CASE AUTH/2969/8/17

SENIOR PRACTICE NURSE v ASTRAZENECA

Conduct of a representative

A senior practice nurse complained about the conduct of a medical representative with AstraZeneca UK. The representative was promoting Forxiga (dapagliflozin) which was indicated to improve glycaemic control in adults aged 18 years or over with type 2 diabetes, either as monotherapy or as add-on combination therapy.

The complainant stated that there had been several occasions when the representative had come into surgery asking to see him/her; all of which had been self-presentations at reception with no forwarding or booked appointment. When the representative was advised by the receptionists that the complainant was in surgery seeing patients he/she became quite insistent that the complainant be contacted. The representative was advised to email the complainant directly. The complainant stated that on one occasion he/she had to go into reception in the middle of a minor surgery procedure with a GP to collect a consent form. The representative proceeded to try to talk to him/her in view and ear shot of other patients (after being told that the complainant was busy and needed in surgery) telling him/her that he/she should be changing all diabetic patients from canagliflozin (Invokana, marketed by Janssen) to Forxiga in view of recent surveys linking canagliflozin to increased lower limb amputation.

The representative continued to follow the complainant down the corridor telling him/her how bad canagliflozin was. The complainant stated that he/she was happy to see representatives who wanted to advise him/her about their products but he/she found the AstraZeneca representative to be very unprofessional in his/her approach, basically slagging off her rival company.

The complainant had since spoken to the canagliflozin representative to gain clarification on this matter and had decided to no longer see the AstraZeneca representative as his/her attitude was very threatening and unprofessional.

The detailed response from AstraZeneca is given below.

The Panel noted that according to the complainant his/her receptionist would confirm the representative's frequent visits and that he/she could be quite persistent. The complainant also described the representative's behaviour as threatening and unprofessional. The Panel noted AstraZeneca's submission that the representative did not recall being told that the complainant was in minor surgery when he/she asked to see him/her and denied following the nurse down the corridor in an attempt to continue the conversation. The Panel noted that the complainant confirmed that the representative was fully aware that he/she was in minor surgery and did follow him/her down the corridor which he/she stated was witnessed by receptionists. According to the unsigned statement of the representative's line manager he/she had never witnessed the representative insist on seeing a health professional if told that he/she was busy. In relation to the allegation that the conversation at issue took place within earshot and in full view of patients the Panel noted that the parties' accounts differed. It was not possible to determine where the truth lay. The complainant bore the burden of proof and in this regard the Panel did not consider that the complainant had established a breach of the Code on this point as alleged. No breach of the Code was ruled.

Similarly, in relation to the general allegation that the representative's behaviour was threatening and unprofessional the Panel considered that this had not been established by the complainant and no breach of the Code was ruled on this point.

According to AstraZeneca the named doctor and complainant had given the representative verbal consent to call upon them whenever there were new updates in relation to Forxiga which was why the representative intended to discuss the amputation data with him/her and did not consider that he/she had raised it proactively. The Panel noted that the complainant made no particular comment in this regard but had described the representative's visits as self-presentations at reception with no forwarding or booked appointment. AstraZeneca's HCP Interactions Guidance stated that a 'solicited contact may be recorded if during a prior interaction, the HCP or ORDM had 'given permission to call back at an agreed date and time or specific topic'. It was unclear whether the Guidance covered an open-ended consent to call-back which applied until such consent was withdrawn or otherwise terminated. The Panel made no judgement on the acceptability of open-ended call backs. The Panel was concerned that the guidance did not refer to recording such permission. The Panel was concerned that AstraZeneca was relying on unrecorded verbal consent and the representative's recollection of the same to apparently categorise subsequent calls as solicited. The impression given to health professionals by these arrangements was important bearing in mind the requirements of the Code including that such visits should not cause inconvenience and that the wishes of individuals must be observed. The Panel considered that as a matter of good governance such consent should be recorded internally and in writing to the health professional so that all parties were clear about what had been agreed verbally. It was of particular note that the complainant described the representative's visits as self-presentations and raised concerns about their frequency.

The Panel noted that the HCP Interactions Guidance defined solicited contacts as set out above and stated that a solicited contact might be attendance at a group meeting including HCPs or ORDMs. The following page of the document describing AV/Rep Led meetings stated that these occurred normally with more than one HCP and appeared to suggest that group calls were all solicited by definition. The Panel noted that the representative had recorded meetings with the complainant and a named doctor as a group call on more than one occasion and on one occasion the doctor had not attended, however, it was still recorded as such. The Panel queried whether AstraZeneca's definition of a solicited call or group call or permission to call back satisfied the requirement of a solicited call as referred to in the Code.

