CASE AUTH/3654/5/22

HEALTH PROFESSIONAL v NOVARTIS

Allegations about an Entresto (sacubitril/valsartan) promotional video on a learned society's website

CASE SUMMARY

This case was in relation to a Novartis promotional symposium video hosted on a learned society's website following its conference in September 2021.

The Panel ruled a breach of the following Clauses of the 2021 Code for failing to state that Entresto should not be initiated in patients with SBP [systolic blood pressure] < 100 mmHg or serum potassium level >5.4 mmol/l and for failing to include Entresto prescribing information within the video:

Breach of Clause 6.1	**Misleading material that was not sufficiently complete to enable viewers to form their own opinion of the therapeutic value of the medicine**
Breach of Clause 12.1	**Failing to include prescribing information**
Breach of Clause 5.1	**Failing to maintain high standards**

The Panel ruled no breach of the following Clauses of the 2021 Code as:

- **The video had been certified.**
- **The complainant had made a very narrow allegation with regard to checking hepatic function as per the SPC, however, Novartis submitted that monitoring of liver function was not a specific requirement of Entresto.**
- **There was no allegation that information in the video was not capable of substantiation.**
- **The Panel considered that the matter in relation to the omission of prescribing information was covered by its ruling of breaches of Clauses 12.1 and 5.1 and an additional ruling of a breach of Clause 2 was not required.**
- **Whilst concerned about the editing of the video, overall, the Panel considered that health professionals would likely be left with the impression that there were important clinical considerations with the use of Entresto, including in relation to potassium and blood pressure, prompting them to refer to more detailed information such as the SPC prior to use of Entresto; on balance, the Panel did not consider that the video meant that Novartis had reduced confidence in, or brought discredit upon, the industry.**

No Breach of Clause 6.1	**Requirement that information must not be misleading**
No Breach of Clause 6.2	**Requirement that information must be capable of substantiation**
No Breach of Clause 8.1	**Requirement to certify promotional material**

No Breach of Clause 5.1	**Requirement to maintain high standards**
No Breach of Clause 2	**Requirement that activities or material must not bring discredit upon, or reduce confidence in, the pharmaceutical industry**

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

FULL CASE REPORT

A complaint was received from an anonymous, contactable complainant, who described themselves as a health professional, about Novartis Pharmaceuticals UK Ltd.

COMPLAINT

The complainant alleged that Novartis had organised and funded a promotional session via the 2021 annual conference of a learned society titled 'Addressing health inequalities in heart failure: a real world case study'. This was referred to on the learned society's main website (link provided). The complainant referred to a tab called 'click here to view' underneath the reference to the Novartis event, which showed the video of the talk (MLR ID 166435, November 2021). The complainant provided a direct video link. The complainant submitted that Novartis had paid for 3 named health professionals to present on this promotional session around its medicine Entresto.

The complainant alleged that there was no prescribing information provided within the video; the prescribing information was a crucial part that was needed as a health professional and this was, according to the complainant, a clear and obvious breach of Clauses 12.1, 5.1 and 2. The complainant asserted that it was hugely worrying that Novartis had not presented the Entresto prescribing information which could only mean the content had not been certified in breach of Clauses 8.1, 5.1 and 2.

The complainant stated that around 6 minutes, 25 seconds into the video, the second speaker started his/her discussion named 'Recent international guidelines in Heart Failure'. At 11 minutes and 12 seconds, he/she presented an algorithm which was titled 'Figure 1. Modified from Management algorithm for NICE guideline: "Chronic Heart Failure in Adults: diagnosis and management". In the recommendations algorithm to the right-hand side for heart failure with reduced ejection fraction, the arrow to the blue box then showed 3 options to offer: Number 1 was sacubitril valsartan if EF <35%*. The '*' then took the viewer to a tiny footnote at the bottom, which stated to measure serum sodium, potassium and renal function before and after starting and after each dose increment. The complainant alleged that this was fundamentally misleading as the clear value around hyperkalemia was not given. It was not as simple as what the slide said to just check potassium. The summary of product characteristics (SPC) for Entresto was very clear on this:

