CASE AUTH/2799/10/15

ANONYMOUS ONCOLOGIST v PIERRE FABRE

Promotion of Vinorelbine

An anonymous, non-contactable complainant complained about promotional material for Navelbine (vinorelbine), available on the Pierre Fabre stand at the European Society for Medical Oncology (ESMO) Congress held in Vienna in September 2015.

The complainant noted the phrase 'Rare Cumulative Toxicity' which appeared on the stand panels and similar phraseology which appeared in materials available on the stand. The complainant had used vinorelbine for many years and had not found its side-effects to be a rarity; most of his/her patients had had some adverse reaction, particularly gastrointestinal side-effects.

The complainant queried claims in an efficacy brochure including the majority of patients (79%) were able to dose escalate to 80mg/m^2 and 'Easily Manageable Adverse Events'. In the complainant's practice, most patients were only able to bear 60mg/m^2. The complainant further submitted that adverse events were certainly not easy for clinicians or patients to manage, let alone endure.

The complainant stated that when he/she questioned the Pierre Fabre representative on the stand regarding the above, he/she was told that vinorelbine had a rare cumulative toxicity because patients only took the medicine for three weeks out of four (toxicities reduced during the rest week) after which, the cycle continued. The complainant submitted that this explanation was nonsensical because as long as the patient took the medicine, there were toxicities, and therefore the statement 'rare cumulative toxicities' was misleading.

The complainant queried whether patient safety might be at risk.

The detailed response from Pierre Fabre is given below.

The Panel first considered whether the promotion of Navelbine at the ESMO Congress in Vienna, from an exhibition stand organised and funded by the French global team, came within the scope of the Code. UK employees provided substantial support to the global team by manning the stand together with representatives from other affiliates. The welcome pack provided to 20 UK based oncologists invited by the UK company to attend the congress included details of where to find the Pierre Fabre stand. In that regard, the Panel considered that Pierre Fabre in the UK had invited the UK health professionals to view the promotional material on the stand. Further, in the Panel's view, it was more than likely that when UK delegates, and particularly the 20 invited by the UK affiliate, Pierre Fabre Limited, visited the Pierre Fabre stand, they would talk to UK representatives. The Panel noted its comments above about the UK company directing UK delegates to the stand and therefore considered that the promotion of vinorelbine to UK health professionals on the stand at the ESMO Congress fell within the scope of the UK Code.

The Panel noted that the claim 'Rare Cumulative Toxicity' on the front page of an efficacy brochure detailing the use of Navelbine in metastatic breast cancer and advanced non small cell lung cancer (NSCLC) was referenced to Petrelli *et al* (2011) and Aapro and Finek (2012). Aapro and Finek reviewed 31 studies which included more than 1,000 patients with metastatic breast cancer. Petrelli *et al* referred specifically to the lack of risk of major cumulative toxicity when vinorelbine was administered in combination with labatinib in metastatic breast cancer. Aapro and Finek stated that 'As shown in different studies, oral vinorelbine based-regimens allowed a longer duration of treatment, as a result of their activity and the absence of cumulative toxicities'. In the Panel's view, there was a difference between cumulative toxicity and acute toxicity and the claim was not misleading as alleged; it did not imply that acute toxicity was rare but rather that cumulative toxicity was rare. Pierre Fabre had provided relevant data regarding cumulative toxicity. Given all the circumstances, the Panel ruled no breaches of the Code.

The claim that the majority of patients (79%) were able to dose escalate to 80mg/m^2 appeared on a page detailing the use of Navelbine in metastatic breast cancer. The Panel noted that the claim actually read '79% of patients were able to escalate to the standard dose of 80mg/m^2' and was referenced to Steger *et al*, a poster presented at ESMO in 2014 which included the results of a phase II study to evaluate the efficacy and safety of single agent oral vinorelbine as first line chemotherapy in 70 breast cancer patients presenting with bone metastases without visceral involvement. The Panel further noted that the summary of product characteristics (SPC) stated that the first three administrations of Navelbine should be 60mg/m^2 of body surface area, once weekly. It was recommended that beyond the third administration, the dose should be increased to 80mg/m^2 once weekly except in those patients whose neutrophil count dropped below certain parameters. The Panel considered that whilst the claim was based on the poster, it unequivocally implied that around 4 in 5 of all patients could tolerate a dose escalation to 80mg/m^2. The study, however, was only conducted in a small specific population and the claim did not make it clear that there were certain patients in whom dose escalation would not be appropriate. In that regard the Panel did not consider that a statement on two other pages of the brochure which provided a means of calculating doses and which read 'Continue with standard dose of 80mg/m^2/week depending on blood count' was sufficient

