CASE AUTH/2893/11/16

ANONYMOUS NON-CONTACTABLE v GE HEALTHCARE

Promotion of Vizamyl

An anonymous, non-contactable complainant who stated that he/she had worked with positron emission tomography (PET) amyloid tracers for a number of years in clinical research complained about the promotion of ^{18}F flutemetamol injection by GE Healthcare. Flutemetamol (^{18}F) was a PET scanning radiopharmaceutical containing the radionuclide fluorine-18, used as a diagnostic tool for Alzheimer's disease.

The complainant alleged that GE Healthcare had actively approached some of his/her colleagues in PET centres to try and get them to use Vizamyl by supplying flutemetamol. GE Healthcare did not have a UK manufacturing site on its marketing authorisation for Vizamyl (^{18}F flutemetamol injection), and so could not produce Vizamyl in the UK. The company had a specials licence and could produce a variation chemical compound in the form of flutemetamol (^{18}F) injection in the UK but this was not the same as the European licensed product, Vizamyl.

The complainant alleged that GE Healthcare was in breach of the Code with regard to disguised promotion and training of relevant staff, which demonstrated a lack of understanding of ABPI standards. Further, the complainant alleged that at the European Association of Nuclear Medicine (EANM) meeting in Barcelona in October, GE Healthcare had promoted Vizamyl to UK customers despite having no way of supplying the product in the UK. On the advertising booth, GE Healthcare informed everyone that GE Healthcare could supply flutemetamol while it sorted out its supply in the UK they just needed to ask for it.

The detailed response from GE Healthcare is given below.

The Panel noted that Vizamyl, which contained ^{18}F flutemetamol, although licensed in the UK, was not available in the UK. None of the manufacturers listed in the marketing authorisation were UK based and so, as the medicine had a very short half-life, once made, it would not reach a UK patient in time to be used. GE Healthcare could instead manufacture ^{18}F flutemetamol in the UK but as this was not a licensed medicine it could only be supplied for use in a clinical trial or on a named patient basis as a 'special'. To date it had not been supplied as a 'special'. The complainant stated, and was not contradicted by GE Healthcare, that Vizamyl and ^{18}F flutemetamol were not the same and the two should not be confused.

The Panel noted that some of the material on the company stand at the EANM meeting included UK prescribing information which gave the cost of the product in pounds sterling, referred to the Medicines and Healthcare products Regulatory Agency (MHRA) and prominently displayed the UK company address. The Panel considered that the use of such material misleadingly implied that Vizamyl was commercially available in the UK which was not so. A breach of the Code was ruled. The Panel further considered that as such material was bound to solicit questions from the UK delegates about the UK availability of the medicine, it would lead on to questions about ^{18}F flutemetamol. The Panel considered that on the balance of probabilities, UK delegates at the EANM meeting would have been told about the unlicensed ^{18}F flutemetamol. A breach of the Code was ruled. The Panel considered that high standards had not been maintained. A breach of the Code was ruled.

The Panel noted that there was no evidence to show that, as alleged, GE Healthcare had actively approached PET centres to try to get them to use Vizamyl by supplying ^{18}F flutemetamol. GE Healthcare submitted that all conversations with UK centres were as a result of an unsolicited enquiry. No ^{18}F flutemetamol had been supplied to date on a named patient basis. The burden was on the complainant to prove his/her point. No breaches of the Code were ruled.

The Panel again noted that there was no evidence to show that on the balance of probabilities, GE Healthcare had disguised the promotion of Vizamyl or that relevant staff had not been appropriately trained. No breaches of the Code were ruled.

The Panel noted its comments and rulings above but did not consider that in the circumstances a ruling of a breach of Clause 2, a sign of particular censure, was warranted. No breach was ruled.

An anonymous, non-contactable complainant who stated that he/she had worked with positron emission tomography (PET) amyloid tracers for a number of years in clinical research and had had various dealings with all major manufacturers, complained about the promotion of ^{18}F flutemetamol injection by GE Healthcare. Flutemetamol (^{18}F) was a PET scanning radiopharmaceutical containing the radionuclide fluorine-18, used as a diagnostic tool for Alzheimer's disease.

