ANONYMOUS v GENZYME

Conduct of a Representative

An anonymous complainant referred to the conduct of a named Genzyme employee during a meeting to discuss Aubagio (teriflunomide).

Aubagio (teriflunomide) was licensed for the treatment of adults with relapsing remitting multiple sclerosis. Its summary of product characteristics stated that liver enzymes should be assessed before treatment and monitored every two weeks for the first six months.

The complainant explained that the employee met a consultant neurologist and a pharmacist to discuss Aubagio. Concerns had been raised regarding the need to accommodate the monitoring of patients on Aubagio every two weeks for the first six months. In response the employee said that another hospital unit was not going to follow the licence and was looking at monthly monitoring. The complainant stated that it was inappropriate to suggest that licensed guidelines were not followed. The complainant was concerned that the employee could be having further off-licence discussions with health professionals and possibly bringing the industry into disrepute.

The detailed response from Genzyme is given below.

The Panel noted that the parties' accounts differed. In such circumstances it was difficult to determine precisely what was said at the meeting and therefore where the truth lay. A judgement had to be made on the available evidence bearing in mind that the complainant had to establish his/her case on the balance of probabilities.

The Panel noted the complainant's allegation that the named employee had stated during a meeting with a doctor, pharmacist and a Genzyme representative that a hospital unit was looking at monthly monitoring for Aubagio patients which was outwith the product licence. The representative had raised concerns with the manager after the meeting but the manager did not recollect a discussion about off-label monitoring. Had this been raised, the manager would have reported the matter to the employee's manager. In addition, the Panel noted that the representative's record of the meeting referred to setting up central monitoring but did not indicate that anything untoward had occurred.

According to Genzyme, the named employee denied making the comments alleged and stated that in response to the doctor raising concerns about the difficulty of monitoring every two weeks, the employee stated that a number of centres were similarly concerned and referred to another hospital's shared care plan. One of the health professionals present might have mentioned monthly monitoring but the named employee could not be sure if it was mentioned at all or if it was, who might have mentioned it. The named employee was not aware of the plans for monthly monitoring but knew about the shared care plan from a medical science liaison (MSL).

According to Genzyme, the pharmacist present corroborated the named employee's position. The pharmacist thought that the doctor might have referred to monthly monitoring but disagreed with the complainant's version of the meeting. There was no evidence from the doctor before the Panel.

The Panel noted that the named employee stated that 'they discussed monitoring further'. The Panel had no information about the detail of that general discussion. The Panel considered that it was likely that if monthly monitoring had been raised by a health professional the Genzyme staff present would have responded to this concern. The Panel noted that the relevant objection handler about monitoring discussed the licensed requirements and referred the health professional to in depth hepatic safety data.

Whilst noting its concern and comments above the Panel noted that the complainant had to establish his/her case on the balance of probabilities. The complainant had been asked to comment on Genzyme's response but had stated that he/she had no additional comment to make. Given the parties' differing accounts of the meeting in question, it was impossible to determine precisely what had been said. The Panel therefore ruled no breach of the Code including Clause 2.

A complaint was received about the conduct of a named Genzyme employee during a meeting to discuss Aubagio (teriflunomide) from someone who was contactable but wanted to remain anonymous.

Aubagio (teriflunomide) was licensed for the treatment of adult patients with relapsing remitting multiple sclerosis (MS). Elevation of liver enzymes had been observed in patients treated with Aubagio and so liver enzymes should be assessed before treatment and every two weeks during the first six months of treatment and every eight weeks thereafter (Aubagio summary of product characteristics (SPC)).

COMPLAINT

The complainant explained that a named Genzyme employee (employee 1) met a consultant neurologist and a pharmacist to discuss Aubagio. The complainant stated that various questions and concerns had been raised by the health professionals as they had yet to prescribe the medicine for their

patients. The health professionals would struggle to accommodate the monitoring of patients every two weeks for the first six months to which employee 1 replied that another unit in another named hospital was not going to follow the licence and was looking at monthly monitoring. The complainant stated that it was highly inappropriate for employee 1 to suggest that licensed guidelines were not followed. The complainant was concerned that employee 1 could be having further off-licence discusions with health professionals and possibly bringing the industry into disrepute.