The Panel noted that the representative appeared to have called on the complainant four times between January and July. Two calls were described by AstraZeneca as group calls in an internal email dated 29 August summarising the calls at the named surgery, however, AstraZeneca confirmed that only the complainant was present at one of these calls and the second group call did not actually take place. The Panel further noted that the same summary described a meeting with the complainant on 17 January as a 1:1 call, however it appeared that the call report described the call type as group detail. It appeared that the representative called on the complainant three times at the named surgery within the six month period and all were recorded as 'solicited' calls. The Panel noted that the complainant's concerns were broader than calls and contacts and included attendances at reception.

Notwithstanding all of the points outlined above and noting the complainant's burden of proof the Panel considered that there was insufficient evidence to establish on the balance of probabilities whether the number of unsolicited calls on the complainant exceeded 3 on average. The Panel therefore ruled no breach of the Code. Nonetheless, the Panel noted that serious concerns remained about the company's governance in this area, including the poor guidance to representatives about permission from a health professional to call back and unclear guidance about, and poor recording of calls and contacts as set out above. In this regard the Panel considered that the company had failed to maintain high standards. A breach of the Code was ruled. In addition, the Panel noted the poor governance shown by the representative with regards to call recording and the lack of detail therein meant that the representative had failed to maintain high standards and a breach of the Code was ruled.

The Panel noted that there was no record of, or recollection from the representative in question of a discussion about the amputation data on 27 June; the call record was blank and did not detail discussion. The call of 27 June was logged implying that a dialogue had occurred which was in contrast to the representative's recollection. The Panel noted that when questioned how, in general, he/she might discuss the amputation data, the representative noted that he/she always clarified that all SGLT2is had a warning on the respective summary of product characteristics (SPCs) in relation to the risk of amputations and that canagliflozin had more clinical findings on the SPC but it was unknown whether this constituted a class effect.

In relation to the conversation in question the Panel noted that according to the representative's statement during the interaction the complainant asked if there was anything new to discuss about Forxiga; the representative recalled that he/she said that he/she had some safety information on Forxiga and the SGLT2i class but that the word amputation was not used. The Panel noted AstraZeneca's submission that according to the representative canagliflozin was only referred to in order to inform the complainant that he/she should raise any questions about this medicine with the canagliflozin representative. The Panel noted that the complainant and his/her receptionist remembered the representative saying canagliflozin was dangerous and patients should be switched to dapagliflozin.

The Panel considered that whilst it was likely that canagliflozin was discussed it was impossible to establish precisely what was said during the conversation and therefore it was not possible to determine on the balance of probabilities whether the representative had made misleading claims which were incapable of substantiation with regard to the amputation data for Forxiga or canagliflozin. No breaches of the Code were ruled. The Panel did not consider that evidence had been provided by the complainant to show whether on the balance of probabilities the representative had disparaged canagliflozin as alleged and no breach of the Code was ruled.

In relation to the briefing material the Panel noted that the sales force was first briefed about the increased risk of lower limb amputation with canagliflozin in July 2016 to enable the sales force to respond reactively to questions from health professionals about the emerging data in relation to canagliflozin and, *inter alia*, toe amputations. The sales force was specifically instructed that they must not prompt a health professional to ask a question about this. The Panel noted that the briefing stated that the information could be discussed in response to a direct HCP enquiry or proactively with a HCP known to have a safety concern in relation to the SGLT-2 inhibitor class. The briefing did state 'Do not prompt an HCP in conversation by saying, for example, 'Have you seen the news about the fractures with canagliflozin?'.

An update was provided to the sales force on the amputation data for SGLT2is in a presentation dated March 2017 which informed the sales force of the likely changes to the SPCs for all SGLT2is. The presentation detailed further studies including CANVAS-R wherein the incidence of lower limb amputations for canagliflozin v placebo was not statistically significant. It further stated that a higher incidence of amputation was not observed across 12 other completed Phase 3/4 clinical trials'.

It reproduced expected label updates for Forxiga and canagliflozin.

An email in June 2017 advised the sales force that the CANVAS results must not be proactively discussed with customers. An objection handler was issued in July 2017 which was only to be used reactively in response to questions relating to the risk of lower limb amputation for Forxiga vs canagliflozin. According to AstraZeneca the information included was based on the factual wording in the medicines' SPCs. The Panel noted that both the objection handler and the March 2017 presentation stated that 'to date there had been no increased risk seen in the clinical trial programme for Forxiga' and 'To date we are not aware of any imbalance in lower limb amputations in the Forxiga clinical trial program'. The Panel further noted the representative's line manager's interview statement that it was now known that it was not a class effect. The Panel queried whether this was entirely consistent with the Forxiga SPC which stated that it was unclear whether there was a class effect.

