ANONYMOUS v CHUGAI

Conduct of a representative

An anonymous, non-contactable haematologist from a district general hospital complained that pharmaceutical company representatives encouraged the use of medicines by referencing inaccurate information. The complainant referred in particular to a recent meeting with a Chugai representative who had promoted Granocyte (lenograstim).

The complainant had a number of concerns including that the representative had shown information that was of no benefit to the complainant and wasted both of their time; the information included data showing a recommendation from a European transplant group which was not a stipulation and that the representative had suggested that data from healthy donors could be extrapolated to fit neutropenia patients who were normally ill with cancer.

The complainant also alleged that the representative had told a senior nurse that the commissioning of Granocyte now came direct from the new NHS commissioning board. The complainant was concerned that the representatives had been given incorrect information by Chugai.

The detailed response from Chugai is given below.

The Panel noted that extreme dissatisfaction was usually required on the part of an individual before he/she was moved to complain. The Panel considered that Chugai was in a difficult position given that the complainant was anonymous and had not identified a hospital or a geographical location or named the representative. The Panel noted that Chugai had interviewed the representatives and provided copies of, *inter alia*, the Granocyte e-sales aid, and the relevant briefing document. Conversely, the complainant, who had the burden of proving his/her complaint on the balance of probabilities, had not provided any material to support his/her allegations. As the complainant was non-contactable, it was not possible to obtain more information from him/her. A judgement had to be made on the evidence provided by the parties.

The Panel noted the allegation that the representative had wrongly suggested that data from healthy donors could be extrapolated to neutropenic patients. Chugai agreed that such extrapolation was neither ethical nor correct. The Panel noted that neither the e-sales aid nor the briefing document implied that such extrapolation was possible. In that regard the Panel did not consider that the briefing material advocated a course of action which would be likely to lead to a breach of the Code and no breach was ruled. Bearing in mind the materials used by the representatives, the Panel considered that the complainant had not demonstrated that the representative had claimed that data from healthy donors could be extrapolated to neutropenic patients. No breach was ruled.

The Panel noted Chugai's submission that although the use of Granocyte to mobilise stem cells in patients and donors was more likely in tertiary units, subsequent care was typically managed at the district general hospital. In the Panel's view it was thus not unreasonable that haematologists in secondary care might be informed about the use of Granocyte in tertiary units. In that regard, based on the material before it, the Panel did not consider that the representative in question had failed to maintain a high standard of ethical conduct by wasting the complainant's time as alleged. No breach of the Code was ruled.

The Panel noted that the e-sales aid contained the statement 'The use of biosimilar [granulocyte colony-stimulating factors] G-CSFs for mobilisation of stem cells in healthy donors is NOT recommended by the [European Group for Bone Marrow Transplants] EBMT'. The Panel did not consider that the statement misleadingly implied a stipulation as alleged. No breach of the Code was ruled.

The Panel noted that the complainant was further concerned that the representative was said to have told a senior nurse that the commissioning of Granocyte now came direct from the new NHS commissioning board and not from the local clinical commissioning groups. It appeared that the complainant had not been party to the interaction between the nurse and the representative. The Panel noted that Chugai had provided a link to the NHS England website and a screen shot to show that Granocyte was a medicine which was not reimbursed through national prices set in the National Tariff and directly commissioned (and reimbursed) by NHS England.

The Panel did not consider that the complainant had established that, on the balance of probabilities, the representative had given the senior nurse inaccurate information as alleged. The Panel ruled no breach of the Code. The Panel further noted that there was no evidence that Chugai had incorrectly briefed its representatives about Granocyte reimbursement. The Panel ruled no breach of the Code. With regard to the alleged interaction with the senior nurse, the Panel did not consider that the complainant had established that the representative had failed to maintain a high standard of ethical conduct. The Panel ruled no breach of the Code.

The Panel noted its rulings above and considered that there had been no breach of Clause 2 of the Code.

An anonymous, non-contactable haematologist from a district general hospital complained in general that pharmaceutical company representatives encouraged the use of medicines by referencing inaccurate information, both in relation to available pharmaceuticals and the changes to commissioning within the new NHS. The complainant referred in particular to a recent meeting with a Chugai Pharma representative who promoted the company's granulocyte colony-stimulating factor (G-CSF) - Granocyte (lenograstim)

Granocyte was indicated in adults, adolescents and children older than 2 years for the reduction of the duration of neutropenia in patients (with non myeloid malignancy) undergoing myeloablative therapy followed by bone marrow transplantation and considered to be at increased risk of prolonged severe neutropenia, the reduction of the duration of severe neutropenia and its associated complications in patients undergoing established cytotoxic therapy associated with a significant incidence of febrile neutropenia and the mobilisation of peripheral blood progenitor cells, for patients as well as healthy donors.