COMPLAINT

The complainant was concerned that GE Healthcare had not fully engaged with the right authorities or followed correct procedures like other pharmaceutical companies. GE Healthcare did not have a UK manufacturing site on its marketing authorisation for Vizamyl (^{18}F flutemetamol injection), and so could not produce Vizamyl in the UK. The company could produce a variation chemical compound in the form of flutemetamol (^{18}F) injection at its head office in the UK but this was not the same as the European licensed product, and should be not be confused with Vizamyl.

The complainant alleged that GE Healthcare had actively approached some of his/her colleagues in PET centres to try and get them to use Vizamyl by supplying flutemetamol. This muddied the water as the two were completely different. Whilst the complainant understood that GE Healthcare had a specials licence, the company's approach was not in accordance with the Medicines and Healthcare Products Regulatory Agency (MHRA) Guidance Note 14 – The supply of unlicensed medicinal products (specials). The complainant stated that he/she would raise this separately with the MHRA.

The complainant particularly noted points 2.2 and 2.6 of the MHRA guidance. The complainant commented that there were equivalent licensed medicines available that could meet the patients' needs and that GE Healthcare had sent unsolicited emails asking clinicians to 'try' flutemetamol with their patients - indicating/promoting that GE Healthcare could supply on a specialist route or named patient basis. Named patient basis should not be confused with specialist supply – again no transparency.

The complainant stated that the GE Healthcare employee in question was in breach of Clause 12, Disguised Promotion and Clause 16, Training, which the complainant believed demonstrated a lack of understanding of ABPI standards. The complainant assumed that all GE Healthcare staff had accreditation from the ABPI. Further to this, at the European Association of Nuclear Medicine (EANM) meeting in Barcelona in October, GE Healthcare had promoted Vizamyl to UK customers despite having no way of supplying the product in the UK. On the advertising booth, GE Healthcare informed everyone that it could supply flutemetamol while it sorted out its supply in the UK; people were even informed that they just needed to ask for it. The complainant stated that the future of PET tracers in the UK rested heavily on funding and he/she sincerely believed that everyone needed to work in the highest standards of compliance with industry. The complainant requested anonymity as he/she did not want any of his/her research activities to be questioned, but considered that the GE Healthcare Vizamyl UK marketing team needed to be investigated.

When writing to GE Healthcare, the Authority asked it to consider the requirements of Clauses 2, 3.1, 3.2, 7.2, and 9.1 of the Code in addition to Clauses 12 and 16 cited by the complainant.

RESPONSE

GE Healthcare explained that Vizamyl (^{18}F flutemetamol) was a radiopharmaceutical indicated for PET imaging of β-amyloid neuritic plaque density in the brains of adult patients with cognitive impairment who were being evaluated for Alzheimer's disease and other causes of cognitive impairment. Vizamyl was granted a marketing authorisation from the European Medicines Agency (EMA) on 22 August 2014 via the centralised procedure.

GE Healthcare also supplied flutemetamol for investigator and pharmaceutical company sponsored clinical trials only under an Investigational Medicinal Product Dossier (IMPD) as approved by the MHRA as part of the clinical trial applications submitted by trial sponsors.

Finally, GE Healthcare held a 'specials' licence for the supply of aseptically produced PET radiopharmaceuticals such as flutemetamol (^{18}F) injection from its manufacturing site in Amersham. Whilst it had considered the feasibility of supplying ^{18}F flutemetamol under the terms of the 'specials' licence, to date it had not done so.

GE Healthcare explained that the manufacturers listed in the Vizamyl summary of product characteristics (SPC) as being responsible for batch release, were all located outside the UK. Due to the short half-life (110 minutes) of the fluorine-18 radioactive isotope used for labelling Vizamyl, it was not logistically feasible to ship it from any of the currently licensed manufacturing sites to the UK. Flutemetamol (^{18}F) injection was supplied in the UK under the authorisation of an investigational medical product dossier (IMPD) solely for the purposes of third party investigator sponsored studies. Flutemetamol was also theoretically available for supply under a specials licence, but GE Healthcare had not supplied any third party pursuant to any unsolicited request to date.

GE Healthcare stated that as the complainant had not provided any further information, it had assumed that the other licensed products he/she was likely to be referring to were Vizamyl, Neuraceq and Amyvid. GE Healthcare noted that these products were not equivalent and had different diagnostic characteristics.