The Panel noted the line manager's statement that there was no instruction to lead on a discussion of the SPC changes. AstraZeneca clarified that in the line manager's previous statement 'Where there is high cana use I am comfortable that my team discuss the side effect profile proactively with HCPs, including the amputation data' he/she was referring to the amputation data in the Forxiga detail aid which was in relation to Forxiga only and made no reference to canagliflozin. The Panel considered that this was in contrast to AstraZeneca's submission that the representative confirmed that he/she intended to discuss the changes to the Forxiga SPC and the SGLT2i class, and would have expected canagliflozin to have been discussed in that context, albeit the representative did not think that it was being raised proactively as he/she had verbal permission to call on the complainant with any new Forxiga data. It was also inconsistent with AstraZeneca's submission that in response to questioning the representative's line manager stated that the representative when discussing the amputation data noted that there was data to indicate an increased risk with canagliflozin but that it was unknown whether this was a class effect for all SGLT2is.

The Panel noted its general concerns about the briefing material as outlined above but did not consider that there was evidence to show that on the balance of probabilities AstraZeneca had provided briefing that advocated, either directly or indirectly, any course of action which would be likely to lead to a breach of the Code. No breach of the Code was ruled.

The Panel noted its concerns and rulings above but did not consider that a ruling of a breach of Clause 2 was warranted and no breach of Clause 2 was ruled.

A senior practice nurse (lead diabetes nurse), complained about the conduct of a medical representative with AstraZeneca UK Limited. The representative was promoting Forxiga (dapagliflozin) which was indicated to improve glycaemic control in adults aged 18 years or over with type 2 diabetes, either as monotherapy or as add-on combination therapy.

COMPLAINT

The complainant stated that there had been several occasions over the last few weeks when the representative had come into surgery asking to see him/her. All these occasions had been self-presentations at reception with no forwarding or booked appointment. When the representative was advised that the complainant was in surgery seeing patients he/she became quite insistent that the complainant be contacted. The representative was advised to email the complainant directly. The complainant stated that on one occasion he/she had to go into reception in the middle of a minor surgery procedure with a GP to collect a consent form. The representative proceeded to try to talk to him/her in view and ear shot of other patients (after being told that the complainant was busy and needed in surgery) telling him/her that he/she should be changing all diabetic patients from canagliflozin (Invokana, marketed by Janssen) to Forxiga in view of recent surveys linking canagliflozin to increased lower limb amputation.

The representative continued to follow the complainant down the corridor telling him/her how bad canagliflozin was. The complainant stated that he/she was happy to see representatives who wanted to advise him/her about their products but he/she found the AstraZeneca representative to be very unprofessional in his/her approach, basically slagging off her rival company. The complainant reiterated that this was not in a closed environment but down a corridor.

The complainant had since spoken to the canagliflozin representative to gain clarification on this matter and had decided to no longer see the AstraZeneca representative as his/her attitude was very threatening and unprofessional.

When writing to AstraZeneca, the Authority asked it to respond in relation to the requirements of Clauses 7.2, 7.4, 8.1, 9.1, 15.2, 15.4, 15.9 and 2 of the Code.

RESPONSE

AstraZeneca submitted that it strove to ensure that all of its interactions with health professionals were courteous, appropriately informative and conducted within both the spirit and letter of the Code. AstraZeneca submitted that it was, therefore, extremely disappointed to have received this complaint and accordingly had undertaken an extensive investigation that had involved formal interviews with the representative, his/her line manager, a review of all relevant call notes and all relevant briefing material to sales representatives. On the basis of this testimony and evidence AstraZeneca had been unable to substantiate the complainant's allegations. AstraZeneca believed that the representative acted reasonably and in a professional manner consistent with AstraZeneca's instructions. However, the complainant had clearly

misconstrued the representative's intent and actions and AstraZeneca apologised for any irritation or offence that had been caused.

AstraZeneca submitted that as noted above, the representative in question had been interviewed in relation to this complaint. It appeared that he/she called on the named surgery approximately every 6-8 weeks. This was reflected in the customer relationship management (CRM) system records. The calls were usually to do one of the following: to speak with one of the doctors at the surgery, to speak to one of the nurses, ie the complainant; or to hold a lunchtime meeting. It appeared that both a named doctor and the complainant had given the representative consent to call upon them whenever there were new updates in relation to Forxiga. AstraZeneca submitted that although the representative was not notified of the complainant's name during the investigation of this complaint, the representative had raised the complainant's name spontaneously during his/her interview.

It was likely that the 'recent' call to which the complainant referred was an interaction that took place at the surgery in June 2017. As noted in the interview notes provided, the representative asked at reception whether the complainant was free to speak with him/her. Staff at reception informed the representative that they would see if the complainant was free. The representative did not recall being told that the nurse was in minor surgery.

The representative then met the complainant in the corridor; the representative assumed that the complainant had been notified of his/her presence by reception and that the complainant had decided to come to meet with him/her. The conversation that followed implied that this had indeed been the case. The complainant asked if there was anything new to discuss about Forxiga; the representative recalled that he/she said that he/she had some safety information on Forxiga and the SGLT2i class but that the word amputation was not used. This conversation took place in the corridor but the representative recalled checking that there was no one else within earshot. The complainant then told the representative to make an appointment with him/her to discuss this data but not to book the next free appointment as the complainant was meeting with the canagliflozin representative. The representative recalled that he/she said it was not her job to discuss canagliflozin and advised the complainant to take up any questions about canagliflozin with that representative.

