CASE AUTH/3727/1/23

COMPLAINANT v JANSSEN

Symposium video on Janssen Medical Cloud website

CASE SUMMARY

This case concerned a video of a symposium on pulmonary arterial hypertension published on a Janssen website which the complainant alleged was misleading by presenting:

- **relative risk reduction information without the absolute risk reduction,**
- **a Kaplan–Meier curve labelled with incorrect absolute risk reduction information, and**
- **secondary outcome data without providing the context of the study, including its failure to achieve the primary endpoint.**

The Panel ruled a breach of the following Clauses of the 2021 Code:

Breach of Clause 5.1	**Failing to maintain high standards**
Breach of Clause 6.1 (x3)	**Making a misleading claim**

In relation to allegations about off-label promotion of macitentan and the location of the prescribing information, the Panel ruled no breach of the following Clauses of the 2021 Code:

No Breach of Clause 11.2 (x3)	**Requirement that a medicine must be promoted in accordance with the terms of its marketing authorisation and must not be inconsistent with the particulars listed in its summary of product characteristics**
No Breach of Clause 12.1	**Requirement to include prescribing information**
No Breach of Clause 12.6	**Requirement to include a prominent statement as to where the prescribing information can be found on promotional material on the internet**

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

FULL CASE REPORT

A complaint was received from a contactable complainant about a video of a symposium on pulmonary arterial hypertension published on a Janssen Limited website.

The presentation referred to Opsumit (macitentan) and Uptravi (selexipag).

Opsumit was licensed, as monotherapy or in combination, for the long-term treatment of pulmonary arterial hypertension (PAH) in adult patients of WHO Functional Class (FC) II to III.

Efficacy had been shown in a PAH population including idiopathic and heritable PAH, PAH associated with connective tissue disorders, and PAH associated with corrected simple congenital heart disease.

Uptravi was licensed for the long-term treatment of pulmonary hypertension (PAH) in adult patients with WHO functional class (FC) II-III, either as combination therapy in patients insufficiently controlled with an endothelin receptor antagonist (ERA) and/or a phosphodiesterase type 5 (PDE-5) inhibitor, or as monotherapy in patients who are not candidates for these therapies. Efficacy had been shown in a PAH population including idiopathic and heritable PAH, PAH associated with connective tissue disorders, and PAH associated with corrected simple congenital heart disease.

COMPLAINT

The complainant stated that they were a UK cardiologist with special interest in management and treatment of pulmonary hypertension and that they had been directed by a representative from Janssen UK to the website to watch a video of a recent symposium led by Janssen at the European Society of Respiratory Conference (ERS) in 2021 titled 'Connect, confirm, combine in pulmonary arterial hypertension'.

The complainant stated that they were concerned about the following allegedly misleading information within the presentation titled 'Combining therapies: Having a PAH plan' in this video and had raised those concerns directly with the representative, however with no success.

Therefore, they requested the PMCPA investigate this issue as it could spread misleading information and understanding about pulmonary hypertension treatment to healthcare professionals.

1. The speaker presented a slide titled 'Initial double combination therapy delays the progression of PAH [pulmonary arterial hypertension] compared with monotherapy'. The slide stated '50% reduction in the risk of disease with initial double therapy' and '50% risk reduction for disease progression with initial double therapy vs monotherapy'. The complainant stated it was a well-established principle across the medical and scientific community that relative risk reduction in clinical trials could be misleading when presented in isolation as it could exaggerate the effect of the medicine. They believed this was also an established principle in the Code. Therefore, they were surprised to watch the presentation of the data on this slide in this way without the inclusion of relative risk reduction [sic] to provide the viewers with an unbiased view of the data.

2. The speaker presented a slide titled 'Patients initiating double oral therapy can also expect improvements in how they function' and comparing three different studies: Ambition, Optima and Triton:

   The Optima study investigated the effect of initial combination therapy of macitentan with tadalafil. However, the complainant alleged that macitentan was licensed in the UK for use as add on treatment and not for initial combination therapy. In macitentan's phase III clinical trial, referred to in section 5.1 of the summary of product characteristics, the majority of the patients (64%) were treated with a stable dose of specific therapy for PAH. Therefore, they alleged, the promotion of macitentan for initial combination therapy was off label and not aligned with the details within the summary of product characteristics.

