HEALTH PROFESSIONAL v NOVARTIS

Presentation at Speaker Meeting

An anonymous, contactable health professional who described themselves as a general practitioner complained about a presentation on Entresto (sacubitril and valsartan) delivered by a local consultant cardiologist at an event organised and sponsored by Novartis Pharmaceuticals UK. Entresto was indicated for the treatment of adults with symptomatic chronic heart failure with reduced ejection fraction.

The complainant alleged that the presentation on heart failure and Novartis' new product, Entresto, was not fair or balanced. Only the positive attributes of the medicine were presented and the audience was not given any information about potential side-effects or adverse reactions. In the complainant's view, the presentation was not sufficient such as to allow him/her to form his/her own opinion of the value of the medicine.

The detailed response from Novartis is given below.

The Panel noted that the meeting was designed to explore the 'myth of clinical stability in heart failure', the local burden of the condition and its impact on clinical resources. The Panel noted the timings and summarised content of the three presentations as set out in Novartis' response.

The first presentation discussed the economic burden of heart failure and the heart failure audit and did not mention Entresto. The second presentation 'Diagnosis and Management in Primary Care' discussed, *inter alia*, the causes, local prevalence, investigation and education and lifestyle management of heart failure. The treatment section discussed, *inter alia*, angiotensin receptor blockers, ACE inhibitors, beta blockers and mineralocorticoid receptor antagonists. Comparative efficacy and adverse event data for Entresto versus enalapril from PARADIGM-HF (McMurray *et al* (2014)) was discussed in 5 slides (3 efficacy, 1 adverse event and 1 summary slide). Four slides, each referenced to the Entresto summary of product characteristics, covered the practical prescribing of Entresto including initiating therapy, contraindications, dosing and special populations.

The third presentation, which appeared to be the subject of the complaint, titled [New York Heart Association] NYHA class and clinical outcomes in heart failure focussed on stratifying risk in patients with heart failure including patients with milder symptoms. The Panel noted Novartis' submission that this presentation referred to McMurray *et al* as that study contained data on the associated risks of sudden death between NYHA classes. The Panel noted that the presentation also included promotional claims and the final bullet point of the final slide 'Take home messages', in relation to sacubitril/valsartan and NYHA class read 'patients with NYHA class II symptoms should [be] switched if otherwise appropriate'.

The Panel also noted the safety findings in McMurray *et al* and that fewer patients stopped their study medication overall or because of an adverse event in the Entresto group than in the enalapril group. The authors noted that because of its greater vasodilator effects, treatment with Entresto was associated with a higher rate of symptomatic hypotension but there was no increase in discontinuation due to possible hypotension related adverse events.

The Panel noted that the presentation in question did not refer to potential side-effects or adverse reactions as stated by the complainant. The preceding presentation included some adverse event data from McMurray *et al* and information on contraindications and special populations from the SPC.

On balance, the Panel considered that the primary message of the presentation in question concerned NYHA classification and most of the data from McMurray *et al* was presented in that context. The complainant had not identified precisely what side effects/adverse reactions he/she considered were missing from the presentation in question. In this regard the Panel noted that the complainant bore the burden of proof. It was not for the Panel to infer such matters. The Panel therefore ruled no breach of the Code.

An anonymous, contactable health professional who described him/herself as a general practitioner complained about a presentation on Entresto (sacubitril and valsartan) delivered by a local consultant cardiologist at an event organised and sponsored by Novartis Pharmaceuticals UK Ltd. Entresto was indicated for the treatment of adults with symptomatic chronic heart failure with reduced ejection fraction.

COMPLAINT

The complainant alleged that the presentation on heart failure and Novartis' new product, Entresto, was not fair or balanced, in breach of Clause 7.2. Only the positive attributes of the medicine were presented and the audience was not given any information about potential side-effects or adverse reactions. In the complainant's view, the presentation was not sufficient such as to allow him/her to form his/her own opinion of the value of the medicine.

RESPONSE

Novartis stated that the promotional speaker meeting in question took place in 2019 at a named

venue; it started at 6:15pm and ended at 9pm. Three health professionals were engaged to present at the meeting:

- The meeting chair delivered a 15 minute introductory presentation which focussed on the economic burden of heart failure and then discussed some of the key findings within the National Heart Failure Audit 2016/2017. This presentation was non-product specific and did not contain any element of promotion of Entresto.

- The second presentation (45 minutes) on 'Diagnosis and Management in Primary Care' contained an illustration of a variety of treatment options (slide 30 onwards). Entresto was discussed within this section as a treatment option among others, and the efficacy and safety of Entresto were discussed: specifically 5 slides focussed on efficacy and 6 slides focussed on safety. With specific regard to the safety slides, the presentation outlined information from the clinical trial PARADIGM-HF (McMurray *et al* (2014)) and included practical advice for prescribing Entresto, special populations and contraindications.