As Vizamyl was not currently commercially available in the UK, there had been no formal product launch and product training for UK representatives. Such training was planned for when Vizamyl would be available in the UK. It would not be appropriate under the Code to conduct product training at the current time. GE Healthcare stated that all of its representatives were ABPI qualified. The company had specific employees which worked across Europe, with one based in the UK, including countries where Vizamyl was commercially available. Technical product training for this team had therefore been conducted using the Vizamyl Electronic Reader Training Programme. The programme was educational and had been approved by the MHRA in the UK, as required by the EMA before a planned launch of the product in any EU member state. The training programme was an EMA requirement for the correct usage of amyloid imaging agents. As such, GE Healthcare had provided the programme to investigators that used ^{18}F flutemetamol in investigational studies.

^{18}F flutemetamol was and had been used in the UK as an investigational product as well as being discussed at scientific congresses. As such, GE Healthcare occasionally received unsolicited requests from clinicians asking how they could access flutemetamol or Vizamyl in the UK. There might be a number of reasons for these requests, including

the clinician's preference for a particular tracer and image interpretation method and limitations in access to licensed amyloid imaging agents. In response to the case preparation manager's request for copies of emails sent by company staff asking clinicians to try flutemetamol, GE Healthcare explained that due to the absence of staff, it required any further information to help narrow down the search parameters as to where the alleged emails originated from, or from what date the alleged unsolicited requests to clinicians were made.

GE Healthcare noted that it was a key sponsor of the EANM meeting and as such had a booth at the meeting. PET amyloid imaging was promoted on the GE Healthcare booth. It was a European meeting with international attendees. Vizamyl was approved in all, and available in many, EU member states, including Spain, the host country of the EANM meeting. No materials were given to UK health professionals, although the following printed Vizamyl materials, which had been reviewed in accordance with Spanish requirements, were available at the booth:

1 Vizamyl technologist guide which outlined the technical aspects of conducting a Vizamyl scan (ref JB6680/PRT/OS UK); and

2 Vizamyl image interpretation guide which summarised the principles of image interpretation and was typically used as a summary for clinicians that had completed reader training (ref JB6772/PRT/OS UK).

The Vizamyl SPC was also available on the booth. A list of the promotional materials for Vizamyl as shown at the EANM meeting was provided.

GE Healthcare booth staff were from several European countries including the UK. The staff briefing for the meeting was provided. Those manning the booth were specifically reminded of the presence of medical affairs on the booth and how to direct questions. The relevant extracts of the EANM briefing, which also included a staff rota, were provided.

GE Healthcare stated that representatives were fully trained as to which products were available in their local markets. The company could not fully exclude that UK physicians might have sought information at its booth and it would be logistically impossible to exclude specific nationals from visiting the booth at an international meeting.

GE Healthcare conducted the following activities at the EANM meeting in relation to ^{18}F flutemetamol:

1 A Vizamyl image reader training session (available by registration only) which was conducted by GE Healthcare's Medical Affairs team. No UK clinicians attended.

2 An ^{18}F flutemetamol user group meeting conducted by GE Healthcare's medical affairs team. This was by invitation only for clinicians who had experience with flutemetamol, either in clinical routine or investigational use. No UK clinicians attended.

3 A lunchtime open symposium as part of the congress programme, open to any registered congress attendee. The symposium consisted of four presentations, each by a non-UK health professional. One of the four talks was about the clinical utility of ^{18}F flutemetamol and the speaker was a doctor from Holland. GE Healthcare reviewed the content of the speaker's presentation, which was purely educational and non-promotional in content; a copy was provided. From the attendee list, GE Healthcare was aware that some UK health professionals had attended the symposium although it was not aware of that at the time.

GE Healthcare denied any breach of Clauses 2, 3.1, 3.2, 7.2, 9.1, 12 and 16 of the Code.

In response to a request for further information, GE Healthcare noted that it always encouraged responsible use of its products as patient safety was important. GE Healthcare submitted that it had a strong compliance culture and treated the anonymous complaint very seriously. The company strongly refuted all of the complainant's allegations and denied any breach of the Code. GE Healthcare submitted that in an abundance of caution, it would undertake additional internal training about unlicensed medicines, in particular the supply of Vizamyl.

