CASE AUTH/2979/9/17

HEALTH PROFESSIONAL v PHARMAMAR

Certification and Promotion of Yondelis

An anonymous, non-contactable complainant who described him/herself as a health professional complained about a 'Meetings Highlights' document with the disclaimer 'This newsletter has been funded by an unrestricted educational grant provided by PharmaMar S.A. PharmaMar S.A has not been involved in the production, review or distribution of this material'. The document was on the website of the British Sarcoma Group (BSG). The complainant alleged that PharmaMar had been involved in the preparation of the material which referred to the off-label, early use of its medicine Yondelis (trabectedin).

The complainant also listed a number of promotional materials which he/she had been informed had not been certified. The complainant alleged that one piece of material unfairly compared Yondelis with a competitor and another contained unsubstantiated claims.

The detailed response from PharmaMar is given below.

With regard to the Meetings Highlights document, the Panel noted that it was possible for a company to sponsor material, produced by a third party, which mentioned its own products, and not be liable under the Code for its contents, but only if, *inter alia*, there had been a strictly arm's length arrangement between the parties. In practical terms the arrangements must be such that there could be no possibility that the pharmaceutical company had been able to exert any influence or control over the final content of the material.

The Panel considered that the initial arrangements for the production of the Meetings Highlights document were such that PharmaMar was responsible for the content. There was no arm's length arrangement. The Panel did not change its view based on the amendments to the arrangements such that PharmaMar gave the money to BSG so that it could deal with the medical writer etc after the document had been drafted and the company realised the difficulties with the references in the document to the unlicensed use of Yondelis. The Panel also noted that the Meeting Highlights document had been used by the company for a promotional purpose.

The Panel considered that the Meeting Highlights document was the responsibility of PharmaMar and as it promoted a medicine for an unlicensed use, the Panel ruled a breach of the Code as acknowledged by the company. The disguised promotional nature of the document was compounded by the inclusion of the disclaimer noted above which was not an accurate description of the company's role. The Panel ruled a breach of the Code as acknowledged by PharmaMar.

The Panel ruled that high standards had not been maintained in breach of the Code as acknowledged by the company. The Panel considered that the circumstances brought discredit upon, and reduced confidence in, the pharmaceutical industry and a breach of Clause 2 was ruled as acknowledged by the company.

The Panel was extremely concerned that the circumstances showed a very poor understanding of the Code. It was also concerned that an email from a senior executive provided by the complainant showed a disregard for the Code. The Panel noted, however, that this email could not be located on the company's server. PharmaMar submitted that thus its origin and authenticity were not clear. The senior executive in question denied sending the email at issue.

The Panel upheld the allegations of an unfair comparison of Yondelis vs a competitor and of unsubstantiated claims. Breaches of the Code were ruled.

The Panel was concerned about PharmaMar's arrangements for certification. There was no standard operating procedure and no records of the certificates for the items listed by the complainant. The company could not demonstrate their date of first use or that the materials had been certified. The Panel therefore ruled a breach of the Code as acknowledged by the company.

The Panel considered that high standards had not been maintained and that the circumstances brought discredit upon, and reduced confidence in, the pharmaceutical industry. Breaches of the Code were ruled including Clause 2.

The Panel was extremely concerned about the conduct of senior employees and the lack of procedures for certification which it considered warranted consideration by the Code of Practice Appeal Board. The Panel therefore decided, in accordance with Paragraph 8.2 of the Constitution and Procedure, to report PharmaMar to the Appeal Board.

The Panel also decided that in accordance with Paragraph 7.1 of the Constitution and Procedure PharmaMar should suspend use of the Meeting Highlights document pending the final outcome of the case.

The Appeal Board considered that this case raised serious concerns about PharmaMar's processes and Code knowledge. The Appeal Board queried how such a fundamental failure of compliance on what should be well understood principles of the Code could occur. The Appeal Board considered that PharmaMar's investigation into this issue was wholly inadequate. The Appeal Board noted that

in response to questioning, PharmaMar stated that its investigation into this case had comprised an IT investigation run by human resources, which found no record of two of the emails provided by the complainant. PharmaMar had provided no documentary evidence to verify its IT investigations.

The Appeal Board noted that the PharmaMar representatives submitted that the company had taken advice on this issue from its external review agency yet it provided no documentary evidence to support this.

It was wholly unclear why the HR investigation had focussed on the narrow point about the veracity of the two emails rather than giving any consideration to the broader and significant compliance issues pertaining to the newsletter. It was inexplicable that those matters had not been addressed and the Appeal Board queried whether the company truly understood the gravity of the situation including the importance of self-regulation.