> 'Treatment should not be initiated if the serum potassium level is >5.4 mmol/l. Use of sacubitril/valsartan may be associated with an increased risk of hyperkalaemia, although

> hypokalaemia may also occur (see section 4.8). Monitoring of serum potassium is recommended, especially in patients who have risk factors such as renal impairment, diabetes mellitus or hypoaldosteronism or who are on a high potassium diet or on mineralocorticoid antagonists (see section 4.2).'

The complainant stated that the exact level of potassium should have been written on the slide as measuring potassium without clear recommendations was dangerous.

The complainant stated that blood pressure also needed checking pre- and post-initiation with clear guidance from the SPC:

> 'Treatment should not be initiated unless SBP is ≥100 mmHg. Patients with SBP <100 mmHg were not studied (see section 5.1). Cases of symptomatic hypotension have been reported in patients treated with sacubitril/valsartan during clinical studies (see section 4.8)'.

The complainant stated that hepatic function should also be checked as per the SPC:

> 'Sacubitril/valsartan is contraindicated in patients with severe hepatic impairment, biliary cirrhosis or cholestasis (Child-Pugh C classification) (see section 4.3)'.

The complainant alleged that Novartis had not mentioned these 3 important factors within this slide or during the presentation at any point. Even the health professional kept talking about accelerating treatments but without presenting these specific parts. Patient safety would be at a major risk without checking all aspects that were required as described in the SPC prior to initiation and during treatment. Novartis had cherry-picked a few (sodium, renal function and ambiguous mention of potassium) and had not provided a balanced presentation. The complainant alleged breaches of Clauses 6.1, 6.2, 5.1 and 2. The complainant alleged that it was poor to see an unbalanced presentation considering the high risk nature of heart failure alongside the non-provision of prescribing information and that the industry had been brought into disrepute and confidence had been shattered. The complainant could not understand why Novartis felt they could do such promotional events without presenting the facts.

When writing to Novartis, the Authority asked it to consider the requirements of Clauses 2, 5.1, 6.1, 6.2, 8.1 and 12.1 of the 2021 Code as cited by the complainant.

RESPONSE

Novartis submitted that this complaint caused it concern and it had taken its content seriously. Novartis wanted to highlight that it was committed to operating in accordance with the required standards and meeting the relevant requirements and expectations.

Novartis promotional symposium at the learned society conference

The learned society hosted its annual Conference, 'Shaping Healthy Communities: Focusing on Cardiovascular Care' in September 2021 (the '**Conference**'). The Conference was hosted virtually on the learned society's website.

The learned society approached Novartis regarding sponsorship opportunities for the Conference. Novartis agreed to sponsor the Conference, and the parties entered into a sponsorship agreement to cover the arrangement (the '**Sponsorship**').

As part of the benefits received by Novartis pursuant to the Sponsorship, Novartis hosted a 30-minute virtual symposium at the Conference, which was entitled '*Addressing health inequalities in heart failure: a real-world case study'* (the '**Novartis Symposium**'). As could be seen from the title, the Novartis Symposium focused on health inequalities in heart failure, complementing the Conference agenda. Novartis made reference to the following declaration 'This promotional symposium was organised and funded by Novartis' which it submitted was prominently and clearly stated.

Novartis decided on its symposium topic and selected speakers based on their expertise in heart failure. As a promotional event, the target audience of the Novartis Symposium was health professionals (including GPs, specialists/consultants, nurses and pharmacists).

Engagement of the speakers by Novartis

Novartis submitted that it engaged 3 health professionals to perform services in relation to its symposium. A contract was put in place between each health professional and Novartis.