   In addition, the Triton study referred to on the slide did not meet its primary endpoint. Therefore, the complainant alleged it was misleading to present the secondary outcomes of the study as an improvement of treating pulmonary arterial hypertension patients as these results lacked clinical and statistical robustness.

3. The speaker presented a slide titled 'GRIPHON: Sequential oral triple therapy with selexipag improves long term outcomes, particularly in FC II'. The slide referred to '64% reduction in risk of disease progression compared to placebo in FC II patients on double background therapy' citing an absolute risk reduction (ARR) of 64%. It further referred to '26% reduction in risk of disease progression compared to placebo in FC III patients on double background therapy citing an absolute risk reduction (ARR) of 26%. The complainant stated it was nearly impossible in clinical trials for absolute risk reduction and relative risk reduction to be the same. The complainant alleged that this misleading information about absolute risk reduction was exaggerating the benefit of the company's treatment and misleading healthcare professionals about what to expect from using their treatments.

4. The speaker presented a slide titled 'Conclusions'. The second conclusion stated: 'Initial double combination therapy is recommended for the majority of PAH patients in low/intermediate risk, as this improves outcomes compared to monotherapy'. The complainant alleged that, given the lack of licence for macitentan to be used in initial combination therapy, this recommendation was encouraging off label use of a medicine which may put patients at risk. This was also repeated in the slide titled 'Take home messages: Combine'. The second bullet point stated: 'At diagnosis: Initial double combination therapy is recommended for the majority of PAH patients in low/intermediate risk', which the complainant alleged encouraged the use of macitentan off label.

5. The complainant stated that, unfortunately, the company referred the viewer to the prescribing information of both medicines only at the very end of the hour-long video to avoid the risk of any viewer identifying these 'fatal' errors.

The complainant requested these issues be investigated and asked that Janssen issue corrective information to healthcare professionals to avoid any harm to patients on the back of this biased misleading information distributed by the Janssen.

When writing to Janssen, the Authority asked it to consider the requirements of Clauses 5.1, 6.1, 11.2, 12.1 and 12.6 of the Code.

RESPONSE

Janssen stated that it was very disturbed by the allegation that the complainant attempted to raise their concerns regarding this video content directly with a representative with no success. Following internal enquiry, none of the current Janssen employees working in the PAH therapy area had any record or recollection of directing any healthcare professionals to this content, nor of any concerns as described by the complainant being raised with them noting that had this been the case such concerns would have been escalated to the medical department as was routine practice. Should the complainant still wish to discuss their concerns with Janssen, the company would be very happy to facilitate a meeting with a member of Janssen's medical affairs team as the company believed there was some misunderstanding regarding the licensed indication for one of its therapies, as well as of the evidence base and guidelines supporting combination therapy in PAH.

Janssen stated that it appreciated some of the observations made by the complainant which had highlighted a human error in graph labelling. Janssen found it unfortunate that the complainant described these as 'fatal errors' as Janssen took very seriously its responsibility to ensure the completeness, accuracy, objectivity and unambiguity of the information Janssen provided to healthcare professionals. As Janssen would detail below, the objective of this symposium was to educate on best practice and evidence-based guidance on therapy in PAH. Janssen submitted that the data presented were consistent with the marketing authorisation for the company's products, sufficiently complete to enable the audience to form their own opinion of the therapeutic value of combination therapy in PAH, and consistent with recognised standards of care as presented by world leading experts in pulmonary hypertension.