The Appeal Board noted that the company had provided no record that the member of staff had provided the advice that the company stated it had subsequently followed and that had led to the failings and breaches of the Code. The Appeal Board noted that in response to questioning PharmaMar stated that the member of staff to whom responsibility for the Code was delegated was not a registered signatory. When asked what Code training the company had given the answers were unsatisfactory and vague.

The Appeal Board noted that it appeared that the review process was not carried out correctly. The Appeal Board noted that the company's external agency had provided external medical review and in that regard the Code only required one signatory. The company's online approval system did not keep a record of medical certification. PharmaMar had acknowledged that it had failed to certify promotional items. The Appeal Board noted the company's submission that all materials were withdrawn and subject to recertification. The Appeal Board considered that it was shocking that PharmaMar had chosen to delegate responsibility for compliance with the Code without confirming the credentials and knowledge of the individual concerned. The Appeal Board was concerned with the company's lack of process around certification. The Appeal Board considered that the certification process, correctly implemented, underpinned self-regulation. It appeared that there were serious issues regarding PharmaMar's arrangements. The Appeal Board considered that the level of Code expertise within the company appeared to be very poor given the fundamental errors and the company's apparent lack of preparation for the report.

The Appeal Board noted the circumstances that gave rise to this case and the company's poor approach to compliance as set out in the Panel's ruling. The Appeal Board noted that PharmaMar had now commissioned a gap analysis to identify, and thereafter start to address, compliance failings. The Appeal Board decided that in accordance with Paragraph 11.3 of the Constitution and Procedure, PharmaMar should be publicly reprimanded for failing to make any meaningful effort to undertake a thorough investigation and to provide evidence to support its position. There were significant omissions in its documentation and the company was unable to provide adequate responses to the Appeal Board questions. Such an approach raised grave concerns about the importance attached to compliance and self-regulation by the company. The Appeal Board also decided to require an audit of PharmaMar's procedures in relation to the Code. The audit would take place as early as practicable in early 2018 and on receipt of the report, the Appeal Board would consider whether further sanctions were necessary.

The Appeal Board also decided to require PharmaMar to issue a corrective statement to all attendees to the BSG conference and its organisers. [The corrective statement, which was agreed by the Appeal Board prior to use, appears at the end of this report].

On receipt of the report for the February 2018 audit the Appeal Board noted the poor internal communication at PharmaMar UK and with its Spanish head office. The Appeal Board considered that PharmaMar in the UK had a very limited compliance structure, compliance expertise and Code knowledge. Leadership on compliance needed to urgently improve. The company lacked many of the basic systems that a company required. It was essential that all staff took an active role in compliance.

The Appeal Board noted that the report of the audit highlighted many issues and concerns to be addressed including certification, attention to detail, updating and introduction of standard operating procedures (SOPs) and training. Significant and sustained commitment by all staff was required to address these issues. On receipt of further information in May and June 2018 the Appeal Board decided that PharmaMar should be re-audited in October 2018. On receipt of the report for the re-audit the Appeal Board would decide whether further sanctions were necessary.

PharmaMar Spain notified the PMCPA that as of 1 July 2018 the promotional and commercial activities of PharmaMar UK would stop. PharmaMar stated it would leave membership of the ABPI but remain a member of EFPIA.

On receipt of this further information at its meeting in July 2018 the Appeal Board noted that as a member of EFPIA, PharmaMar would need to comply with the ABPI Code. The Appeal Board requested further information.

On receipt of further information in September 2018 the Appeal Board considered that the PMCPA should make arrangements to re-audit PharmaMar's policies and procedures for how it was running its arrangements in the UK to ensure that PharmaMar was fulfilling its responsibilities under the ABPI Code. The Appeal Board considered that the re-audit should still go ahead as soon as was practical.

In October 2018 the Appeal Board noted PharmaMar's response with regard to the Appeal Board's decision that the re-audit of PharmaMar planned for October 2018 should still go ahead at a suitable date in November. The position had changed again. PharmaMar noted that it had now entered into an agreement with Impilo Pharma AB (Medical Need Europe) appointing it as exclusive distributors of Yondelis in a number of territories. The agreement became effective for the UK, on 1 September 2018. The agreement included promotional and medical affairs activities in the UK.