to clarify the claim at issue. The claim should be able to standalone. The Panel did not consider that Steger *et al* was sufficiently robust to support the strong claim. In that regard the Panel considered that the claim was misleading and could not be substantiated and breaches of the Code were ruled.

The Panel noted that the claim 'Easily Manageable Adverse Events' was referenced to Bennouna *et al* (2014), a study involving 153 patients (premetrexed/ cisplatin (n=51) or oral vinorelbine/cisplatin (n=102)) with non small cell lung cancer. The discussion section of the paper stated that the safety profile differed across the 2 doublets, but the incidence and severity of adverse events was acceptable and easily manageable in both arms. The study did not provide further detail regarding how the manageability of adverse events was assessed. The Panel noted that it was particularly important not to mislead with regard to side-effects. The Panel, however, noted the highly specialised therapy area and that the material was for use at a European oncology congress. In the Panel's view the audience would be familiar with the side effect profile of cytotoxic medicines generally. The Navelbine SPC listed a number of adverse reactions some of which were reversible or could be managed with supportive treatment. In the Panel's view, given the therapy area and the target audience, the claim 'Easily Manageable Adverse Events' was not unreasonable. In that regard the Panel did not consider that the claim was misleading. The Panel considered that the claim could be substantiated. No breaches of the Code were ruled.

The Panel noted its rulings above of breaches of the Code and considered that high standards had not been maintained and ruled a breach of the Code.

With regard to Clause 2, the Panel noted that prejudicing patient safety was an activity likely to be ruled in breach of Clause 2. The Panel noted that there was no evidence to show that patient safety had been adversely affected. The Panel was, however, concerned about the misleading claim about dose escalation to 80mg/m^2 but noted that it did not suggest that all patients could dose escalate. Other information in the leavepiece referred to administering 80mg/m^2 depending on blood count. On balance no breach of Clause 2 was ruled.

The Panel noted the complainant's allegation regarding the misleading response received when questioning the Pierre Fabre representative on the stand. The Panel noted that Pierre Fabre was not able to identify the oncologist or the representative in question. As the complainant was non-contactable it was not possible to ask him/her for further information. The Panel noted Pierre Fabre's submission that all of the UK employees who had manned the stand denied that such a conversation took place. The Panel noted that a complainant had the burden of proving their complaint on the balance of probabilities. It was impossible to know what had transpired between the parties. Although noting that extreme dissatisfaction was usually required before an individual was moved to complain, on the basis of the information before it the Panel ruled no breaches of the Code.

An anonymous, non-contactable complainant who described him/herself as an oncologist, complained about promotional material for Navelbine (vinorelbine), available on the Pierre Fabre stand at the European Society for Medical Oncology (ESMO) Congress held in Vienna, 25-29 September 2015. The complainant drew particular attention to an efficacy brochure (ref July 2015 – 798979).

Vinorelbine was indicated as a single agent or in combination for the first line treatment of stage 3 or 4 non small cell lung cancer and the treatment of advanced breast cancer stage 3 and 4 relapsing after or refractory to an anthracycline containing regimen.

COMPLAINT

The complainant noted the phrase 'Rare Cumulative Toxicity' which appeared on most of the Pierre Fabre panels. The complainant stated that he/she had used vinorelbine for many years and had not found its side-effects to be a rarity. Most of his/her patients had had some adverse reaction to vinorelbine, particularly gastrointestinal side-effects.

The complainant stated that Pierre Fabre also provided materials on the stand with similar phraseology. The complainant queried some of the statements in a brochure, including the majority of patients (79%) were able to dose escalate to 80mg/m^2, and 'Easily Manageable Adverse Events'. In the complainant's practice, most patients were not able to tolerate the high dose, and were only able to bear 60mg/m^2. Moreover, when making such a decision, there were a majority of factors that needed to be taken into consideration including underlying comorbidities, previous treatments, etc. The complainant submitted that adverse events were certainly not easy for clinicians or patients to manage, let alone endure.