- The third presentation (45 minutes) was on 'NYHA [New York Heart Association] Classes and Clinical Outcomes in Heart Failure'. The presentation focussed on using NYHA classes to stratify risk in patients with heart failure and highlighted the risk to those patients with milder symptoms. As PARADIGM-HF contained data on the associated risks of sudden death between NYHA classes, the presentation included subgroup data from this trial to support the delivery of this message.

The presentations were delivered together in the order stated above so as to ensure an organic overview of heart failure and related treatments, including Entresto. To this end, the third presentation was purposefully delivered after the second presentation, so as to provide an objective and unambiguous panorama of the wider topic subject matter of the meeting and ensure the required balance to the information provided.

The speakers were engaged in light of their expertise in cardiology. Details were outlined in the relevant meeting approval form. As indicated on that form, the objectives for this meeting were:

> '1) Upskill local clinicians on the burden of heart failure in the community, (2) Identification, referral and management of heart failure and (3) Benefits of Entresto vs ACE inhibitors for heart failure.'

The invitation/agenda clearly outlined what would be presented at the meeting:

> 'We invite you to be part of the heart failure conversation. During this meeting we will explore the myth of clinical stability in heart failure, the burden of the condition in your locality and its impact on clinical resources. We will debate how to improve patient outcomes and raise awareness of the unmet needs of patients in a constantly changing NHS.'

The invitation/agenda contained the Entresto prescribing information.

Novartis stated that the meeting was promotional with a strong educational focus, it was attended by 12 health professionals, all of whom arrived within the first 10 minutes of the start of the meeting and stayed to the end. Therefore, all attendees were present for the delivery of all the presentations and were able to receive both the safety and efficacy data presented throughout the entirety of the meeting. Furthermore, the prescribing information for Entresto was included at the end of the second and third presentations and was also available in hard copy format at the meeting.

In summary, Novartis submitted that the content shared at the meeting, including information on Entresto, was fair and balanced and not in breach of Clause 7.2.

PANEL RULING

The Panel noted that according to its agenda the meeting was designed to explore the 'myth of clinical stability in heart failure', the local burden of the condition and its impact on clinical resources. The Panel noted the timings and summarised content of the presentations as set out in Novartis' response.

The Panel noted that the complainant's allegation was in relation to the third presentation.

The first presentation discussed the economic burden of heart failure and the heart failure audit and did not mention Entresto. The second presentation was titled 'Diagnosis and Management in Primary Care' and discussed, *inter alia*, the causes, local prevalence, investigation and education and lifestyle management of heart failure. The pharmacology treatment section began at slide 30 and discussed, *inter alia*, angiotensin receptor blockers, ACE inhibitors, beta blockers and mineralocorticoid receptor antagonists. Comparative efficacy and adverse event data for Entresto versus enalapril from PARADIGM-HF (McMurray *et al* (2014)) was discussed in 5 slides (3 efficacy, 1 adverse event and 1 summary slide). Four slides, each referenced to the Entresto summary of product characteristics, covered the practical prescribing of Entresto including initiating therapy, contraindications (7 listed), dosing and special populations (elderly, renal impairment and hepatic impairment).

The Panel noted that the third presentation which appeared to be the subject of the complaint was titled NYHA class and clinical outcomes in heart failure which focussed on using NYHA classes to stratify risk in patients with heart failure including patients with milder symptoms. The Panel noted Novartis' submission that this presentation referred to McMurray *et al* as that study contained data on the associated risks of sudden death between NYHA classes. The Panel noted that the presentation went

beyond stratifying risk in certain heart failure patients; it also included promotional claims and the final bullet point of the final slide titled 'Take home messages', in relation to sacubitril/valsartan and NYHA class read 'patients with NYHA class II symptoms should [be] switched if otherwise appropriate'.

The Panel noted Entresto's use in special populations, its contraindications, special warnings and precautions for use, interactions and undesirable effects as set out in its SPC. The Panel also noted the safety findings in McMurray *et al* and the study authors' statement that fewer patients stopped their study medication overall or because of an adverse event in the Entresto group than in the enalapril group. The study authors noted that because of its greater vasodilator effects, treatment with Entresto was associated with a higher rate of symptomatic hypotension but there was no increase in discontinuation due to possible hypotension related adverse events.

The Panel noted that the presentation in question did not refer to potential side-effects or adverse reactions as stated by the complainant. The preceding presentation included some adverse event data from McMurray *et al* and information on contraindications and special populations from the SPC.

On balance, the Panel considered that the primary message of the presentation in question concerned NYHA classification and most of the data from McMurray *et al* was presented in that context. The complainant had not identified precisely what side effects/adverse reactions he/she considered were missing from the presentation in question. In this regard the Panel noted that the complainant bore the burden of proof. It was not for the Panel to infer such matters. The Panel therefore ruled no breach of Clause 7.2 of the Code.

Complaint received **14 March 2019**

Case completed **17 September 2019**