The Appeal Board considered that as PharmaMar still held an interest in that it remained the licence holder for Yondelis the re-audit should still go ahead. The re-audit needed to assess how PharmaMar was administering its arrangement with Impilo as to how Yondelis was being marketed in the UK in accordance with the Code. The Appeal Board considered that the re-audit should go ahead as soon as was practical. The Appeal Board noted that the PMCPA would need to see relevant Impilo staff as part of the re-audit.

On receipt of the report for the January 2019 re-audit of PharmaMar and Immedica (previously Impilo) in April 2019 PharmaMar SA stated that if and when commercial or medical involvement of UK health professionals was needed, such as speaking at international congresses PharmaMar SA would contact Immedica.

In its comments Immedica UK addressed each of the recommendations.

The Appeal Board noted from the report of the re-audits that most of the PharmaMar SA staff interviewed considered that the first audit had led to global improvements in culture and processes and they viewed the audit process as an opportunity to improve and change. Staff appeared to show an increased understanding of the importance of compliance.

The Appeal Board noted from the report of the re-audits that Impilo Pharma AB as Medical Need and now Immedica, acquired from PharmaMar SA the rights to market and distribute Yondelis in a number of territories including the UK. Immedica UK was a very new small UK company. The Appeal Board noted that the circumstances were unusual in that Immedica UK had not been ruled in breach of the Code. Those interviewed at Immedica UK acknowledged the importance of compliance and the need to ensure that Immedica UK established a robust compliance infrastructure.

The Appeal Board noted from the report of the re-audits that it appeared from those interviewed that PharmaMar understood that any future relationships with UK health professionals would be via Immedica headquarters in Sweden and Immedica UK. The Appeal Board considered each company separately. It considered that each company should implement the re-audit reports recommendations.

On receipt of further information regarding implementation of recommendations in September 2019 the Appeal Board decided that no further action was required.

An anonymous, non-contactable complainant who described him/herself as a health professional complained about meeting highlights, sponsored by PharmaMar S.A, from the 13th annual conference of the British Sarcoma Group (BSG). The complainant also alleged that several marketing and sales materials for Yondelis (trabectedin) had not been approved.

Yondelis was indicated, *inter alia*, for the treatment of adults with advanced soft tissue sarcoma after failure of anthracyclines and ifosfamide or who were unsuited to receive these agents.

COMPLAINT

The complainant noted that the Meeting Highlights document at issue, available on the BSG website, had the following disclaimer 'This newsletter has been funded by an unrestricted educational grant provided by PharmaMar S.A. PharmaMar S.A. has not been involved in the production, review or distribution of this material'.

The complainant stated, however, that it had been brought to his/her attention that PharmaMar Ltd (UK) had been intrinsically involved in the preparation and content of the material. The material mentioned off-label use of Yondelis. On page 2 under the heading 'Neoadjuvant Chemotherapy' the use of Yondelis was discussed despite it not being licensed for such use. The complainant alleged that this was an attempt to promote off-label early use of the medicine.

The complainant stated that a third-party agency had been involved in the development of the document along with PharmaMar employees as shown by email correspondence provided. In particular, the complainant drew attention to the last message of a senior executive about the BSG newsletter; dated 9 March 2017, it stated 'It is compliant as long as the PMCPA and Madrid are not aware of it'.

The complainant added that he/she had been informed that the following marketing and sales materials produced and distributed by PharmaMar had not been signed off by a medical signatory to avoid compliance review:

- i-pad app screenshots – YON1215-924 – unfair comparison against competitor 'Gem/Tax'
- Exhibition panel – YON0117-1069 – unsubstantiated claims
- Exhibition Advert – YON01170-1070
- Dosing Guide – YON1215-925
- BSG Folder – YON0417-1108
- Treatment Administration Booklet – YON3016-958
- Yondelis Patient Information – YON0816-1009
- Yondelis 6+1 booklet – YON0916-1020.

When writing to PharmaMar the Authority asked it to consider the requirements of Clauses 2, 3.2, 9.1 and 12.1 in relation to the Meeting Highlights document and 2, 9.1, 7.2, 7.4 and 14.1 in relation to the materials.

RESPONSE

a) Meeting Highlights document

PharmaMar stated that in November 2016 it asked the BSG co-ordinator if there was a potential opportunity to promote Yondelis given that the independently-organised BSG symposium would discuss this medicine. PharmaMar suggested a medical writing agency attend and write a promotional newsletter. The medical writer was well known to the company and had previously written promotional and non-promotional materials for Yondelis. The medical writer was briefed and provided a fee estimate.

The BSG agreed and accordingly two PharmaMar employees and the medical writer attended the symposium (1/2 March 2017) to listen to the content and prepare the promotional newsletter. Some of the symposium content related to the unlicensed use of Yondelis.