Speaker briefings

Novartis submitted that as part of the process for the engagement of a speaker for a promotional meeting, it briefed the speaker on the requirements of the ABPI Code and relevant Novartis internal policies and processes. Novartis now used an interactive template to create the contracts for this type of engagement. A drop-down list contained within the template itself allowed the selection of whether the proposed activity would be promotional or non-promotional in nature.

Where a briefing was required for a Novartis-organised promotional meeting, the template was automatically populated with the briefing statement. Due to a manual oversight, the incorrect option was mistakenly selected in the drop-down list within the template, which consequently resulted in the speaker briefing element not being included within the relevant contracts with the speakers. Despite this error being made, a verbal briefing was provided by Novartis to each of the speakers. These occurred in August and September 2021. The briefing call covered information regarding the objective of the video, time requirements for the speakers, technical information regarding the video recording and ABPI Code requirements. Novartis teams engaged external health professionals in this manner on a regular basis across a number of settings and were experienced in providing such briefings.

Speaker presentations

Novartis submitted that the speakers each developed the content for their respective presentations to align with the overall Conference theme of health inequalities in heart failure. The speaker presented on the following topics:

- Chair and first speaker– '*Addressing health inequalities in heart failure: a real-world case study*'.
- Second speaker – '*Recent International guidelines in Heart Failure*'.

- Third speaker – '*The Welsh Heart Failure Pathway*'.

As highlighted above, the agenda on the learned society website stated 'This promotional symposium has been organised and sponsored by Novartis'. The speaker presentations were reviewed and certified by Novartis prior to use. The initial slide of each speaker presentation contained the following disclaimer:

> *'This symposium is organised and funded by Novartis Pharmaceuticals UK Ltd. Entresto (sacubitril/valsartan) is indicated in adult patients for treatment of symptomatic chronic heart failure with reduced ejection fraction.1 Prescribing information is available at the end of this presentation 1. Entresto SmPC, 2021.'*

These presentations were pre-recorded, with the speakers dialling in on the day of the Conference to participate in the question-and-answer session forming part of the Novartis Symposium.

Novartis was able to provide a transcript of the Speaker Presentations Video (MLR ID 157520) (Enclosure 17). Novartis did not have a transcript of the full Novartis Symposium video (MLR ID 166435) but offered to prepare one.

Alleged breaches of the 2021 Code

Clause 12.1 of the 2021 Code:
Prescribing Information must be provided on all promotional material

Novartis submitted:

- As explained above, the presentation slides used by each speaker in the pre-recorded element of the Novartis Symposium were certified by Novartis. Each presentation slide deck, when certified, contained the prescribing information for Entresto.
- The video pre-recording of the speaker presentations was carried out in September 2021. Novartis engaged a third party provider in connection with these services. The final version of the video containing the pre-recorded speaker presentations (MLR ID: 157520)) was certified with the prescribing information included.
- The Speaker Presentations Video was hosted on the learned society's website during the Conference and was followed by a live Q&A session.
- After the Conference, at the request of the learned society, a second video was created (MLR ID: 166435) which incorporated the Speaker Presentations Video (which had been certified), plus the recording of the live Q&A session ('**Full Novartis Symposium Video**').
- The learned society requested to host the Full Novartis Symposium Video on their website after the Conference had taken place.
- The Full Novartis Symposium Video was certified by Novartis prior to use by the learned society. Although the prescribing information was included in each of the speaker presentations and the Speaker Presentations Video, the prescribing information had erroneously been removed during the editing of the Full Novartis Symposium Video. This was mistakenly overlooked when Novartis carried out the certification of the Full Novartis Symposium Video. Upon being alerted to this issue, Novartis confirmed with the learned society that the Full Novartis Symposium Video

had been removed from its website. Novartis confirmed that the Full Novartis Symposium Video was no longer available to view on the learned society's website. Novartis were conducting an internal review to determine how the removal of prescribing information during the editing process was mistakenly overlooked during the certification process.

