HEALTH PROFESSIONAL v CEPHALON

Promotion of Effentora

A health professional complained that a Cephalon representative had clearly promoted the sublingual use of Effentora (buccal fentanyl citrate).

Effentora was indicated for the treatment of breakthrough pain in adults with cancer who were already receiving maintenance opioid therapy for chronic cancer pain. The tablets were to be placed in the upper portion of the buccal cavity.

The complainant noted that according to the summary of product characteristics (SPC) Effentora was not licensed for sublingual use. The complainant was concerned that representatives had promoted this 'off licence' use and that inaccurate information had been given to health professionals which could potentially lead to patients being treated on inaccurate data.

In response to a request for further information, the complainant stated that two different representatives had made the claim and that other physicians within the local primary care trust had also heard it.

The detailed response from Cephalon is given below.

The Panel noted that the complainant's identity had not been revealed to Cephalon although the company had been told which PCT he worked in.

The Panel considered that it was impossible to know who had said what to the complainant about sublingual Effentora or whether such information had been given in response to an unsolicited request. The complainant had stated that two different representatives had mentioned that Effentora could be used sublingually. The complainant had also referred to other colleagues within the PCT being told about sublingual use of Effentora although no corroborating evidence was provided in this regard. A judgement had to made on the available evidence and the balance of probability bearing in mind that extreme dissatisfaction was usually required on the part of an individual before he or she was moved to complain.

Darwish *et al* (2009) reported that sublingual use of a fentanyl buccal tablet was a viable alternative to buccal placement in patients who might require an alternative administration site. On 25 February 2009 Cephalon's medical department emailed the sales marketing management to state that Darwish *et al* was outside the product licence and so must not be discussed with customers. Requests from health professionals for information about the study could be forwarded to medical information or to the medical scientific liaison team. The sales representatives were only briefed verbally to forward enquiries to medical information. In the Panel's view it was inadequate to only verbally brief representatives on an off-label issue that was likely to generate interest. No details of that briefing were supplied. In July, after it had received this complaint, Cephalon had written to its staff reminding them that sublingual use of Effentora was outwith the licence and that requests for information on such use should be referred to medical information.

The Panel was also concerned that from Cephalon's response a medical scientific liaison executive might have both a non promotional role ie responding to unsolicited enquiries, and what could be a promotional role ie presenting on technical issues that were beyond the scope of the sales representative. This might have added to the confusion.

The Effentora promotional material referred only to buccal use. An in-house presentation about the Code, used at the Effentora launch meeting, clearly stated that requests for off-label information would be dealt with by the medical information department.

The Panel noted that a complainant had the burden of proving their complaint on the balance of probabilities. The Panel was concerned that, in the first instance, representatives had only been verbally briefed about the sublingual use of Effentora. Nonetheless the training at the Effentora launch meeting clearly explained how off-label queries should be handled. Representatives should have been well aware that sublingual administration of Effentora was outwith the licence. The Panel did not consider that the complainant had provided evidence to show that, on the balance of probabilities, either a representative or a member of the medical scientific liaison team had promoted the sublingual use of Effentora. The Effentora briefing material did not advocate sublingual use. No breach of the Code was ruled.

A health professional complained about the promotion of Effentora (buccal fentanyl citrate) by Cephalon (UK) Limited.

Effentora was indicated for the treatment of breakthrough pain in adults with cancer who were already receiving maintenance opioid therapy for chronic cancer pain. The tablets were to be placed in the upper portion of the buccal cavity.

COMPLAINT

The complainant stated that a Cephalon representative had told him that Effentora could be administered sublingually. The representative was very clear in their promotion of this mode of administration as a benefit of the product. The complainant checked the Effentora summary of product characteristics (SPC) and, in fact, this was an unlicensed mode of administration. The complainant was concerned that representatives had promoted this off licence use having spoken to a number of local fellow clinicians. The complainant was also concerned that Cephalon had given inaccurate information to health professionals when prescribing decisions on these products were being made which could potentially lead to patients being treated on inaccurate data.

When writing to Cephalon, the Authority asked it to respond in relation to Clauses 3.2, 15.2 and 15.9 of the Code.

RESPONSE

Cephalon submitted that the sales representatives had only been briefed on the buccal use and administration of Effentora. No briefings had suggested that other routes of administration were appropriate.

Cephalon submitted that if health professionals referred to a published pharmacokinetic study assessing the bioequivalence of sublingual and buccal fentanyl buccal tablet (Darwish *et al* 2009), sales representatives were verbally briefed to forward any enquiries to medical information. This study was only available from Cephalon via an unsolicited request forwarded to medical information. An email sent on 25 February 2009 to the marketing sales management, emphasised this following publication of the paper.

Cephalon submitted that the complainant referred to a specific representative visit and the alleged off licence use also being promoted locally. Cephalon submitted that the representative who covered the complainant's area could only recollect a question being asked about sublingual delivery of Effentora, in response to which the enquiry was referred to medical information and a member of the medical scientific liaison team. A discussion of this information was then initiated by the health professional, to which the representative concerned stated he was unable to discuss this topic and any further points should be referred to medical information.