On 7 March, the medical writer emailed PharmaMar with suggested content for the newsletter asking for approval and PharmaMar replied that same day with suggestions. It was extremely unfortunate that the reference in the medical writer's email to the unlicensed use of Yondelis (neo-adjuvant chemotherapy for soft tissue sarcoma) was not picked up by the two PharmaMar employees involved or during the symposium itself.

However, the following day (8 March) email correspondence between the two employees who had attended the symposium noted that the suggested content for the newsletter contained information in relation to the unlicensed use of Yondelis, that a promotional newsletter could not include this and that the newsletter would also require prescribing information. The medical writer was not copied in.

PharmaMar submitted that at this point, the promotional newsletter could have simply omitted the unlicensed information but the topic of neo-adjuvant chemotherapy for soft tissue sarcoma was a key highlight of the meeting and could not therefore be left out of a Meeting Highlights newsletter.

It would appear that on advice from one company attendee, the more senior company attendee (a senior executive) contacted the BSG co-ordinator to alert him/her that the newsletter could no longer be promotional, should now be supported by a grant and that the company should have no further involvement. The BSG acknowledged this point and requested disclaimer wording, which was subsequently provided by the less senior company attendee.

On the basis of the senior executive's email, the medical writer would write a comprehensive meeting report (reflecting the content of the symposium and thus containing both licensed and unlicensed information about Yondelis) and the BSG Board would fund and approve this, with no involvement of PharmaMar other than financial support via a grant to the BSG. Therefore, PharmaMar did not review the newsletter.

(PharmaMar provided a copy of the medical writer's invoice to the BSG).

PharmaMar fully acknowledged that it was not possible to establish an arm's length arrangement with the newsletter for the following reasons, and it was thus responsible for its content:

1 The engagement of a medical writer to develop a symposium newsletter was initiated by PharmaMar.
2 Company staff knew the newsletter would in effect promote Yondelis for an unlicensed indication.

Once certain staff understood the full content of the newsletter, they naïvely suggested that it could be supported by a grant from PharmaMar in order to allow the publication to continue and provided a declaration of sponsorship in that regard. This demonstrated a poor understanding of the requirements of the Code by those involved.

PharmaMar stated that it did not deliberately intend to breach the Code but accepted that the content of a publication for which it was responsible promoted one of its medicines for an unlicensed indication, and was disguised in that regard. With this in mind, PharmaMar acknowledged breaches of Clauses 3.2, 12.1, 9.1 and 2 and apologised unreservedly.

PharmaMar stated that it was unfortunate that its senior executive appeared to have acted in good faith but was badly advised on this approach by a less senior colleague and that no-one involved with the publication (including the experienced medical writer) recognised the inappropriate nature of the activity, despite their senior positions and industry experience.

PharmaMar stated that the email in which it was stated 'It is compliant as long as the PMCPA and Madrid are not aware of it', provided by the complainant, could not be located on any of its servers and thus its origin and authenticity was not clear. The attributed author categorically denied that he/she had ever stated, either verbally or in writing, that the report was 'compliant as long as the PMCPA and Madrid are not aware of it'.

b) Review and Certification

In order to describe the process of review and approval of promotional and non-promotional materials, PharmaMar provided some background and important dates including:

- September 2015: PharmaMar Ltd UK affiliate was formally established and the two employees at issue (and others) were transferred to PharmaMar Ltd UK. A third party was retained to provide external medical review of material
- April 2016: The company joined the ABPI
- August 2016: New UK Country Manager appointed
- September 2016: The contract with the external review agency was extended to include certification as well as review support.

PharmaMar provided a copy of its current Global standard operating procedure (SOP) on 'Drafting and approval of promotional materials for the EU and

Switzerland' which stated that the approval process might involve several different reviewers (Spain marketing, Spain regulatory, UK marketing and UK medical). The online approval system, CLEARANCE, stored a record of the PharmaMar UK approval of each item but not the comments made by the external review agency or the medical certification of each. Storage of the agency's comments and approval relied solely on emails between it and PharmaMar (specifically the two employees at issue).

PharmaMar submitted it was highly regrettable that an equivalent UK SOP on the approval of promotional and non-promotional activities and materials was not in place – it was being developed as a matter of urgency with implementation anticipated no later than 31 October. PharmaMar thus had no record of the requisite certificates having been signed to verify signatory confirmation of compliance with the Code for any of the items referred to by the complainant, nor did it have a record of the date of first use of each item.