The complainant stated that when he/she questioned the Pierre Fabre representative on the stand regarding the above mentioned observations, he/she was met with bemusement and was told that vinorelbine had a rare cumulative toxicity because patients only took the medicine weekly for three weeks, and then broke for a week (toxicities reduced during this rest week). After which, the cycle continued. The complainant submitted that this explanation was nonsensical because as long as the patient took the medicine, there were toxicities, and therefore the statement 'rare cumulative toxicities' was misleading.

The complainant stated that having worked with Pierre Fabre in the past, he/she was extremely disappointed with the quality of its current materials as patient safety might be at risk.

When writing to Pierre Fabre, the Authority asked it to consider the requirements of Clauses 7.2, 7.4, 7.9, 9.1 and 2 of the Code.

RESPONSE

Pierre Fabre submitted that the 2015 ESMO Congress was an international meeting attended by medical oncology experts from around the world including,

as it was held in Europe rather than the US, a large number from the UK. The Pierre Fabre stand was organised and funded by Pierre Fabre SA, the French global team, which had full responsibility for preparation of the panels and all materials on the stand. The UK affiliate (Pierre Fabre Limited) was not involved in the organisation of the stand or any materials on it but representatives employed by the UK supported Pierre Fabre SA by manning the stand, together with representatives from other affiliates. In addition Pierre Fabre Limited invited 20 UK oncologists to attend the congress.

Pierre Fabre submitted that after considering the Code and the complaint, it did not consider that materials distributed from the Pierre Fabre stand at ESMO fell within the scope of the Code.

The supplementary information to Clause 1.11 stated 'Activities carried out and materials used by a pharmaceutical company located in a European country must comply with the national code of that European country as well as the national code of the country in which the activities take place or the material are used'.

Furthermore, the supplementary information to Clause 1.1, which defined the scope of the Code stated 'It also applies to promotion to UK health professionals and other relevant decision makers at international meetings held outside the UK, except that the promotional material distributed at such meetings will need to comply with local requirements'.

Pierre Fabre submitted that the Pierre Fabre SA stand at ESMO and the materials on it had to comply with the requirements of the Austrian and French Codes; as the meeting was held outside the UK and the UK affiliate was not involved in the organisation of the stand or preparation of the materials, they did not fall within the scope of the UK Code.

Pierre Fabre noted that the complainant did not state the location of the ESMO Congress or the Pierre Fabre entity that organised the stand. According to Pierre Fabre, in these circumstances, the PMCPA could not know whether the subject of the complaint fell within the scope of the Code and therefore within its jurisdiction. Based on the above and the clear wording of the Code, Pierre Fabre did not believe that the stand or associated materials fell within the jurisdiction of the PMCPA and, therefore it did not provide a detailed response to the complaint with respect to those matters.

Pierre Fabre submitted that it was concerned to cooperate fully in relation to any genuine complaint made to the PMCPA within the scope of the Code and if the Panel disagreed with Pierre Fabre's analysis of the issue it would provide further information.

A number of UK employees were present on the stand organised by Pierre Fabre SA during the course of the congress. The complainant did not identify the representative with whom he/she had a discussion and Pierre Fabre accepted that this could have been a UK employee.

Pierre Fabre submitted that it had spoken with every UK employee who was at the ESMO Congress and none recalled having any discussion with any oncologist or other person consistent with the description provided in the complaint. All employees stated that they would not have responded to an enquiry in the manner alleged due to a full verbal briefing provided by the UK prior to the meeting.

In response to a request from the case preparation manager for a complete response to the complaint and additional information, Pierre Fabre provided a list of the global signatories and their job titles and noted that in addition to the stand, Pierre Fabre SA organised a scientific symposium that took place on 26 September.

The Pierre Fabre stand was manned by some of the affiliates that attended the congress. The UK promotional team manned the stand for the majority of the timeslots available. A full rota was included in the internal briefing document which was provided. The global briefing in relation to stand duty was done on the morning of 25 September.