GE Healthcare had interviewed the employee in question and gave brief details of his/her role. GE Healthcare explained that the employee and his/her colleagues supported customers with training and education on GE Healthcare's molecular imaging products and responded to customers' technical questions. GE Healthcare's account managers generally dealt with any commercial information about the products, however, due to the highly technical nature of the PET market, these employees were also typically the first point of contact for requests about named patient supply or interest in clinical studies. The employee did not proactively call on customers for promotional purposes; contact with customers regarding any product or issue was made at the request of the account manager or when the customer requested such information directly from the employee.

The employee in question confirmed that in his/her role he/she did not send unsolicited emails asking clinicians to try flutemetamol. The interactions with UK PET centres occurred in response to unsolicited requests for information and meetings about Vizamyl and/or flutemetamol. Specifically, he/she had had interactions with a number of named hospitals. In some cases, he/she said that it was not always clear which product a health professional wanted access to and why, since many requests referred to either the brand name or the international non-proprietary name. Also, health professionals who typically made these requests were often involved in clinical studies and/or made requests for individual patients. As already indicated, GE Healthcare manufactured various types of flutemetamol, including Vizamyl (although not for the UK market) and ^{18}F flutemetamol for clinical

studies. GE Healthcare could also manufacture and supply flutemetamol on a named patient basis, and it considered each unsolicited request on a case-by-case basis. In any of these meetings the employee in question confirmed that he/she informed health professionals that Vizamyl was not available in the UK. If physicians wanted access to flutemetamol, he/she would explain that GE Healthcare might be able to supply ^{18}F flutemetamol on a so-called specialist route, ie on a named patient basis, or as part of a clinical trial. No product claims were made about flutemetamol and no encouragement was given to supply the product on this basis. In some instances, GE Healthcare had reached the stage of proposing a means of supply to include the necessary named patient supply agreement, dosing instructions, timings of delivery (all linked to manufacturing capacity) and price but to date had not supplied in this way.

GE Healthcare clarified the employment history of the employee in question which was such that there were no email exchanges between him/her and UK health professionals about Vizamyl or flutemetamol before November 2016. The employee attended EANM 2016 and the autumn BNMS congress. GE Healthcare explained that such support was available at such meetings to give product presentations and technical training. The employee had attended the EANM congress to assist with the ongoing training of a new staff. UK health professionals approached the employee at these meetings about the supply of Vizamyl and/or flutemetamol as detailed below, however, no specialist supplies of flutemetamol had been made to UK PET centres.

GE Healthcare interviewed another employee who covered the above employee's role during absences and who had interacted with two UK PET centres in response to unsolicited requests for information and meetings about flutemetamol. Due to this employee's technical knowledge of flutemetamol/Vizamyl and knowledge about PET tracer supply, such requests were directed to him/her from time to time by the commercial teams or occasionally medical affairs in a situation where the product was not commercially available. The employee explained to the PET centres that 'while Vizamyl has a European marketing authorisation, we currently do not have a production site on our marketing authorisation that is located in the UK and that we currently only produce flutemetamol for research purposes in the UK' and provided details of obtaining flutemetamol by special request when specifically asked.

GE Healthcare submitted that both employees had acted in accordance with GE Healthcare's global procedure on the Supply of Pharmaceuticals and Medical Devices as Unlicensed Product in relation to unlicensed flutemetamol. GE Healthcare provided a copy of the procedure (ref MDGP-0082) which reiterated that the company was forbidden to promote the use of unlicensed products but might, under certain conditions, supply unlicensed products to health professionals. This procedure was also consistent with the MHRA Specials Guide. GE Healthcare provided relevant emails prior to 1 November 2016 and submitted that all email communication was reactive and factual in nature. The information provided did not contain any product claims or suggest that either of the GE Healthcare employees at issue had proactively reached out to health professionals to encourage the supply of unlicensed flutemetamol. Rather, the emails tended to provide logistical information about specialist supply of flutemetamol in response to requests for information from UK PET centres about the supply of Vizamyl/flutemetamol, and also included information clarifying the licensing and supply status of Vizamyl. This was entirely consistent with managing queries about named patient supply. It was necessary to discuss such logistical information before initiating the actual process for the specialist supply of flutemetamol due to the challengingly short half-life of the product, meaning it must be supplied on the correct day at the correct time to allow for a scan. Also, there were specific contractual and other safeguards that needed to be put in place before GE Healthcare could supply in this way.