PharmaMar acknowledged that it had failed to certify promotional items, in breach of Clause 14.1 due to failings in its certification process. It also acknowledged that this amounted to a failure to maintain high standards, in breach of Clause 9.1.

With respect to the allegation of 'unfair comparison vs Gem/Tax' (gemcitabine/docetaxel) in the ipad app (ref YON1215-924), the table in the ipad app compared various attributes such as recommendations from the National Institute for Health and Care Excellence (NICE) and European Society for Medical Oncology (ESMO) – this information was intended to be accurate but on further scrutiny of the guidelines, the information in the app was incomplete and therefore did not fully represent the evidence. Therefore PharmaMar accepted the comparison was unfair and in breach of Clause 7.2 in this regard.

With respect to the allegation that the claim 'Gem/Tax – Higher toxicity' on stand material could not be substantiated, although this information appeared to be from head-to-head data, this was not actually the case and therefore the misleading impression could not be substantiated. PharmaMar accepted a breach of Clause 7.4.

PharmaMar acknowledged that the lack of a robust process in relation to certification, which was essential for self-regulation, amounted to a breach of Clause 2 and it gave its assurance that it was addressing this failing as a matter of urgency.

Summary

In summary, PharmaMar stated that it took very seriously its commitment to adhere to the Code and appreciated that self-regulation was a privilege. In that vein, it would be immediately implementing corrective and preventative actions to avoid future breaches of the Code. This would include, *inter alia*, the following:

- PharmaMar Ltd UK would hire a head of medical affairs to act as final medical signatory. This individual would also have compliance responsibilities and oversight.
- UK-specific SOPs would be created to cover all activities and materials under the scope of the UK Code. These would be trained out to UK staff and implemented effectively.
- Code training had taken place in the past but PharmaMar would provide refresher training to all relevant staff on the requirements of the Code.
- Relationships with third party agencies would be reviewed to ensure due diligence at the outset, that they were trained and had sufficient experience and knowledge of the Code to continue to provide support.
- Certification systems and processes would be overhauled so that Clause 14 requirements around signatories, certificates and archival were met.
- Further action with employees would be considered if the above activities were insufficient.

PANEL RULING

The Panel noted that the complainant was anonymous and non-contactable. The Constitution and Procedure stated that anonymous complaints would be accepted, but that like all other complaints, the complainant had the burden of proving his/her complaint on the balance of probabilities. All complaints were judged on the evidence provided by the parties. The complainant could not be contacted for further information.

With regard to the Meetings Highlights document, the Panel noted that it was possible for a company to sponsor material, produced by a third party, which mentioned its own products, and not be liable under the Code for its contents, but only if, *inter alia*, there had been a strictly arm's length arrangement between the parties. In practical terms the arrangements must be such that there could be no possibility that the pharmaceutical company had been able to exert any influence or control over the final content of the material. Factors which might mean there had not been a strictly arm's length arrangement would include, but not be restricted to:

- Initiation of the material, or the concept for it, by the pharmaceutical company
- Influence from the pharmaceutical company on the content/balance/scope of the material
- Choice/or direct payment of the authors by the pharmaceutical company
- Influence from the pharmaceutical company on the list of persons to whom the material was sent.

The Panel noted the initial arrangements for the Meetings Highlights document. It did not considered that PharmaMar had sponsored that content. The company's initial involvement in making all the arrangements for production of the Meetings Highlight document was such that in the Panel's view the company was responsible for the content. It was not an arm's length arrangement. The Panel did not change its view based on the amendments to the arrangements made by the company such that PharmaMar gave the money to BSG so that it could deal with the medical writer etc after the document had been drafted and the company realised the difficulties with the references in the document to the unlicensed use of Yondelis.

The Meeting Highlights document had been used by the company for a promotional purpose.

The Panel considered that the Meeting Highlights document was the responsibility of PharmaMar and as it promoted a medicine for an unlicensed use, the Panel ruled a breach of Clause 3.2 of the Code as acknowledged by the company. The document was disguised promotion. The disguised nature was compounded by the inclusion of the disclaimer that 'This newsletter had been funded by an unrestricted educational grant provided by PharmaMar S.A. PharmaMar S.A. had not been involved in the production review or distribution of this material' which was not an accurate description of the role of the company. The Panel ruled a breach of Clause 12.1 of the Code as acknowledged by the company.

The Panel ruled that high standards had not been maintained in breach of Clause 9.1 of the Code as acknowledged by the company. Clause 2 was a sign of particular censure and was reserved for such use. The Panel considered that the circumstances brought discredit upon, and reduced confidence in, the pharmaceutical industry and a breach of Clause 2 was ruled as acknowledged by the company.