The UK affiliate did not see the stand panels or any of the material that was available on the stand prior to the meeting. That being the case, on the afternoon of 25 September, the UK team was given guidance on how to man the promotional stand. Given that the promotional items had not been through the UK approval process, the representatives were directed not to use any material or allude to any materials/panels on the stand. If a UK health professional came to the stand, the representatives were instructed to take their details and follow up if appropriate upon their return to the UK.

Pierre Fabre submitted that there was no opportunity nor was it feasible to prepare a formal brief for the UK representatives and certify it before the start of the congress; the UK team was due to man the stand the following day.

'Rare Cumulative Toxicity'

Pierre Fabre disagreed with the complainant's view that the above claim was misleading, and could not be substantiated. The company believed that the oncologist was confused with the terminology used; cumulative toxicity vs acute toxicity. It was clear that the complainant was concerned about acute side-effects. Chronic or cumulative toxicity manifested as a result of continuous exposure to a chemical, in this case vinorelbine. However, Pierre Fabre believed that the complainant meant adverse reactions based in the acute setting, hence his/her description of gastrointestinal side-effects.

Petrelli *et al* (2011) stated '…combination of lapatinib with oral vinorelbine as first line chemotherapy in patients with HER2-neu-positive metastatic breast cancer …is characterised by good tolerability and activity, and can be applied for a prolonged period without the risk of major cumulative toxicity in either first or subsequent lines of treatment..'.

Aapro and Finek (2012) stated '…in different clinical trial settings, oral vinorelbine-based regimens allowed a longer duration of treatment, as a result of their activity and the absence of cumulative toxicities.'

Pierre Fabre submitted that the claim 'Rare Cumulative Toxicity' was not misleading, was capable of substantiation and reflected available evidence on adverse reactions and it denied breaches of Clauses 7.2, 7.4 and 7.9.

Majority of patients (79%) were able to dose escalate to 80mg/m²

The claim in the leavepiece read '79% of patients were able to escalate to the standard dose of 80mg/m²'. The claim referred to a first line phase II study, Steger *et al* (2014) that reported out of the 70 patients enrolled, 79% managed to dose escalate to 80mg/m² from the initial dose of 60mg/m². Moreover, the oral vinorelbine SPC had the following guidance on dosing:

> 'As a single agent, the recommended regimen is:
> first three administrations
> 60mg/m²
>
> Subsequent administrations
> Beyond the third administration it is recommended to increase the dose of Navelbine to 80mg/m² once weekly except in those patients for whom the neutrophil count dropped once below 500/mm³ or more than once between 500 and 1000/mm³ during the first three administrations at 60mg/m².
>
> For combination regimens, the dose and schedule will be adapted to the treatment protocol.'

Pierre Fabre stated that it was important to note that oral vinorelbine's licence was different across Europe and it had clearly indicated the aforementioned with the following statement '… NAVELBINE Oral is registered on a national basis …. Please refer to the Summary of Product Characteristics (SmPC) of your specific country …' on the front page of the leavepiece. Oral Vinorelbine was indicated in the UK as a single agent or in combination for the first line treatment of stage 3 or 4 non small cell lung cancer and the treatment of advanced breast cancer stage 3 and 4 relapsing after or refractory to an anthracycline regimen.

Pierre Fabre was unable to comment on the particular practice of the complainant but submitted that the information provided was fair, balanced and unambiguous. The reference that supported 79% of patients escalating up to 80mg/m² was capable of substantiation and hence, Pierre Fabre denied breaches of Clauses 7.2 and 7.4.

'Easily Manageable Adverse Events'

The claim 'Easily Manageable Adverse Events' was taken directly from an international randomized phase II study in non small cell lung cancer (Bennouna *et al*, 2014). Bennouna *et al* compared 153 patients on pemetrexed/cisplatin and vinorelbine/cisplatin, and found 'the safety profile differed across the 2 doublets, but the incidence and severity of adverse events was acceptable and easily manageable in the 2 arms …'

Pierre Fabre summarised the safety section of the study and considered that the claim 'Easily Manageable Adverse Events' was not misleading; it was balanced, fair, capable of substantiation and reflected current evidence on adverse reactions for the product and therefore was not in breach of Clauses 7.2, 7.4 and 7.9.

