CASE AUTH/2933/2/17

HEALTH PROFESSIONAL CONSULTANT TO A PHARMACEUTICAL COMPANY v CHIESI

Promotion of Fostair

A complaint was received in a private capacity from a health professional who stated that he/she worked as a consultant to a pharmaceutical company. It had previously been decided, following consideration by the then Code of Practice Committee and the ABPI Board of Management, that private complaints from pharmaceutical company employees had to be accepted. To avoid this becoming a means of circumventing the normal procedures for intercompany complaints, the employing company would be named in the report. The complainant would be advised that this would happen and be given an opportunity to withdraw the complaint.

The principles set out above were applied to this complaint. Consultancy status should not be used to circumvent the normal rules for inter-company complaints.

The complainant was advised that if he/she wished to proceed with the complaint in a private capacity Novartis would be named in the case report; and the respondent company would be informed of his/her professional status and the connection with pharmaceutical companies. The complainant so agreed.

The complaint concerned an online advertisement for Fostair (beclomethasone and formoterol) issued by Chiesi. The advertisement included the claim 'Efficacy with only 3 steps per inhalation' and 'See the features of the Fostair NEXThaler device'. The advertisement also claimed 'Efficacy with only 3 steps per inhalation, 'open – inhale – close'. The claim was referenced to the Fostair NEXThaler 100/6 summary of product characteristics (SPC) and Kanniess *et al* 2015.

Fostair was indicated for the treatment of asthma and chronic obstructive pulmonary disease (COPD).

The complainant compared the claim that there were three steps per inhalation – open, inhale, close to the five steps listed in the patient information leaflet (PIL). Those five steps had additional points beneath each including crucially the requirement to hold one's breath for 5-10 seconds to receive a therapeutic dose. The complainant alleged that the prescribing information was also out-of-date and omitted the special warning regarding pneumonia.

The complainant stated that the prescribing information on the website was similarly out-of-date.

The detailed response from Chiesi is given below.

The Panel noted Chiesi's submission about the timing of the update to the prescribing information. The update to the prescribing information had been prepared in July 2016 ahead of the formal approval of the summary of product characteristics (SPC) variation on 5 September 2016. The Panel considered that the prescribing information for the online advertisement and on the website was up-to-date and therefore ruled no breach of the Code.

The Panel noted that the Fostair NEXThaler 100/6 SPC dated 7 September 2016 stated that correct use was essential in order for the treatment to be successful. The PIL stated that optimal lung delivery was obtained if the patient inhaled by breathing in quickly and deeply through the inhaler. A breath holding period of 5-10 seconds, or as long as comfortable for the patient was suggested before breathing out. The PIL instructions which were also in the SPC referred to four steps, visual check, open, inhale, close. Each of these steps had a number of instructions. The 'open' section included an instruction 'before inhaling breathe out as far as is comfortable'.

The advertisement in question referred to 'Efficacy with only 3 steps per inhalation. See the features of the Fostair NEXThaler device. The Panel accepted that as far as the device was concerned it had to be opened by the patient, used for an inhalation and closed by the patient. However to take the medicine correctly in order for the dose to be efficacious there were more than three steps. These were set out in full in the PIL. In addition as far as the device was concerned the PIL referred to four steps. The Panel decided that the advertisement was misleading as it was inconsistent with the SPC and the PIL. A breach the Code was ruled.

The Panel did not consider that the advertisement failed to meet high standards and nor did the circumstances warrant a ruling of a breach of Clause 2 and ruled accordingly.

The complainant stated at the time of submitting the complaint that he/she was a health professional who worked as a consultant to Novartis. It had previously been decided, following consideration by the then Code of Practice Committee and the ABPI Board of Management, that private complaints from pharmaceutical company employees had to be accepted. To avoid this becoming a means of circumventing the normal procedures for intercompany complaints, the employing company would be named in the report. The complainant would be advised that this would happen and be given an opportunity to withdraw the complaint.

This issue came to the fore many years ago when an employee of a pharmaceutical research company complained in a private capacity about a journal advertisement issued by GlaxoSmithKline UK Ltd

(Case AUTH/1498/7/03). In Case AUTH/1498/7/03 it was decided that the pharmaceutical research company would be named in the case report whilst making it clear that the complaint was made in a private capacity.

The case preparation manager decided that the principles set out above would apply to consultants. Consultancy status should not be used to circumvent the normal rules for inter-company complaints.