The representative categorically denied following the nurse down the corridor in an attempt to continue the conversation. The representative recalled that the interaction was brief as the nurse was busy but that it was pleasant and professional.

Following this interaction, the representative tried to call on both the named doctor and the complainant at the surgery in July but was unable to speak with either of them. Although not consistent with the complainant's recollection of when this interaction took place according to the representative's testimony and call records, the representative had previously called on the complainant in April 2017, but the representative could not recall whether the amputation data vs canagliflozin was discussed or not at that meeting.

From the representative's testimony and call records, it appeared any interaction between the two was brief and no reference was made to amputation data at all. On the basis of this evidence, AstraZeneca did not consider that the representative made any misleading or unsubstantiated statements and so it denied a breach of Clauses 7.2 and 7.4. Canagliflozin was only referred to in order to inform the complainant that he/she should raise any questions about this medicine with the canagliflozin representative; no disparaging statements were made and AstraZeneca did not consider that this interaction constituted a breach of Clause 8.1.

When questioned how, in general, he/she might discuss this data, the representative noted in his/her interview that he/she always clarified that all SGLT2is had a warning on the respective summary of product characteristics (SPCs) in relation to the risk of amputations; canagliflozin had more clinical findings on the SPC but it was unknown whether this constituted a class effect. Given this, and the materials and briefings received by the sales force about the risk of amputation (AstraZeneca referred to the details below), AstraZeneca did not consider that any discussion the representative had had in relation to the data had been misleading, was incapable of substantiation or was disparaging to canagliflozin.

AstraZeneca had also spoken to the representative's line manager in relation to joint calls with the representative and his/her observation of the representative's conduct, both generally and in relation to his/her discussion of the amputation data. The representative's line manager had stated that he/she typically accompanied the representative on calls every 4-6 weeks, although he/she had never called on the surgery at issue with the representative. The representative's line manager had never witnessed the representative discussing clinical data in an area where the discussion could be overheard by patients or reception. The most recent occasion on which the representative's line manager accompanied the representative on calls was late July 2017; on that date they called at three separate surgeries and all the clinical conversations took place in surgery rooms with closed doors.

The representative's line manager had never witnessed the representative insist on seeing a health professional when he/she had been told that he/she was busy. When told this, the representative might ask reception to let the health professional know that he/she was there if the health professional wanted to speak with him/her, but he/she did not insist that this was done.
In response to questions around whether he/she had seen the representative discuss amputation data compared to canagliflozin, the representative's line manager stated that he/she had and that his/her recollection was consistent with that of the representative's as noted above ie he/she noted that

there was data to indicate an increased risk with canagliflozin but that it was unknown whether this was a class effect for all SGLT2is.

AstraZeneca noted that some of the representative's line manager testimony in relation to the strategy of his/her team when discussing the amputation data raised some concerns, in particular, that there might have been an informal briefing to his/her team that was not certified. AstraZeneca had been unable to complete further investigations on this new matter prior to its deadline for responding to the original matter. AstraZeneca would, of course, continue to investigate this and act accordingly should it discover further evidence confirming activities had taken place which were contrary to the Code, including submitting a voluntary admission to the Authority.

Following the interview with the representative's line manager, the representative was spoken to again to clarify whether he/she had in fact asked the complainant what the canagliflozin representative might have said to him/her about the amputation data. The representative had reiterated that he/she did not; the only reason canagliflozin was raised during the interaction in June was because the complainant stated that he/she was seeing the canagliflozin representative at her next appointment and the representative replied that the complainant should raise any questions about this medicine with the canagliflozin representative. The representative also confirmed, as in his/her testimony, that she did not raise the amputation data proactively; the complainant had requested that the representative provide him/her with updates in relation to Forxiga and this was why she intended to discuss the amputation data with him/her.

AstraZeneca submitted that the representative had maintained high standards in his/her discussion of the amputation data, consistent with the requirements of Clause 15.2 and AstraZeneca denied the allegation of a breach of this clause.

Although there was no record or recollection from the AstraZeneca representative in question of a discussion of the amputation data in June, AstraZeneca would like to assure the Panel that all company-developed briefing materials and instructions to the field force were appropriate. As background, it was important to clarify the position of the class of medicines sodium-glucose cotransporter-2 inhibitors (SGLT2i), of which AstraZeneca's Forxiga was one of three licensed such medicines (Forxiga, Invokana and Jardiance). In relation to the risk of lower-limb amputation, the SPC for Invokana (canagliflozin), in Section 4.2, Special warnings and precautions for use, stated:

> **'Lower limb amputations**
>
> In ongoing, long-term clinical studies of canagliflozin in type 2 diabetes patients with cardiovascular disease (CVD) or at high risk for CVD, an increase in cases of lower limb amputation (primarily of the toe) has been observed in patients treated with canagliflozin. As an underlying mechanism has not been established, risk factors, apart from general risk factors, for amputation are unknown. However, as precautionary measures, consideration should be given to carefully monitoring patients with a higher risk for amputation events and counselling patients about the importance of routine preventative foot care and maintaining adequate hydration. Consideration may also be given to stopping treatment with canagliflozin in patients that develop events preceding amputation such as lower-extremity skin ulcer, infection, osteomyelitis or gangrene.'