Inappropriate response from a representative

Pierre Fabre was unable to comment on what was discussed with the complainant as it could not identify the oncologist or the representative in question. The UK affiliate checked with all of its employees who manned the stand for the duration of the congress and confirmed that no such conversation took place. Moreover, all of the UK employees were briefed on Friday 25 September, not to use any of the materials on the stand or the stand panels as none of the materials were certified/approved by the UK team.

Pierre Fabre provided the briefing that was shared with all internal personnel before the congress started. The briefing included the following:

- You are invited to address questions or share scientific information about our products within their labelling in a fair, balanced, and scientific manner, in full compliance with the applicable regulations
  - The aids mentioned in the previous slide and available on the booth will support you in this task
- Beware that [Navelbine] is approved at national and not centralised level and there can be differences in its labelling from one country to another
- If asked questions not related to the products' approved labelling kindly refer the health professional to Medical Affairs staff on the scientific corner
- If confronted with a question you do not know how or cannot answer and there is no appropriate functions on site to address it, ask your physician to fill in a request card available on the booth and reassure him/her that the appropriate function will follow up locally after the congress
- Please do not venture in answers you do not fully master: regulations and products' labelling do vary from one country to another
- Whenever in doubt, refrain from taking initiative and rather refer the [health professional] to any of the [Pierre Fabre] Global MKTG (marketing) or Medical team
  - If no global staff is available, kindly ask the [health professional] to leave his/her contact details on the request card or to come back at a later time
- An [adverse event] form is available on site and should be used according to the pharmacovigilance regulations in the same way you would use it in your daily field activity.'

Pierre Fabre submitted that not only had it briefed its employees adequately, the UK affiliate additionally had a second briefing session for the UK employees that would man the stand. Thus, Pierre Fabre submitted that it had maintained high standards at all times and it denied a breach of Clause 9.1.

Pierre Fabre strongly refuted the suggestion that it had brought the pharmaceutical industry into disrepute. It could justify the claims used in its promotional material and had taken the necessary steps to ensure the representatives behaved in a professional manner while manning the stand at ESMO.

Additionally, the UK affiliate did not know beforehand what material would be used for the congress. The UK team was briefed not to use any material on the stand when it became apparent that the material and claims differed to the UK version and that any discussion which required the use of material would have to be done once the individuals concerned were back in the UK, using UK approved material.

Clause 2 was used as a sign of particular censure, and Pierre Fabre submitted that it had not warranted such a reprimand and was thus not in breach of that clause.

In response to a request for further information, Pierre Fabre submitted that eight UK employees attended the congress. Pierre Fabre also provided copies of the meeting application form, the delegate invitation letter, the invitation letters to Pierre Fabre UK delegates, the Pierre Fabre welcome and logistics pack including the itinerary for Pierre Fabre UK delegates, the Pierre Fabre Symposium invitation and details of the Pierre Fabre stand as well as email confirmation of hospitality review under the Austrian Code. The relevant certificates were also provided for all of the items listed. Pierre Fabre submitted that one of the final signatories did not certify the itinerary as he only received that job bag on the penultimate day of the congress.

PANEL RULING

The Panel noted that, as a preliminary issue, it had to consider whether promotion of Navelbine, at the ESMO Congress, by Pierre Fabre came within the scope of the Code. Clause 1.1 stated that the Code applied to the promotion of medicines to members of the UK health professions and to other relevant decision makers. Furthermore, the supplementary information to Clause 1.1, Scope of the Code, stated that it also included 'promotion to UK health professionals and other relevant decision makers at international meetings held outside the UK, except that the promotional material distributed at such meetings will need to comply with local requirements'.

The Panel noted Pierre Fabre's reference to the supplementary information to Clause 1.11, Applicability of Codes, which stated that activities carried out and materials used by a pharmaceutical company located in a European country must comply with the national code of that European country as well as the national Code of the country in which the activities took place or the material was used. Pierre Fabre submitted that the stand at ESMO and the materials on it had to comply with the requirements of the Austrian and French Codes but that, in circumstances where the meeting was held outside the UK and Pierre Fabre Limited had no involvement in the organisation of the stand or preparation of the materials, that these did not fall within the scope of the Code.