The Panel was extremely concerned that the changes to the Meeting Highlights document suggested by PharmaMar showed a very poor understanding of the Code. It was also concerned that the email, allegedly from a senior executive, showed a disregard for the Code. The Panel noted, however that the email could not be located on the company's server. PharmaMar submitted that thus its origin and authenticity were not clear. The employee categorically denied stating that '… it is compliant as long as the PMCPA and Madrid are not aware of it'.

The Panel noted that with regard to the ipad screenshots and the reference to the unfair comparison of 'Gem/Tax' (gemcitabine and docetaxel) and Yondelis, PharmaMar acknowledged that the information about NICE and ESMO was incomplete. The Panel therefore ruled a breach of Clause 7.2 in relation to the acknowledged misleading comparison.

The Panel also ruled a breach of Clause 7.4 with regard to a failure to substantiate a claim that Gem/Tax had a higher toxicity noting PharmaMar's submission that the data appeared to be from a head-to-head study and this was not so.

The Panel was concerned about PharmaMar's arrangements for certification. There was no SOP and there were no records of the certificates for the items listed by the complainant. The company could not demonstrate their date of first use or that the materials had been certified. The Panel therefore ruled a breach of Clause 14.1 in relation to the promotional items as acknowledged by the company. The Panel noted that the case preparation manager had not cited any other sub-clause in relation to these allegations. There was no certification record for patient materials as required by Clause 14.2 and Clause 14.6 set out the requirements for preserving certificates and other documentation.

The Panel considered that high standards had not been maintained with regard to the arrangements for certification at PharmaMar and it thus ruled a breach of Clause 9.1 of the Code as acknowledged by the company. The Panel considered that the circumstances brought discredit upon, and reduced confidence in, the pharmaceutical industry and therefore ruled a breach of Clause 2 of the Code.

The Panel was extremely concerned about the conduct of senior employees and the lack of procedures for certification which it considered warranted consideration by the Code of Practice Appeal Board. The Panel therefore decided, in accordance with Paragraph 8.2 of the Constitution and Procedure, to report PharmaMar to the Appeal Board.

The Panel also decided that in accordance with Paragraph 7.1 of the Constitution and Procedure PharmaMar should suspend use of the Meeting Highlights document pending the final outcome of the case.

COMMENTS FROM PHARMAMAR ON THE REPORT FROM THE PANEL

At the consideration of the report the representatives from PharmaMar stated that the company had accepted the Panel's rulings of breaches of the Code and it sincerely apologised for the failings in this case. The company intended to do whatever was necessary to ensure that this issue was not repeated. In that regard the company had invested in third party Code expertise that had detected gaps in its processes and its priority was to address these issues. The company was also employing the services of a third party signatory and it was in the process of hiring a permanent head of medical affairs. All previous promotional material had been withdrawn and a review process of compliance was ongoing.

APPEAL BOARD CONSIDERATION OF THE REPORT FROM THE PANEL

The Appeal Board noted the Panel's comments and rulings above including the ruling of a breach of Clause 2 which PharmaMar had accepted. The Appeal Board also noted that PharmaMar apologised for its failings in this case.

The Appeal Board considered that this case raised serious concerns about PharmaMar's processes and Code knowledge. The Appeal Board queried how such a fundamental failure of compliance on what should be well understood principles of the Code could occur. The Appeal Board considered that PharmaMar's investigation into this issue was wholly inadequate.

The Appeal Board noted that in response to questioning PharmaMar stated that its investigation into this case had comprised an IT investigation run by human resources, which found no record of two of the emails provided by the complainant dated 9 March. These comprised an email to a senior executive that stated '…I have to inform you that

the newsletter as it is will not be compliant'; and the reply that stated 'It is compliant as long as the PMCPA and Madrid are not aware of it'. PharmaMar had provided no documentary evidence to verify its IT investigations. The Appeal Board noted the submission of the company representatives about the veracity of the emails at the hearing which included matters of style, format and the whereabouts of the senior executive on 9 March. The company confirmed that the preceding email sent to the senior executive on 8 March was genuine. The email stated 'From a Code Compliance point of view this will be considered promotional as it mentions trabectedin. This will mean it will require Prescribing Information and the neo adjuvant part has to be taken out as it is off label'. The sender then asked to be provided with details of the arrangements with two named individuals to see if he could come up with an alternative solution and finished '… call me if you need more clarification'. The Appeal Board considered that contrary to the inferences of the company representatives, this email appeared to give the correct initial advice and yet in response to questioning the PharmaMar representatives stated that that they did not know and had not investigated what response the senior executive had given to this email. At the hearing in response to questioning the senior executive stated that he/she did not know how he/she had responded to the email.