COMPLAINT

The complainant explained that as a consultant haematologist he/she worked in a typical district general hospital and saw a broad range of industry personnel, many from the same company which was frustrating.

The complainant stated that he/she had recently seen a Chugai representative; as the two had met before, the complainant hoped that the representative would know the complainant's workload very well. Yet despite previous conversations and knowing that the complainant's trust referred all patients who required stem cell transplants to the local teaching hospital, the representative insisted on showing the complainant an electronic slide show on his/her iPad to demonstrate the benefits of using G-CSF in healthy donors (relatives who gave their stem cells to assist a family member). When the complainant reminded the representative that the trust did not do any stem cell transplants, the representative replied 'If you see these types of results in healthy donors do you not agree that you would expect to see the same in your patients with neutropenia?'

The complainant was concerned that: the representative had not grasped the complainant's workload and the fact that transplant patients were referred to another centre; showing information at a non-transplant centre was of no benefit to the complainant and wasted both the representative's and complainant's time; the meeting was a tick box exercise to demonstrate to the representative's manager that he/she had seen the complainant; the Chugai data showed a recommendation from the European Group for Blood and Marrow Transplants (EBMT) which was a recommendation not a stipulation and as experts in their field, relevant clinicians should be given due respect to use whatever they deemed appropriate; the representative implied that extrapolation of data to fit another criteria was possible which was unethical, especially as patients with neutropenia were ill (normally with cancer) and had been treated with chemotherapy or radiation and healthy donors were fit and well; the representative could not show evidence that Granocyte was effective in patients with neutropenia when asked.

At the beginning of the conversation it was clear that the use of the electronic information was tracked and so the complainant queried whether this meant that representatives just had to see the complainant as a tick box exercise to keep his/her manager happy with no regard for what consultants really did or what was important. If there was new, factual and evidence based information then the complainant wanted to be informed otherwise he/she did not want his/her time wasted.

The complainant also alleged that other information which the representative had discussed with other members of the trust was incorrect. The complainant noted that a few weeks previously one of the senior nurses had asked him/her why the trust did not use Chugai's medicine as the representative had told her that the commissioning of Granocyte now came direct from the new NHS commissioning board and not from the local clinical commissioning groups (CCGs), this meant that whatever was prescribed within the trust would be reimbursed in full. Historically the local primary care trusts (PCTs) picked up the charge and asked the trust to switch to a generic product.

The complainant was concerned that the information was incorrect and gave a false impression of the reality. The complainant was informed by the finance director that 'we were urged by our local PCTs in 2012/2013 to switch away from branded prescribing where we were able to demonstrate a cost saving at every opportunity – today the new NHS commissioning board are asking us to only use branded products with exception as cost savings are essential to the new NHS'. The complainant was further concerned that the Chugai representative was not aware of the real facts and gave out incorrect information which came from head office as it was not aware of the real NHS and commissioning process.

The complainant appreciated that pharmaceutical companies were under pressure to maintain sales in what must be a very competitive market, but to do this by blatant extrapolation and twisting of the truth showed a new level within the UK which must be stopped immediately.

The complainant hoped that an investigation into this sort of practice would ensure that in future he/she and his/her colleagues were visited with only useful factual information and that they were not just a tick box exercise to satisfy a manager.

When writing to Chugai the Authority asked it to respond in relation to Clauses 2, 9.1, 7.2, 7.4, 15.2 and 15.9.

RESPONSE

Chugai noted that the complaint was anonymous, non-contactable and had not submitted any evidence or material to support his/her complaint.

Chugai took these allegations extremely seriously. All staff were aware of their need to maintain high standards between themselves and health professionals in line with the Code.

1 Interaction between the complainant and a Chugai representative

Chugai explained that Granocyte was indicated in adults, adolescents and children older than 2 years for:

- The reduction of the duration of neutropenia in patients (with non myeloid malignancy) undergoing myeloablative therapy followed by bone marrow transplantation and considered to be at increased risk of prolonged severe neutropenia
- The reduction of the duration of severe neutropenia and its associated complications in patients undergoing established cytotoxic therapy associated with a significant incidence of febrile neutropenia
- The mobilisation of peripheral blood progenitor cells, for patients as well as healthy donors.