When writing to Genzyme, the Authority asked it to respond in relation to Clauses 2, 3.2 and 15.2 of the Code.

RESPONSE

Genzyme submitted that it took allegations of misconduct of its employees and potential breaches of the Code very seriously.

Genzyme stated that there were four people at the meeting in question: employee 1, another Genzyme employee (employee 2), a pharmacist and the doctor. Significant efforts were made to contact and interview the doctor but unfortunately Genzyme had been unable to do so during the time allotted.

In addition Genzyme stated that it interviewed a further two Genzyme employees as a result of information which was provided during the interviews of employees 1 and 2.

Genzyme submitted that employee 1 had met the pharmacist and doctor prior to the call in question and was invited to meet to talk about Aubagio. Employee 2 was new to the business and employee 1 agreed to introduce him/her at the meeting.

Genzyme provided a copy of the Aubagio Risk Management Plan which discussed patient monitoring in the first six months of treatment, along with the certificate of approval. No briefing materials were used during the meeting.

Genzyme provided a copy of the Aubagio SPC and submitted that there were no briefing materials which had been sent to the field force or commissioning specialists about the named hospital's alleged proposal not to follow Aubagio's licence with regard to patient monitoring. Employee 1's evidence was that he/she was not aware that this unit had any plan to go off-licence. Genzyme stated that employee 1 had passed the representatives' examination and employee 2's entry on the customer relationship management (CRM) database for the meeting in question was provided.

Genzyme submitted that it had obtained three accounts of the meeting. Employee 2's account concurred with the anonymous complaint. Genzyme submitted that there was strong concordance between the full and detailed accounts of the meeting provided by employee 1 and the pharmacist; both agreed that employee 1 did not state that the other hospital was not going to follow the licence as alleged.

In addition, employee 2 stated that he/she had told the manager of the concern on the day of the meeting and Genzyme therefore interviewed the manager as part of the investigation. While the manager confirmed that employee 2 had raised various concerns about the meeting his/her recollection was that those concerns were about employee 1's poor preparation for the meeting and weakness in objection handling. The manager could not recall any mention of advice or promotion that deviated from the SPC and if told that employee 1 had dealt inappropriately with an 'off-label' question his/her manager would have been contacted as that would have been a more serious issue requiring corrective action.

Employee 1's account

Genzyme submitted that employee 1 had been invited to meet the pharmacist and doctor to talk about Aubagio. Employee 2 was new and was invited to be introduced. During the meeting formulary was discussed and the doctor raised concerns about the difficulty of monitoring patients once every two weeks but employee 1 did not say that the other hospital was looking at monthly monitoring for patients.

Employee 1 stated that a number of centres had raised this concern and the health professionals might have stated that they had heard that the other hospital might be monitoring monthly. Employee 1 stated that he/she had not been aware of this; the licence required monitoring once every two weeks in the first six months of treatment and he/she understood that the other hospital was planning to put a shared care programme in place with GPs to manage the monitoring requirements in the licence. Employee 1 submitted that they discussed monitoring further and he/she suggested that a medical science liaison (MSL) should arrange to discuss the matter in further detail.

Genzyme asked employee 1 how he/she knew what the other hospital was planning to do with regard to monitoring and was told that an MSL colleague had provided the information.

Employee 1 stated that he/she had a difficult relationship with employee 2; employee 1 had raised a grievance against employee 2 which had been upheld ten days before the complaint was received by the PMCPA and he/she considered that that was the reason for the complaint.

Interview with MSL colleague

Genzyme interviewed the MSL who had told employee 1 about the other hospital's plans and asked about these plans without giving the background to the question. The MSL corroborated employee 1's account stating that a named doctor had been quite vocal (including at national conferences) about his thoughts that the science did

not merit monitoring patients once every two weeks in the first six months but that the hospital had nonetheless accepted the recommendations in the SPC. The MSL was very clear that the other hospital planned to enter into a shared care arrangement, initially on a case-by-case basis, with GPs to carry out twice monthly monitoring and had a number of patients with whom such monitoring arrangements had been agreed with GPs.