Cephalon submitted that its sales representatives received Code update training which included specific reference to promotion within the scope of the SPC.

Cephalon refuted the alleged breaches of Clause 3.2, 15.2 and 15.9. A specific briefing had been sent to the sales teams to remind them of the requirement to forward any requests for information on sublingual (and any other information that fell outside the scope of the SPC) to medical information.

FURTHER COMMENTS FROM CEPHALON

In response to a request for further information, Cephalon explained that its medical scientific liaison team was a field-based extension of its medical affairs medical information function. The team reported to the medical director and responded to unsolicited enquiries from health professionals about detailed technical points or aspects that fell outside the marketing authorization. Furthermore, the team might receive requests from health professionals for presentations to clinical teams on technical details that went beyond the scope of the sales representatives. The team also trained clinical teams participating in a phase IV clinical trial, working in partnership with the clinical research organisation managing the trial. This involved education on breakthrough cancer pain, the administration of the fentanyl buccal tablet and dose titration. The job description for the function, which formed the basis of the role briefing, was provided. Two of the three appointees were from medical information/medical affairs backgrounds, and were familiar with the requirements of the Code for such roles. The third came from a clinical science role via sales and had received additional training and coaching.

It was possible that the complainant had seen a member of the medical scientific liaison team. However, the team would have only discussed sublingual Effentora if the health professional had made a specific and unsolicited request for the information, or following a referral from a sales representative who was unable to address the request. It was difficult to verify whether someone from the team saw the complainant in view of their being anonymised for the purposes of the complaint.

Cephalon stated that health professionals might have referred to Darwish *et al*, hence enquiries arising about sublingual use.

The sales representatives were briefed as to how to comply with the Code if asked about any situation that was outside the marketing authorization during the Effentora launch meeting. Several scenarios were provided, and the need to forward any enquires to medical information relating to off-licence use was emphasised verbally.

FURTHER COMMENTS FROM THE COMPLAINANT

The complainant stated that the claim was mentioned to him by two different representatives (he could not remember their level/seniority) and that other physicians within the local primary care trust (PCT) had told him that they had also heard the claim.

PANEL RULING

The Panel noted that the complainant's identity had not been revealed to Cephalon although the company had been told which PCT he worked in.

The Panel considered that it was impossible to know who had said what to the complainant about sublingual Effentora or whether such information had been given in response to an unsolicited request. The complainant had stated that two different representatives had mentioned that Effentora could be used sublingually. The complainant had also referred to other colleagues within the PCT being told about sublingual use of Effentora although no corroborating evidence was provided in this regard. A judgement had to made on the available evidence and the balance of probability bearing in mind that extreme dissatisfaction was usually required on the part of an individual before he or she was moved to complain.

The Panel noted that Darwish *et al* reported that sublingual use of a fentanyl buccal tablet was a viable alternative to buccal placement in patients who might require an alternative administration site. Effentora was indicated only for buccal placement. On 25 February 2009 an email was sent from Cephalon's Medical Department to the sales marketing management which stated that Darwish *et al* was outside the product licence and so must not be discussed with customers. Requests from health professionals for information about the study could be forwarded to medical information or to the medical scientific liaison team who could address the query. The sales representatives were only briefed verbally to forward enquiries to medical information. In the Panel's view it was inadequate to only verbally brief representatives on an off-label issue that was likely to generate prescriber interest. No details of that briefing were supplied. In July, after it had received this complaint, Cephalon sent a written briefing document to its staff reminding them that sublingual use of Effentora was outwith the licence and that requests for information on such use should be referred to medical information.

The Panel was also concerned that from Cephalon's response a medical scientific liaison executive might have two roles, a non promotional role ie responding to unsolicited enquiries, and what could be a promotional role ie presenting on technical issues that were beyond the scope of the sales representative. This might have added to the confusion.

The Panel noted that the Effentora promotional material supplied by Cephalon referred only to the buccal use of the medicine. An in-house presentation about the Code, used at the Effentora launch meeting, clearly stated that requests for off-label information would be dealt with by the medical information department.

The Panel noted that a complainant had the burden of proving their complaint on the balance of probabilities. The Panel was concerned that, in the first instance, representatives had only been verbally briefed about the sublingual use of Effentora. Nonetheless the training on the Code delivered at the Effentora launch meeting clearly explained how off-label queries should be handled. Representatives should have been well aware that sublingual administration of Effentora was outwith the licence. The Panel did not consider that the complainant had provided evidence to show that, on the balance of probabilities, either a representative or a member of the medical scientific liaison team had promoted the sublingual use of Effentora. No breaches of Clauses 3.2 and 15.2 were ruled. The Effentora briefing material did not advocate sublingual use. No breach of Clause 15.9 was ruled.

Complaint received **20 July 2009**

Case completed **16 October 2009**