The same section of the SPCs for both Forxiga and Jardiance stated:

> **'Lower limb amputations**
>
> An increase in cases of lower limb amputation (primarily of the toe) has been observed in ongoing long-term, clinical studies with another SGLT2 inhibitor. It is unknown whether this constitutes a class effect. Like for all diabetic patients it is important to counsel patients on routine preventative foot care.'

Thus, there appeared to be an increased risk of lower limb amputation with canagliflozin that had not been observed with the other medicines in the SGLT2i class. It was not known whether this could indeed be a class effect and a more general precaution continued to appear on the SPCs for the other two medicines.

The sales force were first briefed about this in July 2016 (ref JBN: 996743.011DOP). This briefing was intended to enable the sales force to respond to any questions from health professionals about the emerging data in relation to canagliflozin and, *inter alia*, toe amputations. AstraZeneca referred the PMCPA to this document and stated that the information contained within it was very factual and was intended for reactive use only; the sales force were specifically instructed that they must not prompt a health professional to ask a question about this.

There was an update provided to the sales force on the amputation data for SGLT2is in a presentation in March 2017 (Scientific Leadership, GB-5826 and 7b, Potential Risk of Lower Limb Amputations with SGLT-2is – An Update, GB-5839), which also informed the sales force of the likely changes to the SPCs for all SGLT2is. The instruction to the sales force was to stay on track and focus on the key messages for promoting Forxiga.

The current material and the associated briefing for the diabetes sales force in relation to lower limb amputation vs canagliflozin was provided (SGLT2i Amputations Objection Handler, GB-7857 and Briefing Document Amputations Objection Handler, GB-7927, respectively). These were rolled out to the sales force in July 2017 and AstraZeneca referred the PMCPA to the briefing document and stated that as well as the email invitation to the roll-out (Update on CANVAS, GB-7169) and the presentation used for this roll out (Diabetes Dial-In July 2017, GB-7522), the

objection handler was to be used reactively only, in response to questions relating to the risk of lower limb amputation for Forxiga vs that for canagliflozin. The information included in the objection handler was very much based around the factual wording in the respective current SPCs for Forxiga and Invokana; there was no over-exaggeration or distortion of the situation and no disparaging language was used.

AstraZeneca considered that there was no company-generated briefing for the sales force in relation to this data that advocated, either directly or indirectly, any course of action which would be likely to lead to a breach of the Code and considered that all such briefing was compliant with the requirements of Clause 15.9.

In relation to call frequency, AstraZeneca provided records of calls made on the nurse at the surgery for this year: some of the calls were at associated practices with which it appeared the nurse was also affiliated. Given that the nurse had requested that the representative call on him/her with updated information on Forxiga, AstraZeneca did not consider that there was any evidence that either the frequency or manner of these calls was likely to cause inconvenience. The representative had been questioned as to what he/she did when he/she called on a health professional and found that they were not available to speak with him/her; as could be seen in his/her interview notes, the representative would not insist on seeing that health professional, but would book another appointment for the future.

In addition, all AstraZeneca representatives were trained on the AstraZeneca HCP Interactions Guidance, which detailed, *inter alia*, the requirements of Clause 15.4. The representative acknowledged that he/she had read and understood the requirements of this document in June 2017. In addition, a Contact Planning Brief was rolled out to Regional Business Managers every 6 months; the one relevant to the first half of 2017 referred to the requirements of Clause 15.4. The representative's line manager noted in his/her interview that he/she trained his/her team, including the representative, on each revised version and stated that his/her team were aware that they must not 'pester' health professionals.

Given this, AstraZeneca submitted that the representative's calls on the nurse at the surgery were consistent with the requirements of Clause 15.4.

Given the information above, AstraZeneca did not consider that, as a company, it had failed to maintain high standards in briefing its representatives on the amputation risk with SGLT2is and it denied the allegation of a breach of Clause 9.1. The company had not brought the industry into disrepute and denied a breach of Clause 2.

In response to a request for further information, AstraZeneca submitted that the consent from the two health professionals received by the representative was verbal and consequently there was no written documentation other than calls being logged in the CRM system.

AstraZeneca submitted that the representative confirmed that he/she intended to discuss the changes to the Forxiga SPC and the SGLT2i class, and would have expected canagliflozin to have been discussed in that context.