Employee 2's account

Genzyme interviewed employee 2 who stated that employee 1 had said that the hospital was not going to follow the licence and was looking at monitoring monthly for patients. Employee 2 stated that the doctor had stopped employee 1 as it was not in accordance with the licence and he/she did not want to talk about anything off-label. Employee 2 stated that he/she felt embarrassed and challenged employee 1 about the statement after the meeting. Employee 2 also stated that he/she had informed the line manager in a telephone call after the meeting that employee 1 had made such a statement about monitoring and showed Genzyme an (undated) email on the subject that had been saved but never sent. Employee 2 submitted unprompted that he/she had a difficult relationship with employee 1.

Interview with employee 2's line manager

Genzyme submitted that the line manager stated that he/she had no recollection of employee 2 telling him/her that employee 1 had suggested that the hospital was not going to follow the licence for monitoring of Aubagio. The line manager recalled that employee 2 had called after the meeting, unhappy with the way it had gone. The line manager also recalled that on another occasion employee 2 had mentioned that another health professional at a different centre had mentioned monthly monitoring and on this occasion immediately informed the health professional that the requirement in the licence was to monitor once every two weeks for the first six months. This was to illustrate and provide evidence for the line manager's belief that if employee 1 had promoted off-label he/she would have expected employee 2 to intervene and corrected it and he/she would have reported this to employee 1's line manager.

Account of the meeting from the pharmacist

Genzyme submitted that the pharmacist stated that he/she recalled the meeting because the relationship between the two Genzyme employees seemed strained and he/she wondered if there was difficultly between them. The pharmacist stated that he/she vaguely remembered the conversation about the other hospital; the two doctors in the two hospitals knew each other and the pharmacist thought it was the doctor in the meeting who had said that the other doctor might be going to monitor patients monthly; employee 1 did not say that. When asked whether the doctor in the meeting had stopped employee 1 as he/she did not want to talk about monitoring off-label, the pharmacist stated that it did not sound like something that doctor would say.

Genzyme concluded that given the above, the weight of evidence suggested that the impropriety alleged in the anonymous complaint did not take place.

In response to a request for an explanation regarding what employee 1 knew of the plan to go off-licence with regard to monitoring and what was said about it during the meeting, Genzyme explained that the plan referred to by employee 1 and the MSL was not the same as the plan referred to by employee 2. The plan meant different things to different people. The shared care plan was not off-licence or inappropriate. The evidence suggested that employee 1 believed the other hospital was planning to implement a program of shared care with GPs to monitor every 2 weeks in line with the SPC. It was what employee 1 said he/she believed and the MSL independently confirmed this was what he/she discussed with employee 1.

Employee 1 recounted that when the pharmacist and doctor brought up the fact that they thought fortnightly monitoring presented a challenge, he/she had empathised, confirming that a number of centres felt the same way, but only spoke about shared care as a possible route to a solution. This would not be off-licence. When asked if a monthly monitoring interval was discussed, employee 1 replied to Genzyme that one of the health professionals at the meeting might have mentioned it, but could not remember for sure if it was mentioned at all or, if it was mentioned, who might have mentioned it. Again, employee 1 did not appear to say or do anything inappropriate by this account. Additionally, employee 1's evidence was supported by the pharmacist's recollection who recalled that the doctor spoke a bit about the other hospital, but could not remember for sure if he/she had mentioned monthly monitoring. The pharmacist was very confident however that employee 1 had not mentioned it and no one had taken from the meeting that monthly monitoring might be an option.

It was the MSL's evidence that the other hospital never had a plan to monitor monthly. This was backed up anecdotally by a senior sales manager who was surprised about the nature of the complaint because all his/her conversations with the other hospital had been about monitoring fortnightly in line with the SPC.

Genzyme submitted that the monthly plan would be off-licence and inappropriate. Employee 1's evidence, supported by the pharmacist, was that at no point during the description of the other hospital's plans or what he/she said about them had he/she referred to an inappropriate/off-licence monthly plan.