Janssen's detailed responses to the complaints in the order that they were outlined by the complainant are given below:

1. The complainant referred to the presentation of relative risk reduction for initial double combination therapy with ambrisentan plus tadalafil vs pooled monotherapy, 'without the inclusion of relative risk reduction to provide the viewers with an unbiased view of the data', by which Janssen understood they meant to refer to the absolute risk reduction. Neither of these therapies was a Janssen medicine and the data presented were available in the public domain from the AMBITION study (Galiè *et al* N Engl J Med 2015). The relative risk reduction was presented alongside the full Kaplan–Meier curve including the number of study subjects at risk, thereby enabling the viewer to evaluate the absolute risk reduction and treatment effect at any given timepoint. Furthermore, the results of this competitor-sponsored study positively impacted the treatment guidelines at that time (Galiè *et al*, Eur Respir J 2015). On this basis, Janssen maintained that the information was presented in a manner consistent with the requirements of Clause 6.1 of the Code, being sufficiently complete to enable recipients to form their own opinion of the therapeutic value of the treatment combination in question.

   Finally, as these data related to non-Janssen products, Janssen stated there was no benefit to Janssen presenting the data in a way that was misleading or exaggerated the treatment effect, as suggested by the complainant.

2. The complainant stated that 'macitentan is licensed in the UK for use as add on treatment and not for initial combination therapy' and alleged that 'the promotion of macitentan for initial combination therapy is off label and not aligned with the details

within the summary of product characteristics'. This was incorrect. The licensed indication for macitentan as described in section 4.1 of the Summary of Product Characteristics (Opsumit (macitentan) Summary of Product Characteristics) was as follows:

Opsumit (macitentan), as monotherapy or in combination, was indicated for the long-term treatment of pulmonary arterial hypertension (PAH) in adult patients of WHO Functional Class (FC) II to III.

Efficacy had been shown in a PAH population including idiopathic and heritable PAH, PAH associated with connective tissue disorders, and PAH associated with corrected simple congenital heart disease.

Janssen submitted that it was clear that macitentan could be used as monotherapy or in combination for the treatment of adult patients with PAH of the aetiologies listed above. Promotion of macitentan in initial combination therapy was consistent with the therapeutic indication, in accordance with the requirements of Clause 11.2 of the Code.

The complainant had also raised concerns about the use of data from a study which did not meet its primary endpoint, stating that it was 'misleading to present the secondary outcomes of the study as an improvement of treating pulmonary arterial hypertension patients as these results lack clinical and statistical robustness'.

The TRITON study (Chin *et al*, Efficacy and safety of initial triple oral versus initial double oral combination therapy in patients with newly diagnosed pulmonary arterial hypertension (PAH): results of the randomized controlled TRITON study. Poster presented at American Thoracic Society (ATS) annual congress August 2020 (virtual)) was conducted to assess the efficacy of initial triple combination therapy (selexipag plus macitentan plus tadalafil) compared to initial double combination (macitentan plus tadalafil). Whilst the primary endpoint of this study failed to achieve statistical significance (there was no benefit shown for triple combination vs. double combination therapy over the duration of the study), Janssen submitted that it was reasonable to refer to within-arm treatment effects of the dual combination arm of this study. Along with the OPTIMA study, the data from TRITON was presented as supportive of the evidence from the AMBITION study which was the basis for the guidelines recommending initial double combination therapy.

3. The complainant pointed out that the slide showed the same values for relative risk reduction and absolute risk reduction for sequential triple oral combination therapy with selexipag vs placebo in functional class II and III patients, and that it was nearly impossible in clinical trials for absolute risk reduction and relative risk reduction to be the same.

Unfortunately, the legends had indeed been labelled incorrectly with the relative risk reductions appearing instead of the absolute risk reductions. Janssen thanked the complainant for highlighting this labelling error. Nevertheless, Janssen submitted, the relative risk reduction was presented in the context of the full Kaplan–Meier curves and the numbers of study subjects at risk, still enabling the viewer to evaluate the absolute treatment effect at any given timepoint and allowing them to

form their own opinion of the therapeutic value of selexipag, meeting the requirements of Clause 6.1 of the Code.

4. The complainant stated that conclusions relating to recommendations for initial dual combination therapy for the majority of PAH patients in low/intermediate risk constituted off-label promotion of macitentan. Janssen stated that in relation to two relevant time points the objective of this symposium was to educate the audience on evidence-based guidance on management of patients with PAH. Initial combination therapy of a PDE-5 inhibitor plus an endothelin receptor antagonist (ERA) in low/intermediate risk PAH was consistent with the expert treatment algorithms in both the 2015 ESC/ERS PH guidelines (Galiè *et al*, Eur Respir J 2015) as well as the proceedings of the 6 World Symposium on PH (Galiè *et al*, Eur Respir J. 2019). The option to choose macitentan as the ERA was entirely consistent with its licensed indication as addressed previously in point 2.