The complainant was advised that if he/she wished to proceed with the complaint in a private capacity Novartis would be named in the case report; and the respondent company would be informed of his/her professional status and the connection with pharmaceutical companies. The complainant so agreed.

Novartis stated that it had no knowledge of, or involvement in, the complaint and did not know the complainant's identity.

The complaint concerned an online advertisement for Fostair (beclomethasone and formoterol) issued by Chiesi Limited (ref CHNEX20161340 Dec 16). The advertisement included the claim 'Efficacy with only 3 steps per inhalation' and 'See the features of the Fostair NEXThaler device'. The advertisement also claimed 'Efficacy with only 3 steps per inhalation, 'open – inhale – close'. The claim was referenced to the Fostair NEXThaler 100/6 summary of product characteristics (SPC) and Kanniess *et al* 2015.

Fostair was indicated for the treatment of asthma and chronic obstructive pulmonary disease (COPD).

COMPLAINT

The complainant compared the claim that there were three steps per inhalation – open, inhale, close to the five steps listed in the patient information leaflet (PIL). Those five steps had additional points beneath each. Crucially one step was the requirement to hold one's breath for 5-10 seconds. If patients did not do this, they would not receive a therapeutic dose. The complainant alleged that the prescribing information was also out-of-date and omitted the special warning regarding pneumonia.

The complainant stated that the prescribing information on the website was similarly out-of-date.

In writing to Chiesi attention was drawn to the requirements of Clauses 2, 4.1, 7.2 and 9.1.

RESPONSE

Chiesi stated it was committed to maintaining high standards and strengthening the image of the pharmaceutical industry by operating in a responsible, ethical and professional manner, especially in relation to materials and activities.

1 Prescribing Information

Chiesi stated that the complainant was incorrect.

The hyperlink to the electronic medicines compendium (eMC) showing the history log of updates to the Fostair NEXThaler 100/6 summary of product characteristics (SPC) was provided by the complainant. The current SPC history log displayed five updates with the latest implemented on 7 September 2016. This history log confirmed that this SPC update included, *inter alia*, 4.4 Special warnings and precautions for use – pneumonia in patients with COPD.

The prescribing information for the digital banner advert for Fostair NEXThaler 100/6 (ref CHNEX20161340) was not provided by the complainant. Instead, a hyperlink was provided linking to the Chiesi website, subsequently alleging that the prescribing information for Fostair NEXThaler 100/6 (ref CHWEB20160717) was similarly out of date on the respiratory products section of the Chiesi website.

Chiesi confirmed that the prescribing information contained within the certified, digital banner advertisement for Fostair was the same version (date of preparation July 2016) as that which appeared on the respiratory products section of Chiesi's website.

Although not explicitly stated by the complainant, the clear implication was that prescribing information used in the digital banner advertisement and on the respiratory products section of Chiesi's website could not reflect the updated Fostair NEXThaler 100/6 SPC dated 7 September 2016, because the prescribing information was prepared in July 2016.

Chiesi stated that it took the matter of using up-to-date prescribing information very seriously and at the time of preparation, Chiesi was acutely aware of PMCPA guidance issued on 20 April 2016, that referred to, *inter alia*, some companies incorrectly assuming that there was a period of grace in which up-to-date prescribing information to reflect changes to the SPC was implemented. In response to the release of this guidance Chiesi implemented a risk minimising measure of preparing updated prescribing information in advance of completion of a Type 1A variation to the Fostair NEXThaler SPCs. The intention at the time was to embargo the updated version of the prescribing information until approval of this variation.

In July 2016, Chiesi's corporate regulatory department based in Italy informed the UK affiliate about the requirement to submit a Type 1A variation to implement the outcome of the referral Article 31 including, *inter alia*, 4.4 Special warnings and precautions for use – Pneumonia in patients with COPD, for the marketing authorisations of inhaled corticosteroid containing medicinal products indicated in the treatment of COPD. The specific wording required to update SPCs was made available by the European Medicines Evaluation Agency (EMA) at the time. Internally, within the UK medical affairs department a timetable of actions and activities were initiated by Chiesi:

Timelines and actions for creation of current prescribing information

	Medical Affairs – Communications/Action(s)
18 July 2016	Medical affairs manager briefed medical affairs team including, *inter alia*,: • Fostair SPCs would be updated with information on pneumonia following the PRAC review. • Significant changes in Section 4.4 and 4.8 would impact the Fostair prescribing information. • Update the prescribing information for Fostair. • Note in the job summary that the updated prescribing information would be embargoed until formal approval received from the MHRA (anticipated early September 2016). • Once approved the old prescribing information would be withdrawn and archived.
18 July 2016	Medical affairs manager informed the marketing department, *inter alia*, that: • Fostair SPCs for both NEXThaler and pMDI would be updated with information on pneumonia following the PRAC review. • The medical affairs team will subsequently prepare the updated prescribing information. • Prescribing information will be embargoed for use until approval received from the MHRA.
8 August 2016	Internal approval of updated prescribing information by two Chiesi signatories. Consequently, the date of preparation was July 2016.
9 August 2016	Medical affairs team informed the marketing department, *inter alia*, that: • Updating of Fostair prescribing information was complete. • Updated prescribing information was embargoed until confirmation of MHRA approval which was expected in September. • The prescribing information would be added to the server for use only after the embargo was lifted.
7 September 2016	Medical affairs manager informed the marketing department, *inter alia*, that: • The pneumonia variation for Fostair pMDI 100/6 and Fostair NEXThaler 100/6 were both now approved. • Fostair prescribing information was no longer embargoed.

Chiesi submitted that given the actions undertaken, the Fostair NEXThaler 100/6 prescribing information was not out-of-date as alleged and therefore not in breach of the Code.

The Code stated that the prescribing information consisted of, *inter alia*, a succinct statement of common adverse reactions likely to be encountered in clinical practice, serious adverse reactions and precautions and contra-indications relevant to the indications in the advertisement.

It was not clear why the complainant concluded that a warning related to pneumonia had been omitted other than he/she had incorrectly assumed that the prescribing information could not reflect the updated Fostair NEXThaler 100/6 SPC dated 7 September 2016, because this prescribing information was prepared in July 2016 and did indeed include the pneumonia warning.

Failure to acknowledge the statements related to pneumonia in the prescribing information by the complainant thus appeared to be an oversight and invalidated the related allegation. Chiesi noted that the PMCPA specifically requested the complainant to set out what in his/her opinion, was missing from the prescribing information.

Furthermore, Chiesi submitted that the proactive risk mitigating measures implemented by the medical affairs team (tabulated above) following the release of the April 2016 PMCPA guidance on keeping prescribing information up-to-date, meant Chiesi was actually enhancing the high standards expected and strengthening the image of the pharmaceutical industry, contrary to alleged implications of Clauses 9.1 and 2. Therefore there was no breach of Clauses 4.1, 9.1 and 2.

In response to a request for further information in relation to the delay in using updated prescribing information on the Chiesi respiratory website, Chiesi submitted that an update to the prescribing information for Fostair pMDI and Fostair NEXThaler 100/6 was prepared in July 2016 following an update to the SPC with the pneumonia warning. The prescribing information was examined and approved by two Chiesi signatories on 8 August 2016, ahead of the formal approval of the SPC variation by the MHRA on 5 September 2016. The Chiesi respiratory website was not developed or live at the time of approval of the SPC variation by the MHRA. The Chiesi respiratory website was certified on 22 November 2016 and went live for the first time on 25 November 2016.

2 Alleged misleading claim

Chiesi stated that the claim '3 steps per inhalation –

open, inhale, close' appeared part way through the running of the digital banner advertisement once the gradually building image of the Fostair NEXThaler 100/6 device was fully formed and the claim in question appeared over the top of the fully formed device image.

The primary reference supporting the claim was the Fostair NEXThaler 100/6 SPC to which the complainant did not refer. The Fostair NEXThaler 100/6 SPC included a section entitled 'E. How to use your NEXThaler inhaler'. Directly underneath this were three of four sub-section titles that clearly related to the operational sequence of the Fostair NEXThaler 100/6 device, namely E2 – Open; E3 – Inhale and E4 – Close. E1 – Visual Check, would not ordinarily be considered as part of the operational sequence. These sub-section headings were aligned to the operational sequence of an inhaler device, and supported the claim '3 steps per inhalation – open, inhale, close'. Chiesi submitted that the statement was not misleading and therefore there was no breach of the Code.

Chiesi submitted that the claim was supported by other literature including Corradi *et al* 2014 which described the inhalation steps as '3 Open Inhale Close'.