In response to a request for a copy of employee 1's entry on the customer relationship management (CRM) database for the meeting, Genzyme submitted that there was no such entry. It was Genzyme's policy that if two colleagues were in the same meeting only one of them entered it in the CRM. This was to prevent double counting of visits and misunderstanding its coverage and frequency.

FURTHER COMMENTS FROM THE COMPLAINANT

The complainant had no additional comments on Genzyme's response.

Genzyme subsequently, at the Panel's request, provided a copy of the representatives' briefing material for Aubagio.

PANEL RULING

The Panel noted that the parties' accounts differed. In such circumstances it was difficult to determine precisely what was said at the meeting and therefore where the truth lay. A judgement had to be made on the available evidence bearing in mind that the complainant had to establish his/her case on the balance of probabilities.

The Panel noted that Section 4.4 of the SPC, Special warnings and precautions for use, stated that during treatment blood pressure, alanine aminotransferase (ALT/SGPT), and complete blood cell counts based on signs and symptoms (eg infections) during treatment should be monitored. Liver enzymes should be assessed before initiation of therapy and every two weeks during the first six months of treatment and every eight weeks thereafter or as indicated by clinical signs and symptoms, examples were given. In addition, for ALT (SGPT) elevations between 2- and 3-fold the upper limit of normal, monitoring must be performed weekly. The briefing document on Aubagio's risk management plan referred to the monitoring requirements in the SPC. The Panel noted that in some areas shared care plans existed where monitoring responsibilities in line with the marketing authorisation were shared with primary care.

The Panel noted the complainant's allegation that employee 1 had stated during a meeting with a doctor, pharmacist and employee 2 that a unit in another hospital was looking at monthly monitoring for patients which was outwith the product licence. According to Genzyme, employee 2's account supported the complaint. Employee 2 had raised concerns with his/her manager after the meeting. The manager, however, whilst noting that concerns about the meeting had been raised did not recollect mention of a discussion about off-label monitoring. Had this been raised the manager was sure that he/she would have reported the matter to employee 1's manager. In addition, the Panel noted that employee 2's CRM entry referred to setting up central monitoring but did not indicate that anything untoward had occurred.

According to Genzyme, employee 1 denied making the comments alleged and stated that the doctor present had raised concerns about the difficulty of monitoring every 2 weeks. In response, employee 1 had stated that a number of centres had raised this concern and referred to another hospital's shared care plan to manage the licensed monitoring requirements. One of the health professionals present might have mentioned monthly monitoring but he/she could not be sure if it was mentioned at all, or if it was mentioned, who might have mentioned it. Employee 1's position was that he/she was not aware of the plans for monthly monitoring but he/she knew about the shared care plan from an MSL. According to Genzyme, the MSL in question corroborated employee 1's view and was clear that the shared care arrangement monitored within licence. However, the MSL was also clear that a named doctor from the other hospital had publicly stated that, in his/her view, the science did not merit monitoring patients every two weeks for the first six months of treatment but nonetheless the other hospital would comply with the licensed requirements. It was unclear whether this latter information had been given to employee 1 by the MSL.

According to Genzyme, the pharmacist present corroborated employee 1's position. The pharmacist thought that the doctor present might have referred to monthly monitoring but disagreed with the complainant's version of the meeting. There was no evidence from the doctor before the Panel.

The Panel noted that employee 1 stated that 'they discussed monitoring further'. The Panel had no information about the detail of that general discussion. The Panel considered that given the company's adoption of the needs based selling model which required representatives to actively seek out concerns and objections it was likely that if a monthly monitoring model had been raised by a health professional the Genzyme staff present would have responded to this concern. The Panel noted that the objection handling section of the campaign briefing document (AUBA-UK-12/13-4737) in response to a concern about monitoring, discussed the licensed requirements and referred the health professional to in depth hepatic safety data.

The Panel noted that the complainant had to establish his/her case on the balance of probabilities. The complainant had been asked to comment on Genzyme's response but had stated that he/she had no additional comment to make. Given the parties' differing accounts of the meeting in question, it was impossible to determine precisely what had been said. The Panel therefore ruled no breach of Clauses 2, 3.2 and 15.2 of the Code.

Complaint received **19 June 2014**

Case completed **23 October 2014**