Clause 5.1 of the 2021 Code
Not maintaining high standards, as the prescribing information was not provided

Novartis submitted:

- The certified presentation slides and the certified Speaker Presentations Video contained the prescribing information for Entresto. Novartis accepted that the inclusion of prescribing information did not make it through the editing process to the final video and that this was overlooked during the certification of this aspect of the project. To the extent that the PMCPA considered that this simple human error must lead directly to a finding that Clause 5.1 had been breached, Novartis would accept this decision. However, in Novartis' view, an isolated error made by an individual should not automatically lead to a finding that high standards had not been maintained.
- Novartis addressed the alleged breach of Clause 5.1, as it related to the balance of the presentation below.

Clauses 6.1 and 6.2 of the 2021 Code
Information, claims and comparisons must be accurate, balanced, etc
Information, claim or comparison must be capable of substantiation

Novartis submitted:

Hyperkalemia and Blood Pressure:

- The slide referred to by the complainant was the standard Heart Failure algorithm from an external organisation which was a collaboration between three healthcare organisations. Novartis had no input into the creation of this algorithm; for full transparency this was stated on the second speaker's presentation slides.

- It was not necessary to discuss the hyperkalemia use in detail as the patients being discussed specifically were not hyperkalemia patients. The speakers in the session aimed to create a general view of using Entresto, in line with the guidelines discussed.

- The footnote referred to by the complainant stated:

  '**Measure serum sodium, potassium and assess renal function before and after starting and after each dose increment. If eGFR is 30 to 45 ml/min/1.73 m^2, consider lower doses or slower titration of ACEI/ARBs/sacubitril valsartan or MRAs.'*

  This footnote was not written by Novartis, but by **the external organisation** as part of its Heart Failure guideline. Novartis would expect that an external organisation

operating within the healthcare sector, had researched the facts of the medicine sacubitril/valsartan, alongside other Heart failure medicine classes ACEI, ARBs and MRAs and decided that this information was sufficient relevant information that should be known about the medicine classes when prescribing according to the guideline. This was contrary to the complainant's submission that the information provided was missing some key points. For brevity's sake, it was not reasonably possible to list all the possible adverse events outlined in the Entresto SPC in each meeting, therefore the general reference to 'measure potassium levels' alerted the health professional to the fact that checking potassium levels was important when prescribing Entresto.

- Once serum potassium was measured, as recommended, the health professional would immediately be aware of whether the patient had Hypokalemia, Hyperkalemia, or normal potassium levels. The General Medical Council had issued guidance covering good practice in prescribing and managing medicines and devices. Section 8 of this guidance required medical professionals to recognize and work within the limits of their competence and keep their knowledge up-to-date. Sections 9 to 11 further required the health professional to make use of electronic and other systems to improve the safety of prescribing, including accessing the medicines SPC on the electronic Medicines Compendium (eMC) website. Heart failure was a very specialized area of expertise, and the health professionals were highly trained; it was reasonable to assert that health professionals would be skilled enough to understand that they should check or be aware of the products' SPC before making a prescribing decision.

- The speaker presentation slide decks provided further detail, which had been summarised below:

    - Slide 8 of the third speaker's slide deck mentioned '*Adapt initiation and titration to each patient depending on heart rate, blood pressure, renal function, fluid status and weight*'.

    - Slide 9 of the third speaker's slide deck went into further detail by stating in No 3 recommendation *'Consider Sacubitril Valsartan (NICE EF<35%, ACC EF≤40%). If hypotensive, consider low dose ARB as a bridge to an ARNI'.*

    - Slide 12 of the chair/first speaker's slide deck stated within the section titled 'Medication Advice':
        - *'If transferring to Entresto from ACEI then a 36hr washout period is required. If issues with ACEI or ARB such as hypotension, allergy, renal decline or angioneurotic oedema then Entresto should NOT be started; seek advice.'*
        - On this slide, the systolic blood pressure, creatinine, and potassium general advisable limits were also stated:
            - *'**Systolic Blood Pressure** should not be consistently <110mmHg*
            - ***Creatinine>**200umol or if increase >50% from baseline*
            - ***Potassium** >5.5mmol/l'*