AstraZeneca explained that at the time of its initial response the company had not been able to complete its investigation into comments by the representative's manager which suggested that an informal briefing might have occurred. Having further interviewed the representative's manager and his/her manager AstraZeneca had found no evidence that the representative's manager provided an informal briefing to his/her team. The representative's manager clarified that as part of a routine regional planning discussion, he/she and fellow managers agreed the importance of understanding the differences between the SPCs for the SGLT2i class. There were increasing reports of prevailing misperceptions that all of the side effects were consistent across the class. This was particularly relevant in the context of the amputation data for which there were clear differences in wording in the SPCs. This SPC information was shared with the team to equip them to respond to any questions that a health professional might have raised on the subject in the context of a promotional call. There was no instruction to lead on a discussion of the SPC changes. AstraZeneca submitted that in the line managers' comment in his/her previous statement:

> 'Where there is high cana use I am comfortable that my team discuss the side effect profile proactively with HCPs, including the amputation data.'

The manager clarified that he/she was referring to the amputation data in the Forxiga detail aid which was in relation to Forxiga only and made no reference to canagliflozin.

FURTHER INFORMATION FROM THE COMPLAINANT

The complainant confirmed that the representative's recollection of events was different to what actually happened. With regard to the 'chance meeting' in reception with the representative, the complainant stated that the representative WAS fully aware that the complainant was in minor surgery as he/she expressly told the representative at least twice and as such could not discuss anything with him/her at that time. According to the complainant the whole incident was witnessed by the receptionist who clearly remembered the representative saying canagliflozin was dangerous and patients should be switched to dapagliflozin. The complainant explained that he/she did try to explain to the representative that he/she was seeing the canagliflozin representative the following week and would clarify the situation but was in no position at that time to make any judgement. The complainant stated that he/she gave his/her apologies and continued down the corridor to accompany a GP in minor surgery

but the representative CONTINUED to follow him/her [again all witnessed by the receptionists who were prepared to write a statement if required]. The complainant stated that the receptionists would also confirm the representative's many frequent visits and that the representative could be quite persistent. Therefore, it was with regret that the complainant would no longer continue to have dealings with the representative in the future.

PANEL RULING

The Panel noted that the parties' accounts of the exchange between the complainant and the AstraZeneca representative differed. The Panel noted the difficulty in dealing with complaints based on one party's word against the other; it was often impossible in such circumstances to determine precisely what had happened. Paragraph 2.2 of the Constitution and Procedure stated that a complainant had the burden of proving their complaint on the balance of probabilities. The Panel noted, however, that a high degree of dissatisfaction was usually required before an individual health professional was moved to submit a formal complaint.

The Panel noted that the Code required representatives, *inter alia*, to maintain a high standard of ethical conduct in the discharge of their duties (Clause 15.2) and to ensure that the frequency, timing and duration of calls together with the manner in which they were made did not cause inconvenience. The wishes of individuals on whom representatives wish to call and the arrangements in force at any particular establishment, must be observed (Clause 15.4).

The Panel noted that according to the complainant his/her receptionist would confirm the representative's frequent visits and that he/she could be quite persistent. The complainant also described the representative's behaviour as very threatening and unprofessional. The Panel noted AstraZeneca's submission that the representative did not recall being told that the complainant was in minor surgery when he/she asked to see him/her in June and denied following the nurse down the corridor in an attempt to continue the conversation. The Panel noted that the complainant confirmed that the representative was fully aware that he/she was in minor surgery and did follow him/her down the corridor which he/she stated was witnessed by receptionists. According to the unsigned statement of the representative's line manager he/she had never witnessed the representative insist on seeing a health professional if told that he/she was busy.

The Panel noted that whilst the representative's statement made it clear that the representative would not enter into a discussion in a public area and his/her line manager confirmed that he/she had never seen the representative do this, both the representative and complainant agreed that the conversation took place in the corridor. According to AstraZeneca the representative recalled checking that there was no one else within earshot. The representative's statement did not refer to checking but stated he/she 'believed there was no one in the corridor or within earshot'. The representative's statement explained that the patient waiting room was not along that corridor and that reception was behind a glass/wooden wall in its own separate room. This was at odds with the complainant's account, that the representative proceeded to try to talk to him/her in view and ear shot of other patients and was witnessed by the receptionists. The company document HCP Interactions Guidance dated 7/3/2017 stated that 1:1 calls may not be held where members of the public could overhear. Such guidance was also reflected in a Forxiga briefing document for the Amputation Objection Handler (GB-7927). In relation to the allegation that the conversation at issue took place within earshot and in full view of patients the Panel noted that the parties' accounts differed. It was not possible to determine where the truth lay. The complainant bore the burden of proof and in this regard the Panel did not consider that the complainant had established a breach of the Code on this point as alleged. No breach of Clause 15.2 was ruled.

Similarly, in relation to the general allegation that the representative's behaviour was threatening and unprofessional the Panel considered that this had not been established by the complainant and no breach of Clause 15.2 was ruled on this point.