5. The complainant stated that the prescribing information was shown 'only at the very end of the video after an hour long to avoid the risk of any viewer identifying these fatal errors.' Janssen submitted that this was incorrect. The video was housed and could only be viewed on Janssen's website for UK healthcare professionals. Once on the website, viewers were guided to the location of the prescribing information in both the header and the footer of every page. The viewer was able to access the prescribing information for any relevant Janssen medicines in advance of or at any time during the viewing of any content on the page. The inclusion of the location of the prescribing information at the end of the video was, therefore, additional to the clear directions to its location on the website, which met the requirements of Clauses 12.1 and 12.6 of the 2021 Code.

In summary, Janssen stated that the video content in question provided education on evidence-based clinical guidelines for the treatment of PAH. Janssen acknowledged the graph labelling error and thanked the complainant for bringing this to the company's attention. Notwithstanding this error, Janssen submitted that the graphs and associated data presented by the speaker were not misleading and were sufficiently complete to allow viewers to form their own opinion of the therapeutic value of the medicines discussed. Initial double combination therapy was consistent with the marketing authorisation for macitentan, and secondary endpoint data mentioned from the TRITON study were presented in the context of clinical trial data where PAH patients received initial dual combination therapy. Finally, the website on which the video was located made clear the availability and the location of the prescribing information, in addition to this also being shown at the end of the symposium video. As such, Janssen believed that it had maintained high standards in accordance with the requirements of Clause 5.1 of the Code.

PANEL RULING

The Panel noted the complaint concerned a video recording of a Janssen-sponsored symposium titled 'Connect, confirm, combine in pulmonary hypertension' published on a Janssen website. The symposium, which comprised three presentations, was part of the programme at the European Respiratory Society Congress, 2021. The complainant alleged that the third presentation, 'Combining therapies: Having a PAH plan', contained misleading information and that raising the matter with a Janssen representative had not been successful. The Panel noted that the presentation in question followed those on the importance of collaboration and connecting PAH experts and confirming the diagnosis of PAH.

1. Relative risk reduction in absence of ARR

The Panel noted the complaint concerned a slide titled 'Initial double combination therapy delays the progression of PAH compared with monotherapy' and which contained data from the AMBITION study. The complainant alleged that the presentation of relative risk reduction in clinical trials could be misleading when presented in isolation, as it could exaggerate the effects of the medicine. They also stated that the presentation of relative risk reduction for initial double combination therapy with ambrisentan plus tadalafil vs pooled monotherapy, 'without the inclusion of relative risk reduction to provide the viewers with an unbiased view of the data', was misleading; the Panel considered that the complainant intended to refer to absolute risk reduction in this statement.

The supplementary information to Clause 6.1 Absolute risk and relative risk states 'Referring only to relative risk, especially with regard to risk reduction, can make a medicine appear more effective than it actually is. In order to assess the clinical impact of an outcome, the reader also needs to know the absolute risk involved. In that regard, relative risk should never be referred to without also referring to the absolute risk.'

The slide at issue featured two boxes. One contained the study name, AMBITION, and a brief statement that its objective was 'to look at long term follow-up of patients treated with initial ambrisentan and tadalafil' followed by the claim '50% reduction in the risk of disease progression with initial double therapy'. The Panel noted that the claim was presented in large blue bold type with the exception of the words 'in the risk of'.

To the right was a box containing a Kaplan–Meier curve headed '50% risk reduction for disease progression* with initial double monotherapy vs monotherapy'. The Kaplan–Meier curve compared the percentage of patients with no event against time for double therapy and pooled monotherapy. Beneath the graph the number of patients at risk at the various time points for each group was given. The asterisk to the graph heading linked to a footnote in very small type at the bottom of the slide which stated, '*Clinical failure, which was defined as the first occurrence of a composite end point of death, hospitalisation for worsening pulmonary arterial hypertension, disease progression, or unsatisfactory long-term clinical response. Results were driven by a decrease in disease progression and hospitalisations due to PAH; they do not apply to mortality on its own.'