- Slide 13 of the chair/first speaker's slide deck went into detail about how Entresto should be initiated. The slide provided situations when additional advice was required during initiation or dose increase:
  - *'Systolic Blood Pressure <110mmHg or symptoms of hypotension*
  - *Serum potassium ≥ 5.5mmol/l*
  - *Cr >200umol or if increase >50% from baseline*
  - *eGFR ≤30'*

- The flowchart on slide 13 of the chair/first speaker's slide deck included recommendations such as:
  - **Initiate **Entresto** 24mg/26mg bd*
  - **Check U&Es & BP at 3 weeks*
  - *If BP &U&Es acceptable increase **Entresto** to 49mg/51mg bd*
  - **Check BP at 3 weeks*
  - *If BP & U&Es acceptable increase **Entresto** to 97mg/103mg bd*
  - **Check U&Es & BP at 3 weeks*

- At about 25 minutes into the Full Novartis Symposium Video, the second speaker explained that she had not been able to prescribe two of the four products used for treating heart failure, because the patient was quite frail. In this instance, Entresto was not prescribed due to concerns with blood pressure. The second speaker explained that the patient's vital signs, including his blood pressure, would continue to be monitored to see when the other products could be prescribed. This was contrary to the impression created by the complainant that '*the HCP kept talking about accelerating treatments but without presenting these specific parts*'. There was no risk to patient safety as there were several discussions on blood pressure, hyperkalemia and renal function highlighted during the talk; hence the health professionals would be fully aware that these were side-effects of the product.

- The prescribing information which could be seen at the end of the Speaker Presentations Video, which was shared at the conference, further highlighted the relevant considerations when prescribing Entresto and the health professionals would be able to access this.

- Entresto had been licensed and available for 7 years for the treatment of heart failure; it was not a 'new' product. At this point, most of the prescribers would already be familiar with the product and relevant safety considerations. The aim of this session was not to present new information but to provide a refresher, both on Entresto and other products used for the treatment of heart failure. The discussions were balanced as efficacy and safety was presented. If the prescriber was new to the therapy area or newly qualified, the prompts on the slides and discussion to measure Potassium, Sodium and Renal Function and blood pressure, would be enough to help them decide or prompt them to seek further information from the SPC or more experienced colleagues.

- From 25 minutes and 50 seconds into the Full Novartis Symposium Video until the end of the video at 28 minutes, potential side-effects (eg, potential decline in eGFR and blood pressure effects) were discussed, therefore a health professional would be aware that Entresto had effects on kidney function as well as blood pressure. It was well-known that delegates tended to remember the first and last points mentioned during a presentation, so positioning the side-effect discussion at the end of the presentation,

after the case study session was purposely done to ensure the health professionals would remember the product safety as well as efficacy. This was in addition to the points regarding safety considerations that were made earlier on in the video.

- The patient described in the case study at the end of the Full Novartis Symposium Video, from 18 minutes onwards, had good renal function and blood pressure. Nevertheless, daily blood pressure checks, and U & E renal function checks were conducted, which showed to the health professional the ideal way to initiate the product. Since the patient had good blood pressure and renal function, it would have been confusing for the delegates if concerns about low blood pressure or hyperkalemia were discussed at this stage.

- The complainant also referred to Clause 6.2 of the ABPI Code in their complaint but had not specifically mentioned which of the claims could not be substantiated. All statements and claims in the video regarding Entresto were fully substantiated by the products SPC available on the eMC website.

Hepatic Function:

Novartis submitted:

- Monitoring of liver function was not a specific requirement of Entresto use, especially as it was not stated within the Posology and method of administration section of the SPC.