The Appeal Board noted that the PharmaMar representatives submitted that the company had also taken advice on this issue from its external review agency yet again it provided no documentary evidence to support this.

It was wholly unclear why the HR investigation had focussed on the narrow point about the veracity of the two emails rather than giving any consideration to the broader and significant compliance issues pertaining to the newsletter. It was inexplicable that those matters had not been addressed and the Appeal Board queried whether the company truly understood the gravity of the situation including the importance of self-regulation.

The Appeal Board noted that the company had provided no record that the member of staff had provided the advice that the company stated it had subsequently followed and that had led to the failings and breaches of the Code. The Appeal Board noted that in response to questioning PharmaMar stated that the senior executive and his/her predecessor had delegated responsibility under the Code to this staff member and the company had subsequently discovered that this member of staff was not a registered signatory. When asked what Code training the company had given the member of staff the company's answers were unsatisfactory and vague. The Appeal Board noted that it appeared that the review process was not carried out correctly and in this regard it noted the person's credentials. The Appeal Board noted that the company's external agency had provided external medical review and in that regard the Code only required one signatory. The company's online approval system did not keep a record of medical certification. The Appeal Board noted that PharmaMar had acknowledged that it had failed to certify promotional items. The Appeal Board noted the company's submission that all materials were withdrawn and subject to recertification. The Appeal Board considered that it was shocking that PharmaMar had chosen to delegate responsibility for compliance with the Code without confirming the credentials and knowledge of the individual concerned. The Appeal Board was concerned with the company's lack of process around certification. The Appeal Board considered that the certification process, correctly implemented, underpinned self-regulation. It appeared that there were serious issues regarding PharmaMar's arrangements. The Appeal Board considered that the level of Code expertise within the company appeared to be very poor given the fundamental errors and the company's apparent lack of preparation for the report.

The Appeal Board noted the circumstances that gave rise to this case and the company's poor approach to compliance as set out in the Panel's ruling. The Appeal Board noted that PharmaMar had now commissioned a gap analysis to identify, and thereafter start to address, compliance failings.

The Appeal Board decided that in accordance with Paragraph 11.3 of the Constitution and Procedure, PharmaMar should be publicly reprimanded for failing to make any meaningful effort to undertake a thorough investigation and to provide evidence to support its position. There were significant omissions in its documentation and the company was unable to provide adequate responses to the Appeal Board questions. Such an approach raised grave concerns about the importance attached to compliance and self-regulation by the company. The Appeal Board also decided to require an audit of PharmaMar's procedures in relation to the Code. The audit would take place as early as practicable in early 2018 and on receipt of the report, the Appeal Board would consider whether further sanctions were necessary.

The Appeal Board also decided to require PharmaMar to issue a corrective statement to all attendees to the BSG conference and its organisers. [The corrective statement, which was agreed by the Appeal Board prior to use, appears at the end of this report].

APPEAL BOARD FURTHER CONSIDERATION

On receipt of the report for the February 2018 audit the Appeal Board noted the poor internal communication at PharmaMar UK and with its Spanish head office. The Appeal Board considered that PharmaMar in the UK had a very limited compliance structure, compliance expertise and Code knowledge. Leadership on compliance needed to urgently improve. The company lacked many of the basic systems that a company required. It was essential that all staff took an active role in compliance.

The Appeal Board noted that the report of the audit highlighted many issues and concerns to be addressed including certification, attention to detail, updating and introduction of standard operating procedures (SOPs) and training. Significant and

sustained commitment by all staff was required to address these issues. On receipt of further information in May and June 2018 the Appeal Board decided that PharmaMar should be re-audited in October 2018. On receipt of the report for the re-audit the Appeal Board would decide whether further sanctions were necessary.

FURTHER CONSIDERATION OF THE APPEAL BOARD

PharmaMar Spain notified the PMCPA that as of 1 July 2018 the promotional and commercial activities of PharmaMar UK would stop. PharmaMar stated it would leave membership of the ABPI but remain a member of EFPIA.

On receipt of this further information at its meeting in July 2018 the Appeal Board noted that as a member of EFPIA, PharmaMar would need to comply with the ABPI Code. The Appeal Board requested further information.