The Panel considered the immediate impression to a busy health professional. In the Panel's view, the 50% reduction in the risk of disease progression was the primary take-home message. The Panel noted Janssen's submission that presenting the relative risk reduction alongside the full Kaplan–Meier curve, including the number of study subjects at risk, enabled viewers to evaluate the absolute risk reduction and treatment effect at any given timepoint. In the Panel's view, however, it was not sufficient to rely on a viewer independently deciding that they needed to know the absolute risk reduction and, further, deciding to calculate the absolute risk reduction. In the Panel's view, it was likely that most viewers would not pause the presentation to calculate the absolute risk reduction but noted that it had no evidence before it on this point. It was also unclear whether each viewer would know how to calculate absolute risk reduction. In the Panel's view, the slide emphasised the relative risk reduction without sufficient balance; if relative risk reduction was stated, the absolute risk reduction should be presented together with the relative risk reduction in such a way as to allow the reader to make an immediate assessment of the clinical impact of an outcome.

The Panel considered that the Code was clear on this point and a **breach of Clause 6.1** was ruled.

2. Alleged off-label promotion and misleading presentation of secondary endpoint data

The Panel noted the slide at issue was headed 'Patients initiating double oral therapy can also expect improvements in how they function' and featured a table which referred to three studies, AMBITION, OPTIMA and TRITON, and demonstrated improvements in measures of PAH patients' function by a series of ticks. The description beneath each study read 'Initial combination therapy with macitentan and tadalafil' (OPTIMA and TRITON), and 'Initial combination therapy with ambrisentan and tadalafil' (AMBITION). The functional measures highlighted on the slide were haemodynamics, 6-minute walk distance (6MWD), World Health Organization (WHO) functional class (WHO FC), and N-terminal pro-brain natriuretic peptide (NT-proBNP) levels.

The Panel noted Janssen had provided it with a copy of the AMBITION and TRITON studies but had not provided the OPTIMA study.

i) Alleged off-label promotion of macitentan

The Panel noted the complainant's submission that macitentan was licensed in the UK for use as 'add on treatment and not for initial combination therapy'. The complainant referred to Section 5.1 of the summary of product characteristics (SPC) and macitentan's Phase III clinical trial, where the majority of the patients (64%) were treated with a stable dose of specific therapy for PAH. The complainant alleged that the promotion of macitentan for initial combination therapy was off label and not aligned with the SPC.

In the Panel's view, the purpose of Section 5.1 of an SPC (Pharmacodynamic properties) was, amongst other things, to provide a summary of clinical efficacy and safety data relevant to the licensed indications in Section 4.1 of the SPC. In the Panel's view, the complainant's interpretation of the relationship between Section 5.1 and the licensed indication was incorrect.

The Panel noted that Section 4.1, Therapeutic indications, of the Opsumit SPC stated that Opsumit (macitentan) is licensed as monotherapy or in combination for the long-term treatment of pulmonary arterial hypertension (PAH) in adult patients of WHO Functional Class (FC) II to III. The Panel considered that the slide in question clearly referred to the use of macitentan in initial combination therapy and on this point was promoted in accordance with the terms of its marketing authorisation and was not inconsistent with the particulars listed in its SPC. Section 5.1 of the SPC did not alter the Panel's interpretation of macitentan's licensed indication and the Panel therefore ruled **no breach of Clause 11.2**.

ii) Presentation of secondary outcome data from study which did not meet its primary endpoint

The complainant alleged as the TRITON study had not met its primary objective it was misleading to present secondary outcomes of the TRITON study as these results lacked clinical and statistical robustness. The Panel noted Janssen's submission that TRITON was conducted to assess the efficacy of initial triple combination therapy (selexipag plus macitentan plus tadalafil) compared to initial double combination therapy (macitentan plus tadalafil) and, while no statistically significant benefit was shown for triple combination vs. double combination therapy over the duration of the study, it was reasonable to refer to within-arm treatment effects

of the dual combination arm of this study as supportive of the evidence from the AMBITION study which was the basis for the guidelines recommending initial double combination therapy.