- Given there was no requirement for liver function monitoring with Entresto, and information on initiating in those with liver impairment was summarised in the SPC and prescribing information, this information was not hidden and supported appropriate prescribing and patient safety. Therefore, Novartis denied breaches of Clauses 6.1 or 6.2 on this point.

Clause 5.1 of the 2021 Code
Not maintaining high standards as presentation was not balanced

Novartis submitted that:

- the presentation was fully balanced for the reasons explained in Novartis' response to the alleged breaches of Clauses 6.1 and 6.2 above;

- as such, high standards were maintained in relation to the balance of the Novartis Symposium and Novartis fully refuted breaches of Clause 5.1 on this point.

Clause 8.1 of the 2021 Code
Promotional material must be certified

Novartis refuted any breach of Clause 8.1. As explained above, the speaker presentation slide decks, the Speaker Presentations Video and the Full Novartis Symposium Video were all certified by Novartis.

Clause 2 of the 2021 Code

Novartis strongly refuted any breach of Clause 2 and fully disputed that the '*industry [has] been brought into disrepute and confidence [has] been shattered*'.

Novartis submitted, as explained above, both the certified presentation slides and the certified Speaker Presentations Video contained the prescribing information for Entresto. Despite the prescribing information being included in each of the speaker presentations and the Speaker Presentations Video, due to a genuine human error, the fact that the prescribing information was missing from the Full Novartis Symposium Video was mistakenly overlooked during the certification process.

The actions of Novartis in relation to these materials had not brought discredit upon, or reduced confidence in, the pharmaceutical industry. After becoming aware of the issue, Novartis took prompt action to ensure that the material in question was removed from the learned society's website. In addition, Novartis was carrying out an internal investigation to identify the cause behind the oversight at the point of certification, with the Novartis compliance team also considering any necessary corrective measures to further refine Novartis' internal processes.

The complainant referred to confidence being 'shattered'. It was not clear whether the complainant asserted that this was their personal view or that of some other group. Regardless, Novartis wholly rejected this characterization of the situation. Many of the complainant's points were, at best, issues on which reasonable minds could differ or relate to issues where no reasonable argument could be made that there would be any effect on patient safety or public confidence.

Novartis took its responsibilities under the Code extremely seriously and invested significant resources to ensure its associates developed a deep understanding of the requirements of the ABPI Code. Even with robust oversight, and high standards, human errors would inevitably occur over the course of many thousands of items being reviewed and Novartis welcomed the opportunity for these to be highlighted so that it might correct these promptly and review and further refine its processes as a result.

Conclusion

In summary, the complaint had raised several issues related to the Novartis Symposium at the learned society's Conference. It was Novartis' opinion that there was a legitimate defence to the alleged breaches of Clauses 6.1, 6.2 and 8.1. However, Novartis conceded that Clause 12.1 (in relation to the prescribing information not being provided on the Full Novartis Symposium Video only) had been breached due to a simple human error. In Novartis' view, this breach should not have an automatic effect on any other clauses of the Code.

PANEL RULING

At the learned society's conference in September 2021, Novartis hosted a promotional 30-minute virtual symposium which was entitled 'Addressing health inequalities in heart failure: a real-world case study'.

It appeared to the Panel that the complainant's allegations were in relation to a video of the symposium hosted on the learned society's website following the conference (MLR ID 166435, November 2021), and the Panel made its rulings in relation to this material.

The Panel noted Novartis' submission that the video in question incorporated pre-recorded speaker presentations plus the recording of the live Q&A session, and that the prescribing information had erroneously been removed during the editing of this video, which was mistakenly overlooked when Novartis certified the video in November 2021.

Whilst noting that the certified presentation slides and the certified pre-recorded speaker presentations contained the prescribing information for Entresto, the edited video in question (MLR ID 166435), hosted on the learned society's website, did not include prescribing information and therefore the Panel ruled **a breach of Clause 12.1** as acknowledged by Novartis.