The Panel noted the supplementary information to Clause 22.1 stated that in relation to meetings organised by affiliates outside the UK 'Companies should remind their affiliates outside the UK that the ABPI Code of Practice must be complied with if UK health professionals attend meetings which they organise regardless of whether such meetings occur in the UK or abroad'.

The Panel noted that the stand at the ESMO Congress was organised and funded by Pierre Fabre SA, the French global team, which had full responsibility for preparation of the exhibition panels and all materials on the stand or distributed from it.

The Panel noted Pierre Fabre's submission that ESMO was an international meeting attended by medical oncology experts from around the world including a large number from the UK due to the meeting being held in Europe. Employees of the UK affiliate, Pierre Fabre Limited, who were at the meeting supported Pierre Fabre SA by manning the stand together with representatives from other affiliates. The Panel noted, however, that UK representatives provided just over half the man hours needed for the stand (36.5/66.5). Although there were four time slots where no UK representatives were present they were, for all but one of the remaining eight slots, always in the majority of those on the stand; for two of those time slots, only UK representatives manned the stand. In addition Pierre Fabre Limited invited 20 UK based oncologists to attend the congress. The welcome pack provided to these delegates included details of where to find the Pierre Fabre stand. In that regard, the Panel considered that Pierre Fabre in the UK had invited the UK health professionals to view the promotional material on the stand, Further, in the Panel's view, it was more than likely that when UK delegates, and particularly the 20 invited by Pierre Fabre Limited, visited the Pierre Fabre stand, they would talk to UK representatives. The Panel could not understand how the UK representatives could be expected to man the stand without referring to or being seen to use the promotional materials on it as submitted by Pierre Fabre. This submission contradicted the global briefing material which stated that material available on the stand, including the efficacy brochure at issue, would support those manning the stand.

The Panel noted its comments above about the UK company directing UK delegates to the stand and therefore considered that the promotion of vinorelbine to UK health professionals on the stand at the ESMO Congress fell within the scope of the UK Code.

The Panel noted the complainant was anonymous and non-contactable. As stated in the introduction to the Constitution and Procedure anonymous complaints were accepted and like all complaints,

judged on the evidence provided by the parties. Complainants had the burden of proving their complaint on the balance of probabilities.

The Panel noted that the claim 'Rare Cumulative Toxicity' appeared on the front page of an efficacy brochure detailing the use of Navelbine in metastatic breast cancer and advanced non small cell lung cancer. The brochure also referred to 'manageable safety profile' and 'easily manageable adverse events'. The claim was referenced to Petrelli *et al* (2011) and Aapro and Finek (2012). Aapro and Finek reviewed 31 studies which included more than 1,000 patients with metastatic breast cancer. The Panel noted Pierre Fabre's submission that cumulative toxicity manifested as a result of continuous exposure to a chemical. The Panel noted the complainant's view that he/she had used vinorelbine for many years and had not found its side-effects to be a rarity; most of his/her patients had had some reaction to vinorelbine, especially gastrointestinal side-effects. With regard to these side-effects, the Panel noted Pierre Fabre's submission that in its view the complainant was concerned with adverse reactions in the acute setting. The Panel noted that the Navelbine summary of product characteristics (SPC) stated that the most common system organ classes involved during post-marketing experience included, *inter alia*, gastrointestinal disorders. A number of adverse reactions reported were listed by system organ and frequency. The Panel noted that Petrelli *et al* referred specifically to the lack of risk of major cumulative toxicity when vinorelbine was administered in combination with labatinib in metastatic breast cancer. Aapro and Finek stated that 'As shown in different studies, oral vinorelbine based-regimens allowed a longer duration of treatment, as a result of their activity and the absence of cumulative toxicities'. In the Panel's view, there was a difference between cumulative toxicity and acute toxicity. In the Panel's view, the claim was not misleading as alleged as it did not imply that acute toxicity was rare but rather that cumulative toxicity was rare. Pierre Fabre had provided relevant data regarding cumulative toxicity. Given all the circumstances, the Panel ruled no breaches of Clauses 7.2, 7.4 and 7.9.