The Panel noted the slide at issue followed on from the slide at issue in point 1 above and noted its limited content as set out above. Whilst no further detail about TRITON was provided on the slide, the Panel noted the accompanying voiceover. The speaker highlighted that ambrisentan and tadalafil was not the only combination that had been shown to improve functional endpoints; improvements had also been shown with the combination of macitentan and tadalafil in the OPTIMA and TRITON studies. The speaker stated that the TRITON study compared triple therapy (macitentan, tadalafil and selexipag) with dual therapy (macitentan and tadalafil) and that 'what we know is that upfront dual combination therapy across the board improves function as well as other hard outcomes such as morbidity and mortality'. There was, however, no further discussion of the TRITON study and no mention of the primary endpoint or the failure of the study to meet it. Whilst the voiceover was relevant, the Panel noted that the presentation had to be capable of standing alone with regard to the requirements of the Code.

The Panel noted that the TRITON study poster stated that the results of the pre-specified secondary endpoints should be interpreted as exploratory, based on the statistical testing hierarchy, noting a large improvement in 6 MWD, NT-proBNP and other haemodynamic parameters was seen in both treatment groups at Week 26, with no difference between treatment arms.

The Panel considered that, in principle, when a primary endpoint failed to achieve statistical significance it was not necessarily unreasonable to refer to secondary endpoint data, so long as this was placed within the context of the overall study findings. The context and nature of the trial and material might also be relevant. It was unclear from the poster whether the within-arm improvements from baseline were a secondary endpoint in the Triton study, which appeared to be powered to look at between group differences. Within-arm data was provided in a table to illustrate the calculation of the between-group differences.

While the Panel understood that the objective of the presentation as a whole was to highlight that studies had demonstrated the benefit of initiating PAH patients on dual therapy, it was mindful that the Code required material to be sufficiently complete to enable recipients to form their own opinion of the therapeutic value of the medicine. In the Panel's view, the presentation of information regarding the within-arm treatment effects of the dual combination arm of the TRITON study was not placed within the context of the study, including its failure to achieve the primary endpoint, and in this regard was misleading. The Panel ruled **a breach of Clause 6.1**.

3. Misleading absolute risk reduction

The Panel noted the relevant slide was headed 'GRIPHON: Sequential oral triple therapy with selexipag improves long-term outcomes, particularly in FC II' and related to the GRIPHON study which investigated the treatment effect of adding selexipag to background therapy in PAH patients. Two Kaplan–Meier curves were shown. The first was headed '64% reduction in risk of disease progression compared to placebo in FC II patients on double background therapy'. The second Kaplan–Meier curve was headed '26% reduction in risk of disease progression compared to placebo in FC III patients on double background therapy'. Both graphs included the hazard ratio, confidence interval and ARR (absolute risk reduction). In both cases the figure cited for ARR was the same as the relative risk reduction given in the graph's heading.

The complainant alleged that it was nearly impossible in clinical trials for the absolute risk reduction to be the same as relative risk reduction and alleged that in presenting this information Janssen had exaggerated the effect of its medicine and thus had misled health professionals. Janssen accepted that the legends had been mislabelled with the relative risk reductions provided instead of the absolute risk reductions.

The Panel noted, but did not accept, Janssen's submission that the slide showed the full Kaplan–Meier curves with the number of patients at risk and therefore in spite of the error viewers would be able to evaluate the absolute treatment effect at any given timepoint, the inference being that the slide was thereby compliant. The Panel noted its comments above (at point 1) on this point and considered that these were relevant here. In the Panel's view, if relative risk reduction is stated, the absolute risk reduction should also be presented to allow the reader to make an immediate assessment of the clinical impact of an outcome.

In the Panel's view, providing incorrect information about absolute risk reduction was misleading contrary to the requirements of Clause 6.1 and its supplementary information. The Panel ruled **a breach of Clause 6.1**.