GE Healthcare provided a detailed summary of specific interactions with a number of UK PET centres as supported by relevant email correspondence and interviews with relevant staff. These reactions were all reactive in response to unsolicited requests for information and meetings about Vizamyl/flutemetamol.

GE Healthcare submitted that the UK sales team had not been trained on Vizamyl or flutemetamol and had never been asked to talk to customers about it. However, the team the employee in question worked in was familiar with the Image Reader Training Package for Vizamyl which was a required element of the risk management obligations associated with Vizamyl's EMA marketing authorisation. The training was educational and contained relevant sections of the SPC as requested by the EMA (eg on indication, limitations, posology, safety information and pivotal clinical trials), but most of the programme was about how to read the images. The only other materials used in the reader training session were a set of PET amyloid scans displaying in 3 axis views for the training participants to practice/test reading scans to assess whether the scan was positive or negative. The Image Reader Training Package was consistent with the image reader training used in GE Healthcare's clinical trials and had been approved by the MHRA.

GE Healthcare submitted that in response to requests from UK PET centres for information about the supply of Vizamyl/flutemetamol, its two employees in question provided logistical information about the specialist supply of flutemetamol. It was necessary to consider and discuss such logistical information before initiating the actual process for the specialist supply of flutemetamol given its very short half-life as it must be supplied on the correct day at the correct time to allow for a scan. The consideration was conducted on a case-by-case basis and in accordance with company policies, MHRA guidance and the law.

In accordance with GE Healthcare's global procedure on the Supply of Pharmaceuticals and Medical Devices as Unlicensed Product, when it received a request to supply an unlicensed product, the GE Healthcare contact must inform the local quality assurance/regulatory affairs (QA/RA) organization to verify the request and accompanying information. Therefore, the team in which one of the employees in question worked did not have any formal briefing material for such requests; he/she might have to liaise direct with the requestor in relation to issues not handled by medical affairs, such as questions about pricing, intellectual property license conditions and delivery times. Owing to the very short half-life of flutemetamol, the responses to the questions would vary on a case-by-case basis and a discussion of details such as delivery times were required before initiating the process.

In relation to international congresses, the internal certified briefing slides for EANM 2016 were provided. Slide 18 of the EANM 2016 staff briefing slides provided guidance on promotional conduct for those staffing the congress and included a reminder to refer 'all medical related questions to MA [medical affairs] via an introduction'. Slide 27 detailed the selected Vizamyl communications taking place at the congress and slide 28 went on to provide further details of how to handle referrals to medical affairs. Staff at the congress were therefore aware of their role and what requests should be referred to medical affairs colleagues.

Medical affairs conducted a session on the Vizamyl Reader Training Package (as described above) at BNMS 2016. GE Healthcare noted that the UK commercial team had promotional stand panels covering all of the company's molecular imaging products for use at the BNMS 2016 meeting, because at that time GE Healthcare planned to file a variation for a manufacturing site in the UK by the end of Q2 2016. Due to the on-going supply issues, the stands had subsequently been withdrawn from use.

GE Healthcare submitted that in accordance with GE Healthcare's global procedure on the Supply of Pharmaceuticals and Medical Devices as Unlicensed Product, when it received a request for the supply of an unlicensed product, the GE Healthcare contact must inform the local QA/RA organization to verify the request and accompanying information. Market access verified the request, for example asking whether the clinician asked for access to product for research purposes (in which case it would be directed the ISS route); was the clinician requesting access because he/she was engaging in a therapeutic trial (in this case it would be referred to the study clinical research organisation of the sponsor or answered by market access), or had the clinician requested access to the product for clinical use in patients not in a study.

In the latter scenario, market access discussed the legitimacy of this request and liaised with the systems owner of the global procedure on the Supply of Pharmaceuticals and Medical Devices as Unlicensed Product (or local equivalent). However, market access did not deal with questions such as pricing, delivery times so these queries might be dealt with by one of the employee in question's team. In relation to flutemetamol in particular, the very short half-life of the product, meant that these logistical issues must be discussed before engaging in specialist supply of the product.