The Panel noted AstraZeneca's submission that the representative called on the named surgery approximately every 6-8 weeks to either hold a lunchtime meeting or to speak to the complainant or one of the doctors as reflected in the CRM system. In contrast the Panel noted that the representative's statement referred to making such calls every 4-8 weeks. According to AstraZeneca the named doctor and complainant had given the representative verbal consent to call upon them whenever there were new updates in relation to Forxiga which is why the representative intended to discuss the amputation data with him/her and did not consider that he/she had raised it proactively. The Panel noted that the complainant made no particular comment in this regard but had described the representative's visits as self-presentations at reception with no forwarding or booked appointment. The Panel noted that AstraZeneca's HCP Interactions Guidance dated 7/3/2017 stated that a 'solicited contact may be recorded if during a prior interaction, the HCP or ORDM had 'given permission to call back at an agreed date and time or specific topic'. The Panel was also concerned that on such an important matter the relevant sentence, perhaps due to an omission or grammatical error did not make sense. In addition, it was unclear whether the Guidance covered an open-ended consent to call-back which applied until such consent was withdrawn or otherwise terminated. The Panel made no judgement on the acceptability of open-ended call backs and just considered the matter in relation to Clause 15.4. The Panel was concerned that the guidance did not refer to recording such permission. The Panel was concerned that AstraZeneca was relying on unrecorded verbal consent and the representative's recollection of the same to apparently categorise subsequent calls as solicited. The impression given to health professionals by these arrangements was important

bearing in mind the requirements of Clause 15.4 including that such visits should not cause inconvenience and that the wishes of individuals must be observed. The Panel considered that as a matter of good governance such consent should be recorded internally and in writing to the health professional so that all parties were clear about what had been agreed verbally. It was of particular note that the complainant described the representative's visits as self-presentations and raised concerns about their frequency.

The Panel noted that the HCP Interactions Guidance dated 7/3/2017 defined solicited contacts as set out above and stated that a solicited contact might be attendance at a group meeting including HCPs or ORDMs. The following page of the document describing AV/Rep Led meetings and stated that these occurred normally with more than one HCP and appeared to suggest that group calls were all solicited by definition. The Panel noted that the representative had recorded meetings with the complainant and a named doctor as a group call on more than one occasion and on one occasion the doctor had not attended, however, it was still recorded as such. The Panel queried whether AstraZeneca's definition of a solicited call or group call or permission to call back satisfied the requirement of a solicited call as referred to in the Code.

The Panel noted that according to the call notes summary provided by AstraZeneca the representative appeared to have called on the complainant four times between January and July. Two calls were described by AstraZeneca as group calls in an internal email dated 29 August summarising the calls at the surgery, however, AstraZeneca confirmed that only the complainant was present at one of these calls and the second group call did not actually take place. The Panel further noted that the same summary described a meeting with the complainant in January as a 1:1 call, however it appeared that the call report described the call type as group detail. It appeared that the representative called on the complainant three times at the named surgery within the six month period and all were recorded as 'solicited' calls. The Panel noted that the complainant's concerns were broader than calls and contacts and included attendances at reception.

Notwithstanding all of the points outlined above and noting the complainant's burden of proof the Panel considered that there was insufficient evidence to establish on the balance of probabilities whether the number of unsolicited calls on the complainant exceeded 3 on average. The Panel therefore ruled no breach of Clause 15.4. Nonetheless, the Panel noted that serious concerns remained about the company's governance in this area, including the poor guidance to representatives about permission from a health professional to call back and unclear guidance about, and poor recording of calls and contacts as set out above. In this regard the Panel considered that the company had failed to maintain high standards. A breach of Clause 9.1 was ruled. In addition, the Panel noted the poor governance shown by the representative with regards to call recording and the lack of detail therein meant that the representative had failed to maintain high standards and a breach of Clause 15.2 was ruled.

The Panel noted that there was no record of, or recollection from the representative in question of a discussion about the amputation data in June; the call record was blank and did not detail discussion. The Panel noted that according to the representative's interview notes a conversation was only logged in the CRM if product and key selling messages were mentioned and a dialogue ensued. If no dialogue ensued then the representative did not log the call. The call in June was logged in the CRM implying that a dialogue had occurred which was in contrast to the representative's recollection. The Panel noted that when questioned how, in general, he/she might discuss the amputation data, the representative noted that he/she always clarified that all SGLT2is had a warning on the respective summary of product characteristics (SPCs) in relation to the risk of amputations and that canagliflozin had more clinical findings on the SPC but it was unknown whether this constituted a class effect.

In relation to the conversation in question, the Panel noted that according to the representative's statement during the interaction the complainant asked if there was anything new to discuss about Forxiga; the representative recalled that he/she said that he/she had some safety information on Forxiga and the SGLT2i class but that the word amputation was not used. The Panel noted AstraZeneca's submission that according to the representative canagliflozin was only referred to in order to inform the complainant that he/she should raise any questions about this medicine with the canagliflozin representative. The Panel noted that the complainant and his/her receptionist remembered the representative saying canagliflozin was dangerous and patients should be switched to dapagliflozin.