On receipt of further information in September 2018 the Appeal Board considered that the PMCPA should make arrangements to re-audit PharmaMar's policies and procedures for how it was running its arrangements in the UK to ensure that PharmaMar was fulfilling its responsibilities under the ABPI Code. The Appeal Board considered that the re-audit should still go ahead as soon as was practical.

On receipt of further information in October 2018 the Appeal Board noted PharmaMar's response with regard to the Appeal Board's decision that the re-audit of PharmaMar planned for October 2018 should still go ahead at a suitable date in November despite the closing down of Pharma Mar Ltd operations in the UK as of 31 July 2018 and its UK office as of 30 August 2018. The position had changed again. PharmaMar noted that it had now entered into an agreement with Impilo Pharma AB (Medical Need Europe) appointing it as exclusive distributors of Yondelis in a number of territories. The agreement became effective for the UK, on 1 September 2018. The agreement included promotional and medical affairs activities in the UK.

The Appeal Board considered that as PharmaMar still held an interest in that it remained the licence holder for Yondelis the re-audit should still go ahead. The re-audit needed to assess how PharmaMar was administering its arrangement with Impilo as to how Yondelis was being marketed in the UK in accordance with the Code. The Appeal Board considered that the re-audit should go ahead as soon as was practical. The Appeal Board noted that the PMCPA would need to see relevant Impilo staff as part of the re-audit.

On receipt of the report for the January 2019 re-audit of PharmaMar and Immedica (previously Impilo) in April 2019 PharmaMar SA stated that if and when commercial or medical involvement of UK health professionals was needed, such as speaking at international congresses PharmaMar SA would contact Immedica.

In its comments Immedica UK addressed each of the recommendations.

The Appeal Board noted from the report of the re-audits that most of the PharmaMar SA staff interviewed considered that the first audit had led to global improvements in culture and processes and they viewed the audit process as an opportunity to improve and change. Staff appeared to show an increased understanding of the importance of compliance.

The Appeal Board noted from the report of the re-audits that Impilo Pharma AB as Medical Need and now Immedica, acquired from PharmaMar SA the rights to market and distribute Yondelis in a number of territories including the UK. Immedica UK was a very new small UK company. The Appeal Board noted that the circumstances were unusual in that Immedica UK had not been ruled in breach of the Code. Those interviewed at Immedica UK acknowledged the importance of compliance and the need to ensure that Immedica UK established a robust compliance infrastructure.

The Appeal Board noted from the report of the re-audits that it appeared from those interviewed that PharmaMar understood that any future relationships with UK health professionals would be via Immedica headquarters in Sweden and Immedica UK. The Appeal Board considered each company separately. It considered that each company should implement the re-audit reports recommendations.

On receipt of further information regarding implementation of recommendations in September 2019 the Appeal Board decided that no further action was required.

Complaint received	**21 September 2017**
Undertaking received	**27 November 2017**
Appeal Board consideration	**7 December 2017, 18 April, 17 May and 20 June, 19 July, 13 September, 17 October 2018, 10 April, 18 September 2019**
Interim case report first published	**9 April 2018**
Case completed	**18 September 2019**

On 9 April 2018, BSG sent the following corrective statement on behalf of PharmaMar to all attendees to the BSG conference and its organisers.

> 'Corrective statement
>
> Between March and October 2017, the 'British Sarcoma Group 13th Annual Conference, 1st - 2nd March 2017 – Meeting Highlights' newsletter was available. The newsletter mentioned Yondelis (trabectedin) which was marketed by PharmaMar Ltd.
>
> You are being sent this corrective statement because you received or might have received the newsletter.
>
> Following a complaint under the ABPI Code of Practice for the Pharmaceutical Industry, the Code of Practice Panel considered that the newsletter was the responsibility of PharmaMar and it promoted its medicine for an unlicensed use. The document was also disguised promotion and the disguised nature was compounded by the inclusion of the disclaimer that 'This newsletter had been funded by an unrestricted educational grant provided by PharmaMar S.A. PharmaMar S.A. had not been involved in the production review or distribution of this material' which was not an accurate description of the role of the company
>
> The Code of Practice Panel ruled that PharmaMar had failed to maintain high standards and had brought discredit upon and reduced confidence in the pharmaceutical industry. As a result of the above governance concerns, the Panel reported PharmaMar to the Code of Practice Appeal Board which required PharmaMar to issue this corrective statement and to circulate a copy of the published report for the case which contains full details. This is enclosed.

Details of this case (Case AUTH/2979/9/17) are also available on the PMCPA website (www.pmcpa.org.uk).'