This complaint encompassed two alleged interactions that pertained to the indications for Granocyte:

- District general hospitals used Granocyte and other G-CSFs to treat patients with chemotherapy-induced neutropenia. The main treating physician was typically a consultant haematologist or oncologist
- In addition, tertiary care units used Granocyte and other G-CSFs to mobilise stem cells in patients and healthy donors. Subsequent follow-on care of these transplant patients was typically managed by a haematologist at a district general hospital.

Aligned to the above treatment pathways there were a number of reasons for a representative to see a haematologist in a district general hospital. Chugai representatives directly promoted the use of Granocyte to haematologists for use in neutropenic patients and to haematologists who might refer patients to specialist transplant units.

Chugai submitted that the anonymous nature of the complaint, the failure to identify a hospital or a geographical location, or to name the representative, placed Chugai in a difficult position. This complaint could emanate from any consultant haematologist working in the UK. In order to provide an appropriate response the company's compliance officer and its medical director conducted interviews with all of the representatives who promoted Granocyte; all of those interviewed denied any conversation with a consultant haematologist that could have led to this complaint. Furthermore the representatives refuted extrapolating clinical data in the donor population to data in the neutropenic patient setting. All of the representatives had passed the ABPI representative examination and certificates were provided.

In the context of this background information Chugai addressed the six specific items identified by the complainant. The comments were in relation to the alleged actions of the representative and Chugai had addressed the response in that context.

1 The representative had clearly not grasped the complainant's workload and the fact that transplant patients were referred to another centre. At a non-transplant centre, showing information that was of no benefit to the complainant wasted both the representative's and complainant's time.

As indicated earlier there were a number of reasons why Chugai representatives would visit haematologists in a district general hospital to promote Granocyte. There was nothing to suggest that any representative had acted inappropriately or visited an inappropriate customer. During the interviews with the representatives, each had been asked whether they were aware of a customer who had raised any concerns of this nature. No representative could identify any such concerns. Chugai submitted that in the absence of more specific detail it was unable to investigate further; there was no evidence that any representative had acted inappropriately or wasted a customer's time. The company refuted any breach of Clauses 9.1 and 15.2 in this regard.

2 The meeting was a tick box exercise to demonstrate to the representative's manager that he/she had seen the complainant.

Chugai submitted that it had no key performance indicator or required metric which compelled representatives to visit any health professional a specific number of times and it strongly adhered to the Code in that respect. Data collated from the e-sales aid recorded regional use only. Chugai stated that it collated this information so that it could see which pages of the e-sales aid the representatives used and in turn make it more appropriate and useful to its customers. Chugai denied that the use of the e-sales aid was a tick box exercise, and it refuted any breach of Clauses 9.1 and 15.2.

3 The Chugai data showed a recommendation from the EBMT; this was a recommendation not a stipulation so as experts in their field, relevant clinicians should be given due respect to use whatever they deemed appropriate.

Chugai stated that the e-sales aid contained the following quotation from EBMT: 'The use of biosimilar G-CSFs for mobilization of stem cells in healthy donors is not recommended by the EBMT'. This quotation clearly referred to healthy donors. Chugai recognised the expertise of health professionals to use whatever therapy they deemed appropriate, however the Code allowed industry to

use quotations from reputable bodies such as EBMT. There was no evidence that a representative had stipulated otherwise. Chugai refuted any breach of Clauses 9.1 and 15.2 in this regard.

4 Extrapolation of data to fit another criteria was unethical, especially as patients with neutropenia were ill (normally with cancer) and had been treated with chemotherapy or radiation. Healthy donors were fit and well. To suggest a similar outcome was unethical and unfounded.

Chugai categorically agreed that extrapolation of data from healthy donors to patients undergoing cancer treatment was neither ethical nor correct. Neither the e-sales aid nor the briefing document stated that efficacy results in one population were transferable to another. Chugai submitted that during the interview process all representatives denied any such conversation had taken place. In the absence of any evidence Chugai refuted any breach of Clauses 7.2, 7.4, 9.1 and 15.2 in this regard.

2 Granocyte Funding

Chugai submitted that the core concern was whether Granocyte reimbursement was provided by NHS England or the local CCG.

