by direct link on the website where it was accessed. There were also additional links from the same webpage as the video that provided additional information on initiating Entresto including considerations regarding renal function. Use with other therapies and in renal impairment were adequately supported where clinicians had questions arising from the video.

Therefore, Novartis submitted that there were no breaches of Clauses 6.1 and 6.2 and as high standards had been maintained there was no breach of Clauses 5.1 and 2.

PANEL RULING

The Panel noted the allegation that it was inappropriate to play down renal function and say it was acceptable for a renal function drop without any qualification considering the SPC contraindication in relation to concomitant use with aliskiren-containing medicinal products in patients with diabetes mellitus or in patients with renal impairment (eGFR <60 ml/min/1.73 m²).

With specific reference to the complainant's point on concomitant use with aliskiren, Novartis submitted that aliskiren had limited use in the UK and maintained that this, and other cautions related to concomitant RAAS therapies, were provided in the prescribing information included in the video and by direct link on the website where it was accessed. Furthermore, there were also additional links from the same webpage as the podcast that provided additional information on initiating Entresto including considerations regarding renal function. In Novartis' view, use with other therapies and in renal impairment were adequately supported where clinicians had questions arising from the podcast.

The Panel considered that whether a contraindication or special warning/precaution 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/warning/precaution and the content, audience and use of the material.

The Panel noted that although the podcast was originally developed for heart failure specialist nurses it was published on webpages that were part of a general company product website intended for UK health professionals and certified for use with physicians, pharmacists and nurses, it could be reasonably assumed that not all health professionals accessing the material would be familiar with heart failure and Entresto's safety profile.

The Panel noted that the prescribing information was provided at the end of the podcast and noted Novartis' submission about relevant links on the webpage but noted that information necessary for Code compliance should be part of the podcast so that it stood alone in relation to the requirements of the Code. The Panel noted that at the relevant timepoint in the podcast, users were not alerted to important safety information including contraindications, special warnings and precautions.

The Panel considered that, in the circumstances of this particular case, in relation to the impact on patients' renal function, the podcast underplayed an important safety issue. The SPC had additional important and relevant safety information, including that Entresto was not

recommended in patients with end-stage renal disease and that concomitant use with aliskiren-containing medicinal products in patients with diabetes mellitus or in patients with renal impairment (eGFR <60 ml/min/1.73 m²) was contraindicated.

The Panel was concerned about the use of the phrase 'slight but acceptable drop in renal function'. The Panel considered that it was important to be cautious when discussing the safety aspects of a medicine. Noting its comments above, the Panel considered that the phrase in question, in the absence of any qualification, downplayed the importance of renal function as alleged and was misleading and incapable of substantiation. The Panel ruled **breaches of Clauses 6.1 and 6.2**. Noting its rulings above, the Panel considered that Novartis had failed to maintain high standards and accordingly **ruled a breach of 5.1**.

Clause 2 was a sign of particular censure and was reserved for such use. The supplementary information to Clause 2 included prejudicing patient safety as an example of an activity that was likely to be in breach of this clause.

The Panel noted that the phrase at issue was used by the nurse when explaining how he/she would explain the benefit/risk profile in relation to renal function to heart failure patients. The Panel noted its comments above about the importance of caution when discussing safety aspects of a medicine. The Panel considered that patient safety was of the utmost importance and that health professionals should be able to rely on company material to be complete and unambiguous in this regard.

The Panel noted its ruling above that the phrase in question, in the absence of any qualification, downplayed the importance of renal function. The Panel considered that the failure at the relevant point in the interview to qualify or provide further information about an important safety matter, particularly given that the claim at issue downplayed the importance of renal function, was such that Novartis had reduced confidence in, and brought discredit upon, the industry and **a breach of Clause 2** was ruled.

9 Speaker briefing

COMPLAINT

The complainant alleged that it was clear that the nurse in the video was not given a clear brief by Novartis around compliance requirements in breach of Clauses 5.1 and 2.

RESPONSE

Novartis submitted that a clear briefing was given to the speaker in advance of the engagement. A copy of the approved briefing was provided which, Novartis stated, explained the objective of the podcast and gave guidance on relevant aspects of compliance requirements. Before the recording the speaker also received a verbal briefing reiterating the same points and was given the opportunity to address any queries. Novartis submitted that an appropriate briefing was therefore provided and as high standards had been maintained there were no breaches of Clauses 5.1 and 2.

PANEL RULING

The Panel considered that it was well-established that if companies interviewed patients or health professionals and used the output for activities within the scope of the Code, they must

ensure that no part of the content was inconsistent with the Code. In the Panel's view, it was critical that the briefing provided to speakers was clear and took account of the speaker's experience in, and understanding of, the Code. Companies should edit the final material where necessary to ensure compliance.

The complainant alleged that the speaker had not been given a clear briefing. Novartis submitted that both a written and follow-up briefing was given to the speaker in advance of the engagement. The written briefing submitted by Novartis stated the objective of the podcast and gave guidance on relevant aspects of compliance requirements. Novartis submitted that before the recording, the speaker had also received a verbal briefing reiterating the same points as the written briefing and was given the opportunity to address any queries.

The Panel noted that the written speaker briefing referred to the podcast being used in a promotional capacity and stated that the aim of the podcast series was to share real world experience regarding the use of Entresto. The briefing contained, among other things, suggested talking points, that the words 'safe' and 'new' and superlatives should not be used and that the discussion must be in accordance with the licensed indication and be balanced highlighting both safety and efficacy when referring to Entresto.

The Panel was concerned that no guidance or examples about what was meant by 'balanced' were included in the briefing despite the speaker being specifically asked to provide examples of their own and patients' real-life experience of Entresto. The Panel considered that it was particularly important to be clear about the quality standards in the Code if a speaker was going to discuss their personal experience. The speaker had subsequently made a number of strong statements during the podcast that were not qualified. The Panel did not consider that the written briefing overall was sufficiently clear and detailed such that the speaker would understand the relevant requirements of the Code. Noting its comments above and that Novartis had complete editorial control over the material, the Panel considered that Novartis had failed to maintain high standards and therefore ruled **a breach of Clause 5.1**.

The Panel considered its ruling above and noted that Clause 2 was used as a sign of particular censure and reserved for such use. The Panel considered that, in the particular circumstances of this case, the matter ruled upon was adequately covered by the Clause 5.1 ruling and that an additional ruling of a breach of Clause 2 would be disproportionate and therefore ruled **no breach of Clause 2**.

Complaint received **18 April 2022**

Case completed **31 May 2023**