The Panel considered that whilst it was likely that canaglifozin was discussed it was impossible to establish precisely what was said during the conversation and therefore it was not possible to determine on the balance of probabilities whether the representative had made misleading claims which were incapable of substantiation with regard to the amputation data for Forxiga or canagliflozin. No breach of Clauses 7.2 and 7.4 were ruled. The Panel did not consider that evidence had been provided by the complainant to show whether on the balance of probabilities the representative had disparaged canagliflozin as alleged and no breach of Clause 8.1 was ruled.

The Panel noted that Clause 15.9 required, *inter alia*, that briefing material must not advocate, either directly or indirectly, any course of action which would be likely to lead to a breach of the Code. The Panel noted the relevant warnings in Section 4.2 of the canagliflozin and Forxiga SPCs as set out in AstraZeneca's response.

In relation to the briefing material the Panel noted that the sales force was first briefed about the

increased risk of lower limb amputation with canagliflozin in July 2016 to enable the sales force to respond reactively to any questions from health professionals about the emerging data in relation to canagliflozin and, *inter alia*, toe amputations. The sales force was specifically instructed that they must not prompt a health professional to ask a question about this. The Panel noted that the briefing (Ref JBN: 996743.011 DOP July 2016) stated that the information could be discussed in response to a direct HCP enquiry or proactively with a HCP known to have a safety concern in relation to the SGLT-2 inhibitor class. The briefing did state 'Do not prompt an HCP in conversation by saying, for example, 'Have you seen the news about the fractures with canagliflozin?'.

An update (GB-5839) was provided to the sales force on the amputation data for SGLT2is in a presentation dated March 2017 which informed the sales force of the likely changes to the SPCs for all SGLT2is. The presentation detailed further studies including CANVAS-R which enrolled a similar population of patients to the previous CANVAS study and wherein the incidence of lower limb amputations for canagliflozin v placebo was not statistically significant. It further stated that a higher incidence of amputation was not observed across 12 other completed Phase 3/4 clinical trials'. It reproduced expected label updates for Forxiga and canagliflozin.

An email in June 2017 (GB-7169) advised the sales force that the CANVAS results must not be proactively discussed with customers. An objection handler (GB-7857) was issued in July 2017 which was only to be used reactively in response to questions relating to the risk of lower limb amputation for Forxiga vs that for canagliflozin. According to AstraZeneca the information included was based on the factual wording in the medicines' SPCs. The Panel noted that both the objection handler and the March 2017 presentation stated that 'to date there had been no increased risk seen in the clinical trial programme for Forxiga' and 'To date we are not aware of any imbalance in lower limb amputations in the Forxiga clinical trial program'. The Panel further noted the representative's line manager's interview statement that it was now known that it was not a class effect. The Panel queried whether this was entirely consistent with the Forxiga SPC which stated that it was unclear whether there was a class effect. The Panel noted the line manager's statement that there was no instruction to lead on a discussion of the SPC changes. AstraZeneca clarified that in the line manager's previous statement 'Where there is high cana use I am comfortable that my team discuss the side effect profile proactively with HCPs, including the amputation data' he/she was referring to the amputation data in the Forxiga detail aid which was in relation to Forxiga only and made no reference to canagliflozin. The Panel considered that this was in contrast to AstraZeneca's submission that the representative confirmed that he/she intended to discuss the changes to the Forxiga SPC and the SGLT2i class, and would have expected canagliflozin to have been discussed in that context, albeit the representative did not think that it was being raised proactively as he/she had verbal permission to call on the complainant with any new Forxiga data. It was also inconsistent with AstraZeneca's submission that in response to questioning the representative's line manager stated that the representative when discussing the amputation data noted that there was data to indicate an increased risk with canagliflozin but that it was unknown whether this was a class effect for all SGLT2is.

The Panel noted its general concerns about the briefing material as outlined above but did not consider that there was evidence to show that on the balance of probabilities AstraZeneca had provided briefing that advocated, either directly or indirectly, any course of action which would be likely to lead to a breach of the Code. No breach of Clause 15.9 was ruled.

The Panel noted its concerns and rulings above but did not consider that a ruling of a breach of Clause 2 of the Code was a sign of particular censure and reserved for such. In that regard, the Panel did not consider that the matter warranted such a ruling and so no breach of Clause 2 was ruled.

During the consideration of this case, the Panel considered that AstraZeneca would be well advised to review its process for permission to call back for the entire field force bearing in mind the letter and spirit of the Code, and its guidance on calls and contacts. In addition, the company should ensure that its representatives were entering calls and contacts accurately in its CRM system.

Complaint received **3 August 2017**

Case completed **26 January 2018**