A link was provided to the NHS England website. This showed the latest version of its directly-purchased products list. Chugai provided a screen shot (using the spreadsheet filters) to show that Granocyte was on the list. This confirmed that Granocyte was reimbursed by NHS England.

In light of this Chugai refuted that any incorrect information was disseminated by its representatives.

Finally, Chugai noted its concern that the complainant was anonymous and non-contactable and had not supplied any evidence or material to support his/her serious allegations. Chugai was very concerned that this allegation could damage its good reputation.

PANEL RULING

The Panel noted the clauses cited by the case preparation manager, Clauses 2, 7.2, 7.4, 9.1, 15.2 and 15.9 of the Code. The 2014 Code came into operation on 1 January 2014 with a transition period for newly introduced requirements. The clauses cited in this case were the same in the 2014 and 2012 Second Edition (amended) Codes, thus the Panel used the 2014 Code.

The Panel noted that extreme dissatisfaction was usually required on the part of an individual before he/she was moved to complain. The Panel considered that Chugai was in a difficult position given that the complainant was anonymous and had not identified a hospital or a geographical location or named the representative. The complaint could have emanated from anywhere in the UK. The Panel noted that in order to provide an appropriate response Chugai's compliance officer and its medical director had interviewed all of the representatives who promoted Granocyte (ten) and provided copies of, *inter alia*, the Granocyte e-sales aid, and the relevant briefing document. Conversely, the complainant, who had the burden of proving his/her complaint on the balance of probabilities, had not provided any material to support his/her allegations. As the complainant was non-contactable, it was not possible to obtain more information from him/her. A judgement had to be made on the evidence provided by the parties.

The Panel noted the allegation that the representative had wrongly suggested that data from healthy donors could be extrapolated to the treatment of neutropenic patients. Chugai agreed that such extrapolation was neither ethical nor correct. The Panel noted that neither the e-sales aid nor the briefing document implied directly or indirectly that such extrapolation was possible. In that regard the Panel did not consider that the briefing material advocated a course of action which would be likely to lead to a breach of the Code and ruled no breach of Clause 15.9. Bearing in mind the materials used by the representatives, the Panel considered that, on the balance of probabilities, the complainant had not demonstrated that the unidentified representative had made a claim that data from healthy donors could be extrapolated to neutropenic patients. No breach of Clauses 7.2 and 7.4 were ruled.

The Panel noted Chugai's submission that, in district general hospitals, its representatives promoted Granocyte for use in patients with chemotherapy-induced neutropenia. Although the use of Granocyte to mobilise stem cells in patients and healthy donors was more likely in tertiary units, subsequent care of such patients was typically managed at the district general hospital. In the Panel's view it was thus not unreasonable that haematologists in secondary care might be informed about the use of Granocyte in tertiary units. In that regard, based on the material before it, the Panel did not consider that the representative in question had failed to maintain a high standard of ethical conduct by wasting the complainant's time as alleged. No breach of Clauses 9.1 and 15.2 was ruled.

The Panel noted that the e-sales aid contained the statement 'The use of biosimilar G-CSFs for mobilisation of stem cells in healthy donors is NOT recommended by the EBMT'. The Panel noted the complainant's concern that the statement from the EBMT was a recommendation and not a stipulation and that, as experts in their field, relevant clinicians should be given due respect to use whatever they deemed appropriate. The Panel considered that the statement in the e-sales aid clearly reported a recommendation and it noted the complainant's acknowledgement that the e-sales aid showed a recommendation from the EBMT. The Panel did not consider that the statement misleadingly implied a stipulation as alleged. No breach of Clause 7.2 was ruled.

The Panel noted that the complainant was further concerned that the representative was said to have informed one of the senior nurses that the

commissioning of Granocyte now came direct from the new NHS commissioning board and not from the local CCGs. It appeared that the complainant had not been party to the interaction between the nurse and the representative. The Panel noted that Chugai had provided a link to the NHS England website and a screen shot to show that Granocyte was a medicine which was not reimbursed through national prices set in the National Tariff and directly commissioned (and reimbursed) by NHS England.

The Panel did not consider that the complainant had established that, on the balance of probabilities, the representative had provided a senior nurse with inaccurate information about the reimbursement of Granocyte as alleged. The Panel ruled no breach of Clauses 7.2 and 7.4. The Panel further noted that there was no evidence that Chugai had incorrectly briefed its representatives about Granocyte reimbursement. The Panel ruled no breach of Clause 15.9. With regard to the alleged interaction with the senior nurse, the Panel did not consider that the complainant had established that the representative had failed to maintain a high standard of ethical conduct. The Panel ruled no breach of Clauses 15.2 and 9.1.