GE Healthcare did not sponsor UK health professionals to attend the EANM 2016 symposium. Since Vizamyl was not available for supply in the UK, a decision was taken not to invite the UK sales team or sponsor any UK customers.

The EANM booth displayed all GE Healthcare products. Approved information about the symposia and booth location was publicly available, including in the congress programme.

GE Healthcare concluded that, whilst it appreciated the concerns of the complainant, it denied breaches of Clauses 2, 3.1, 3.2, 7.2, 9.1, 12 and 16. GE Healthcare submitted that it treated any complaint very seriously and had ensured that relevant staff were fully aware of the company's position on unlicensed medicines and named patient supply. GE Healthcare would also organise additional internal training, in particular training on the company's global procedure on the Supply of Pharmaceuticals and Medical Devices as Unlicensed Product to reinforce the company's position on the issue. In particular, given the various different preparations of flutemetamol that GE could manufacture and supply on various different legal grounds (licensed, named patient, investigational medicinal product), it had reminded all of its technicians to be very clear going forward in terminology when responding to unsolicited requests since without clear wording it could appreciate that flutemetamol might become interchangeable with Vizamyl.

PANEL RULING

The Panel noted that the anonymous complainant was non-contactable and so could not be asked to provide further details. Anonymous complaints were accepted and like all complaints judged on the evidence provided by the parties. The complainant, who had the burden of proving his/her complaint on the balance of probabilities had not provided any evidence in support of his/her allegations.

The Panel noted that Vizamyl, which contained ^{18}F flutemetamol, although licensed in the UK, was not available in the UK. None of the manufacturers listed in the marketing authorisation were UK based and so, as the medicine had a very short half-life, once made, it would not reach a UK patient in time to be used. GE Healthcare could instead manufacture ^{18}F flutemetamol in the UK but as this was not a licensed medicine it could only be supplied for use in a clinical trial or on a named patient basis as a 'special'. To date it had not been supplied as a 'special'. The complainant had submitted, and it was not contradicted by GE Healthcare, that Vizamyl and ^{18}F flutemetamol were not the same and the two should not be confused.

The Panel noted that the complainant had alleged that GE Healthcare had promoted ^{18}F flutemetamol

to UK health professionals at the EANM meeting in Barcelona, October 2016. In that regard the Panel noted that some of the material on the company stand (A technologist's guide to imaging with Vizamyl and Vizamyl, A summary of image interpretation) both included UK prescribing information which gave the cost of the product in sterling, referred to the MHRA and prominently displayed the UK company address. The Panel considered that the use of such material misleadingly implied that Vizamyl was commercially available in the UK which was not so. A breach of Clause 7.2 was ruled. The Panel further considered that as such material was bound to solicit questions from the UK delegates about the UK availability of the medicine, it would lead on to questions about ^{18}F flutemetamol. The Panel considered that on the balance of probabilities, UK delegates at the EANM meeting would have been told about the unlicensed ^{18}F flutemetamol. A breach of Clause 3.1 was ruled. The Panel considered that high standards had not been maintained. A breach of Clause 9.1 was ruled.

The Panel noted that there was no evidence to show that, as alleged, GE Healthcare had actively approached PET centres to try to get them to use Vizamyl by supplying ^{18}F flutemetamol. GE Healthcare had submitted that all conversations with UK centres were as a result of an unsolicited enquiry. No ^{18}F flutemetamol had been supplied to date on a named patient basis. The burden was on the complainant to prove his/her point. No breach of Clause 3.1 and 3.2 was ruled.

With regard to the complainant's allegations of breaches of Clauses 12 and 16, the Panel again noted that there was no evidence to show that on the balance of probabilities, GE Healthcare had disguised the promotion of Vizamyl or that the representatives had not been appropriately trained. No breach of Clause 12 and of Clause 16 was ruled.

The Panel noted its comments and rulings above but did not consider that in the circumstances a ruling of a breach of Clause 2, a sign of particular censure, was warranted. No breach was ruled.

Complaint received **29 November 2016**

Case completed **31 March 2017**