The Panel was concerned that the removal of prescribing information during editing was not identified during the certification of this video. The Panel considered that a robust certification process underpinned self-regulation and **a breach of Clause 5.1** was ruled.

The Panel considered that the matter in relation to the omission of prescribing information was covered by its rulings above and thus the Panel ruled **no breach of Clause 2** in this regard.

The Panel noted that the video had been certified and **no breach of Clause 8.1** was ruled. The Panel consequently ruled **no breach of Clauses 5.1 and 2** in this regard.

In relation to the allegations about the algorithm slide in the second speaker's presentation, the Panel noted Novartis' submission that this was the standard external organisation's Heart Failure algorithm and that Novartis had no input into the creation of this algorithm. Nonetheless, the Panel considered that the video was Novartis promotional material for Entresto (sacubitril, valsartan) and therefore needed to comply with the requirements of the Code.

The Panel noted that the right hand side of the algorithm, following the box "Heart failure with reduced ejection fraction (HFrEF)" was a blue box which stated:

'Offer:

1. ACEI (or ARB if intolerant of ACE) or Sacubitril valsartan if EF < 35%,*
   and
2. β-blocker, and
3. Mineralocorticoid receptor antagonist (MRA)*'

The '*' led to a footnote in smaller font, at the bottom of the slide and beneath the algorithm boxes, which stated:

> '*Measure serum sodium, potassium and assess renal function before and after starting and after each dose increment. If eGFR is 30 to 45 ml/min/1.73 m2, consider lower doses or slower titration of ACEI/ARBs/sacubitril valsartan or MRAs'.

The Panel noted the complainant's allegation that the exact level of potassium should have been given as measuring potassium without clear recommendations was dangerous; that blood pressure also needed checking pre- and post- initiation as the Entresto SPC stated that treatment should not be initiated unless systolic blood pressure (SBP) is ≥100 mmHg and that hepatic function should also be checked as Entresto was contraindicated in patients with severe hepatic impairment, biliary cirrhosis or cholestasis.

The Panel noted Section 4.2 (Posology and method of administration) of the Entresto SPC stated, amongst other things, that treatment should not be initiated in patients with serum potassium level >5.4 mmol/l or with SBP < 100 mmHg. The SPC further stated in Section 4.4 (Special warnings and precautions for use) that when initiating therapy or during dose titration with sacubitril/valsartan, blood pressure should be monitored routinely. If hypotension occurs, temporary down-titration or discontinuation of sacubitril/valsartan was recommended. This section of the SPC also stated, amongst other things, that monitoring of serum potassium was recommended and discontinuation of sacubitril/valsartan should be considered if serum potassium level is >5.4 mmol/l. Section 4.3 (Contraindications) included, amongst other things, severe hepatic impairment, biliary cirrhosis and cholestasis.

The Panel noted that the algorithm in question referred to measuring potassium before and after starting treatment and after each dose increment for patients on a number of different medicines including patients taking sacubitril/valsartan.

Whilst noting that the chair's certified presentation slides, provided by Novartis, in relation to initiation of Entresto, included: 'Take advice about initiation or dose increase if: Systolic Blood Pressure <110mmHg or symptoms of hypotension; Serum potassium ≥5.5mmol/l …' it appeared that this slide had been edited out of the video in question (MLR ID 166435), in addition to the removal of the Entresto prescribing information slides.

Noting that the allegations were in relation to this video and not the certified speaker's slides, the Panel considered that there was no reference in the video to the Entresto SPC requirement that treatment should not be initiated in patients with serum potassium level >5.4 mmol/l or with SBP < 100 mmHg. However, the algorithm slide in question, which was presented during the video, did include reference to measuring serum potassium before and after starting and after each dose increment, albeit this was a footnote on the slide and not verbalised, and there were some references in the video to checking blood pressure with hypotension being a potential issue with sacubitril/valsartan treatment.