The Panel noted its rulings above and considered that there had been no breach of Clause 2 of the Code.

Complaint received **6 March 2014**

Case completed **11 April 2014**

CASE AUTH/2704/3/14

MEDICINES MANAGEMENT PHARMACIST v FLYNN PHARMA

Circadin journal advertisement

A medicines management pharmacist referred to a claim in a Flynn Pharma Ltd advertisement in Prescriber for Circadin (melatonin) that 'Current guidance states that, when a hypnotic is indicated in patients aged 55 and over, prolonged-release melatonin should be tried first'. The claim was referenced to Wilson *et al* (2010) which the complainant stated was the 'British Association for Psychopharmacology [BAP] consensus statement on evidence-based treatment of insomnia, parasomnias and circadian rhythm disorders'. The complainant alleged that this was hardly current guidance and was misleading as he/she was sure most others would take 'current guidance' to mean that recommended by the National Institute for Health and Care Excellence (NICE) or the All Wales Medicines Strategy Group (AWMSG) in Wales.

The detailed response from Flynn Pharma is given below.

The Panel noted that the complainant stated he/she interpreted the claim to mean guidance recommended by NICE or AWMSG in Wales. The Panel queried how many readers would similarly interpret the claim as such.

The Panel noted that Wilson *et al* was a consensus statement written by eighteen members of BAP. The Panel was unsure of the criteria used to select the authors and noted that guidance from a nationally recognised body was different from that issued by a small consensus group of eighteen members. However, the abstract referred to the document as the 'The British Association for Psychopharmacology guidelines'. The process for agreeing the final document was described in the abstract which stated 'All comments were incorporated as far as possible in the final document which represents the view of all participants although the authors take final responsibility for the document'. BAP published the Journal of Psychopharmacology in which the guidelines appeared. The advertisement at issue included a reference but this did not refer to BAP; only the publication details were cited.

The Panel noted Flynn Pharma's submission that it had played no part whatsoever in the process by which BAP selected the therapy area (insomnia), or formulated its consensus statement and guidelines. The Panel further noted that Flynn Pharma had taken over marketing responsibility for Circadin from Lundbeck in January 2012. The BAP guidelines were published in 2010 following a consensus meeting in May 2009. The Panel noted that although Flynn Pharma had no relationship with BAP, Lundbeck was one of two companies which provided unrestricted grants to partially offset the costs of the BAP consensus statement meeting. The 'method' section of the document explained that observers from the companies were invited to attend but did not participate in the summary proceedings or in drafting the guidelines. The funding arrangements were described on the final page which included 'The costs of the meeting were partly defrayed by unrestricted educational grants from two pharmaceutical companies (Lundbeck and …)'. The Panel further noted Flynn Pharma's submission that one of the authors was a lead investigator in the clinical development of Circadin.

The Panel considered that the claim at issue 'Current guidance states…' was not sufficiently clear that the recommendation came from the 'British Association for Psychopharmacology consensus statement on evidence-based treatment of insomnia, parasomnias and circadian rhythm disorders' nor did it reflect the status of that document and the role of the marketing authorization holder at the time the document was produced. The use of the term 'current guidance' in this context gave insufficient information about the nature and status of the guidance such that the claim at issue was ambiguous and therefore misleading. The Panel considered that on the information provided in the advertisement it was likely that readers would assume that the guidance had been issued by a nationally recognized body such as NICE or AWMSG. That was not so. The Panel ruled a breach of the Code.

A medicines management pharmacist complained about an advertisement (ref Circ/ADV/13/0483) for Circadin (melatonin) placed in Prescriber, Vol 25 issue 1/2 January 2014, by Flynn Pharma Ltd.

Circadin was indicated as monotherapy for the short-term treatment of primary insomnia characterised by poor quality of sleep in patients aged 55 or over.

COMPLAINT

The complainant referred to a claim in the advertisement that 'Current guidance states that, when a hypnotic is indicated in patients aged 55 and over, prolonged-release melatonin should be tried first'. The claim was referenced to Wilson *et al* (2010).

The complainant alleged that this was misleading as he/she was sure most others would take 'current guidance' to mean that recommended by the National Institute for Health and Care Excellence (NICE) or the All Wales Medicines Strategy Group (AWMSG) in Wales. The complainant stated