The claim that the majority of patients (79%) were able to dose escalate to 80mg/m^2 appeared on a page detailing the use of Navelbine in metastatic breast cancer. The Panel noted that the claim actually read '79% of patients were able to escalate to the standard dose of 80mg/m^2' and was referenced to Steger *et al*, a poster presented at ESMO in Madrid in September 2014 which included the results of a phase II study to evaluate the efficacy and safety of single agent oral vinorelbine as first line chemotherapy in 70 breast cancer patients presenting with bone metastases without visceral involvement, enrolled between April 2010 and April 2012. The Panel further noted that the SPC stated that the first three administrations of Navelbine should be 60mg/m^2 of body surface area, once weekly. It was recommended that beyond the third administration, the dose of Navelbine should be increased to 80mg/m^2 once weekly except in those patients for whom the neutrophil count dropped once below 500/mm^3 or was more than once between 500 and 1000/mm^3 during the first three administrations. The Panel considered that whilst the claim was based on the poster, it unequivocally implied that around 4 in 5 of all patients could tolerate a dose escalation to 80mg/m^2. The study, however, was only conducted in a small specific population and it was not clear from the claim in the efficacy brochure that there were certain patients in whom dose escalation would not be appropriate based on their neutrophil count. In that regard the Panel did not consider that a statement on two other pages of the brochure which provided a means of calculating doses and which read 'Continue with standard dose of 80mg/m^2/week depending on blood count' was sufficient to clarify the claim at issue. The claim should be able to standalone. The Panel did not consider that Steger *et al* was sufficiently robust to support the strong claim. In that regard the Panel considered that, on the basis of the material before it, the claim was misleading and could not be substantiated and ruled breaches of Clauses 7.2 and 7.4.

The Panel noted that the claim 'Easily Manageable Adverse Events', was on a page of the brochure detailing the use of Navelbine in non squamous non small cell lung cancer (NSCLC). The claim was referenced to Bennouna *et al* (2014), a randomized phase II study involving 153 patients (premetrexed/cisplatin (n=51) or oral vinorelbine/cisplatin (n=102)) with NSCLC. The discussion section of the paper stated that the safety profile differed across the 2 doublets, but the incidence and severity of adverse events was acceptable and easily manageable in both arms. The study did not provide further detailing regarding how the manageability of adverse events was assessed. The Panel noted that it was particularly important not to mislead with regard to side-effects. The Panel noted, however, that this was a highly specialised therapy area and that the material was for use at a European oncology congress. In the Panel's view the audience would be familiar with the side effect profile of cytotoxic medicines generally. The Navelbine SPC listed a number of adverse reactions most of which were common (≥ 1/100 < 1/10) or very common (≥ 1/10). However some of those reactions were reversible with or without appropriate additional therapy or could be reduced in severity with supportive treatment. In the Panel's view, given the therapy area and the target audience, the claim 'Easily Manageable Adverse Events' was not unreasonable. In that regard the Panel did not consider that the claim was misleading about the adverse events associated with Navelbine. The Panel considered that the claim could be substantiated. No breaches of Clauses 7.2, 7.4 and 7.9 were ruled.

The Panel noted its rulings above of breaches of the Code and considered that high standards had not been maintained and ruled a breach of Clause 9.1.

With regard to Clause 2, the Panel noted that prejudicing patient safety was an activity likely to be ruled in breach of Clause 2. The Panel noted that there was no evidence to show that patient safety had been adversely affected. The Panel was, however, concerned about the misleading claim about dose escalation to 80mg/m^2 but noted that it did not suggest that all patients could dose escalate. Other information in the leavepiece referred to

administering 80mg/m^2 depending on blood count. On balance no breach of Clause 2 was ruled.

The Panel noted the complainant's allegation regarding the misleading response received when questioning the Pierre Fabre representative on the stand. The Panel noted Pierre Fabre's submission that it was not able to identify the oncologist or the representative in question. As the complainant was non-contactable it was not possible to ask him/her for further information. The Panel noted Pierre Fabre's submission that the UK affiliate had checked with all of its employees that had manned the stand for the duration of the congress and all denied that such a conversation took place. The Panel noted that a complainant had the burden of proving their complaint on the balance of probabilities. It was impossible to know what had transpired between the parties. Although noting that extreme dissatisfaction was usually required before an individual was moved to complain, on the basis of the information before it the Panel ruled no breach of Clauses 7.2, 7.4, 7.9 and 9.1 of the Code.

Complaint received **7 October 2015**

Case completed **26 January 2016**