The Panel considered the immediate and overall impression of the slide in question and the entire video.

The video referred to a number of different classes of medicine and a number of specific medicines by name, including Novartis' medicine sacubitril/valsartan, as well as many non-Novartis medicines. The slide in question, which depicted the external organisation's algorithm for management of chronic heart failure in adults, gave an overview of the management pathway and referred to a number of different classes of medicine. As well as reference to sacubitril/valsartan, the slide in question specifically referred to one other medicine by name, dapagliflozin. In the Panel's view, on the balance of probabilities, health professionals would not expect one slide of a treatment pathway algorithm to contain all the relevant information in relation to considerations prior and during use of one of the medicines referred to in that algorithm.

However, given that the algorithm on the slide in question referred to sacubitril/valsartan and the speaker referred to sacubitril/valsartan being "superior to ACE [inhibitors]"; and given that it was a Novartis promotional video that referred to sacubitril/valsartan or "ARNI" on multiple occasions, the Panel considered that the video, overall, should be sufficiently complete to enable viewers to form their own opinion of the therapeutic value of Entresto.

Whilst a footnote on the algorithm slide referred to measuring potassium before and after starting treatment and after each dose increment, noting the primary care audience and lack of prescribing information, the Panel considered that the reference to measuring potassium, without stating anywhere in the material that treatment should not be initiated in patients with serum potassium level >5.4 mmol/l, was misleading and ambiguous as alleged and **a breach of Clause 6.1** was ruled.

As above, noting the audience, lack of prescribing information and that there was no reference within the video that treatment should not be initiated in patients with SBP < 100 mmHg, the Panel considered that the material was not sufficiently complete to enable viewers to form their own opinion of the therapeutic value of the medicine and a **breach of Clause 6.1** was ruled.

Despite being deeply concerned that the video contained no prescribing information to inform readers of Entresto's contraindications which included severe hepatic impairment, noting Novartis' submission that monitoring of liver function was not a specific requirement of Entresto use, the Panel considered, on balance, and based on the complainant's very narrow allegation that 'hepatic function should also be checked as per the SPC', the Panel ruled **no breach of Clause 6.1**.

The Panel noted the complainant had raised Clause 6.2 but had made no allegation that the information in the video was not capable of substantiation and thus the Panel ruled **no breach of Clause 6.2.**

The Panel disagreed with Novartis' submission that the video was balanced. This was an Entresto promotional video that referred to sacubitril/valsartan or "ARNI" on a number of occasions and one of the speakers claimed that sacubitril/valsartan was "superior to ACE [inhibitors]", however, the video contained limited information about considerations for use and the safety profile of Entresto and this was compounded by the absence of prescribing information and by the removal of slides from the Chair's certified slide presentation, which had included more detailed references to clinical considerations in relation to Entresto, including blood pressure and serum potassium. Overall, the Panel considered that Novartis failed to maintain high standards in the creation of this promotional Entresto video and **a breach of Clause 5.1 was ruled.**

Clause 2 was a sign of particular censure and was reserved for such use. Whilst the Panel was deeply concerned about the editing of the video, overall, the Panel considered that the video gave a summary of the management of a highly complex disease and referred to multiple different medicines. In the Panel's view, health professionals would unlikely perceive the video to be a detailed Entresto resource given it referred to many different classes of medicine and the management of heart failure broadly. The Panel considered that health professionals would likely be left with the impression that there were important clinical considerations with the use of sacubitril/valsartan, including in relation to potassium and blood pressure, and that this, on the balance of probabilities, would prompt a health professional to refer to more detailed information, such as the SPC, prior to use of Entresto. On balance, the Panel did not consider that the video meant that Novartis had reduced confidence in, or brought discredit upon, the industry and **no breach of Clause 2** was ruled.

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Complaint received	**23 May 2022**
Case completed	**25 May 2023**