4. Alleged off label promotion of macitentan

The Panel noted the allegation related to two claims; the first appeared as part of the slide headed 'Conclusions' and stated 'Initial double combination therapy is recommended for the majority of PAH patients in low/intermediate risk, as this improves outcomes compared to monotherapy'. The second slide was headed 'Take-home messages: Combine' and the claim in question stated 'At diagnosis: Initial double combination therapy is recommended for the majority of PAH patients in low/intermediate risk'. The complainant alleged that macitentan was not licensed for use in initial combination therapy and therefore the claims in question encouraged the off-label use of macitentan.

The Panel noted the scope of the allegation was very narrow and related solely to the licensed indications for macitentan. The Panel noted its comments above on this matter (at point 2i) and considered that they were relevant here. The Panel noted that Section 4.1, Therapeutic indications, of the Opsumit SPC stated that Opsumit (macitentan) is licensed as monotherapy or in combination for the long-term treatment of pulmonary arterial hypertension (PAH) in adult patients of WHO Functional Class (FC) II to III. The Panel considered that the slides in question clearly referred to the use of macitentan in initial combination therapy and on this point was promoted in accordance with the terms of its marketing authorisation and was not inconsistent with the particulars listed in its SPC. In the Panel's view, the complainant was mistaken about the licensed indication for macitentan. The Panel therefore ruled **no breaches of Clause 11.2 in relation to each slide**.

5. Prescribing information

The Panel noted the allegation regarding reference to where the prescribing information could be found only being available at the very end of the presentation to 'avoid the risk of any viewer identifying these fatal errors'. The Panel noted that it did not appear that the presentation could be downloaded and ruled on this basis.

The Panel noted the location of the prescribing information was clearly signposted at the end of the video, where the statement 'Prescribing information is available on the website in which it is viewed' appeared. The Panel noted that the symposium was 90 minutes long; in its view, it

would be helpful to inform viewers where the prescribing information could be found at the start of a long presentation, as not all viewers would look at the very last slide.

The Panel noted the screenshot of the webpage housing the video within Janssen's website for health professionals. The webpage was dedicated to the 2021 congress of the European Respiratory Society and specifically the pulmonary hypertension highlights from the event. The screenshot indicated that the header of the webpage contained a narrow light blue banner stating that prescribing information and adverse event reporting information could be found at the bottom of the page, where separate links to the prescribing information were provided for each of Janssen's products for pulmonary hypertension. The Panel noted that the complainant appeared to have overlooked the signpost to the location of the prescribing information and the links at the bottom of the webpage. The Panel considered it would be helpful if the contrast between the colour of the header and of the links was improved to aid visibility.

The Panel noted Clause 12.6 of the Code required promotional material on the internet to provide a clear prominent statement as to where the prescribing information can be found. In its view, signposts were available on the webpage and within the material and viewers could access the prescribing information at any point before, during or after watching the video. The Panel considered that the complainant had not established their case and ruled **no breach of Clause 12.6**.

The Panel noted that there did not appear to be an allegation regarding the clarity or legibility of the prescribing information itself or any evidence to suggest that the video was downloadable from the webpage such that the prescribing information was required to be an integral part of it. Accordingly, the Panel ruled **no breach of Clause 12.1**.

Clause 5.1

The Panel noted that the symposium was originally presented at ERS in 2021 and was subsequently included on the Janssen website for health professionals and thus would have been reviewed for compliance with the Code on several occasions. The Panel considered that Janssen had failed to maintain high standards in relation to the presentation of information regarding the within-arm treatment effects of the dual combination arm of the TRITON study that was not placed within the context of the study, including its failure to achieve the primary endpoint, the omission of absolute risk reduction information and the error in labelling relative risk reduction as absolute risk reduction information. The Panel ruled a **breach of Clause 5.1**.

The Panel noted the complainant's references to 'fatal errors' but noted that the Panel had not been asked to consider Clause 2. The complainant had not explained why they considered their concerns were of this magnitude. The complainant bore the burden of proof. The Panel considered that its rulings of breaches of the Code, including a breach of Clause 5.1, adequately covered the complainant's general concerns.

Complaint received **12 January 2023**

Case completed **28 February 2024**