Voshaar T *et al* 2014 undertook a usability study involving the NEXThaler device and noted that '... NEXThaler was a DPI that had been designed to overcome some of the limitations of the currently marketed devices ... had a unique "open-inhale-close" operating sequence that was at least one inhalation step less than that of other existing DPIs and easy for patients to use ....'. In this study involving 66 adult asthma patients, NEXThaler was considered the easiest to use device when compared to two other devices assessed.

Chiesi therefore submitted that the claim '3 steps per inhalation – open, inhale, close', was therefore not misleading and not in breach of the Code.

Chiesi stated that sequences such as opening a device cap, priming/loading a device, inhaling from a device and finally, closing a device were generally well accepted overarching steps related to operational sequences of any inhaler device. Fully opening the inhaler cap of Fostair NEXThaler 100/6 automatically primed the device. So in the case of Fostair NEXThaler 100/6, the operational sequences were: Opening a device cap, inhaling from a device and closing the device cap ie excluding the necessity to prime the device separately.

The complainant alleged that the claim '3 steps per inhalation – open, inhale, close' was misleading because the Fostair PIL contained a section 'E3 – Inhale' where there were 5 sub-points, one of which the complainant stated was crucial.

Chiesi firmly believed it was self-evident that the '3 steps' referred to the operational sequence 'open-inhale-close' and not the sub-points directly underneath 'E3 – Inhale' as seen in the PIL and SPC.

Additionally, the fully formed Fostair NEXThaler 100/6 device image alone placed in the background behind the claim in question also helped with the context of the operational sequence. Chiesi submitted it was self-evident to health professionals that there would be specific actions related to each over-arching step such as holding breath immediately after inhalation, and therefore Chiesi did not accept that the claim was misleading as implied and therefore not in breach of Clauses 7.2, 9.1 and 2 of the Code.

PANEL RULING

The Panel noted that all promotional material must be accurate when it was used and include prescribing information that complied with the Code. The three month time limit that had been previously allowed for prescribing information to be updated was only in relation to changes in cost for a medicine as a result of new Pharmaceutical Price Regulation Scheme (PPRS) agreements.

The PMCPA had always advised that prescribing information had to be up-to-date at the time it was used. It appeared that some in the industry had, in error, interpreted this as three months.

The Panel noted Chiesi's submission about the timing of the update to the prescribing information for the advertisement in question to include the addition of pneumonia in patients with COPD to Section 4.4, Special warnings and precautions for use of the Fostair NEXThaler 100/6 SPC. The update to the prescribing information had been prepared in July 2016 ahead of the formal approval of the SPC variation by the MHRA on 5 September 2016. The Panel considered that the prescribing information for the online advertisement was up-to-date and therefore ruled no breach of Clause 4.1.

The Panel also ruled no breach of Clause 4.1 in relation to the Chiesi respiratory website which according to Chiesi was not available before the approval of the SPC variation. This website went live in November 2016 and included the updated prescribing information which was prepared in July 2016.

The Panel noted that the Fostair NEXThaler 100/6 SPC dated 7 September 2016 stated that correct use of the NEXThaler inhaler was essential in order for the treatment to be successful. The patient should be advised to read the PIL carefully and follow the instructions for use as given in the leaflet. It stated that optimal lung delivery was obtained if the patient inhaled by breathing in quickly and deeply through the inhaler. A breath holding period of 5-10 seconds, or as long as comfortable for the patient was suggested before breathing out. The PIL instructions which were also in the SPC referred to four steps, visual check, open, inhale, close. Each of these steps had a number of instructions. The 'open' section included an instruction 'before inhaling breathe out as far as is comfortable'.

The advertisement in question referred to 'Efficacy with only 3 steps per inhalation. See the features of

the Fostair NEXThaler device. The Panel accepted that as far as the device was concerned it had to be opened by the patient, used for an inhalation and closed by the patient. However to take the medicine correctly in order for the dose to be efficacious there were more than three steps. These were set out in full in the PIL. In addition as far as the device was concerned the PIL referred to four steps. The Panel decided that the advertisement was misleading as it was inconsistent with the SPC and the PIL. A breach of Clause 7.2 was ruled.

The Panel did not consider that the advertisement failed to meet high standards and thus no breach of Clause 9.1 was ruled. The Panel noted that Clause 2 was used as a sign of particular censure and reserved for such use. It did not consider that the circumstances warranted a ruling of a breach of Clause 2 and ruled accordingly.

Complaint received **8 February 2017**

Case completed **2 May 2017**
