CASE AUTH/2694/1/14

ANONYMOUS v PHARMACOSMOS

Promotion of Monofer

An anonymous contactable complainant complained about the advertising of Monofer (iron (III) isomaltoside 1000), by Pharmacosmos UK on two of its linked websites.

The complainant explained that when using the Pharmacosmos website to review two intravenous (IV) iron products he/she noted that the triangle denoting additional monitoring was blue rather than black. The complainant followed the link from the Pharmacosmos website to www.monofer.com. The complainant stated that although it was described as an international site it was linked from the UK website and had a black triangle which indicated that the site was aimed at the UK. Although browsers had to state that they were a health professional, the website stated that 'This medical website focuses on Monofer (iron isomaltoside 1000), a treatment for iron deficiency anemia'. Most other sites did not specify the medicines' uses before visitors had indicated whether they were health professionals. The complainant submitted that a lot of the health professional site was visible behind the initial box and could easily be seen by the general public. The complainant alleged that the summary of product characteristics (SPC) on the website was out of date and alleged that if it was used patients could potentially be discharged without monitoring for 30 minutes and the medicine could be used in contraindicated patients. The Monofer website described the iron matrix technology as new which was not so; Monofer had been available for several years.

The detailed response from Pharmacosmos is given below.

The Panel noted that the Code stated that when required by the licensing authority, all promotional material must show an inverted black triangle to denote that special reporting was required in relation to adverse reactions. The Panel noted Pharmacosmos' submission that the publicly visible UK corporate website was non-promotional in nature. It also considered that Pharmacosmos had changed the relevant part of the website so that the triangle was now black. The Panel noted that the Code only required a black triangle to be included on promotional material and considered that the complainant had not proved his/her complaint on the balance of probabilities that the website was promotional and thus no breach of the Code was ruled.

The Panel noted that the www.monofer.com website was described by Pharmacosmos UK as the international website, however the SPC page appeared to feature the UK prescribing information as the NHS cost was given in £ sterling. This page also referred to www.mhra.gov.uk/yellowcard for reporting side effects in the UK. The prescribing information and monitoring details were not provided for any other country. The Panel noted that the website specifically referred to the availability or use of Monofer in the UK which was one of the factors listed in the Code as bringing such material placed on the internet by a UK company or its affiliate within the scope of the Code. In addition the site was linked from the Pharmacosmos UK website. The Panel considered that although the website stated that 'Monofer.com is a resource for healthcare professionals outside US only. The information on this site is not country-specific and may contain product information otherwise not accessible or valid in your country', the emphasis on the UK was such that on balance the UK Code applied.

The Panel noted that when entering the www.monofer.com site, a pop-up window appeared which stated 'Welcome to Pharmacosmos' international Monofer website. This medical website focuses om [sic] Monofer (iron isomaltoside 1000), a treatment for iron deficiency anemia'. The health professional site was visible behind the pop-up window. The Panel noted from the screenshot that the phrases: 'High dose Infusi', 'up to 20', and 'High dose iron' were visible and part of the letters that formed the words 'in just one visit' were visible on a photograph showing a hand holding a vial of Monofer. Overall, the Panel considered that the claim 'High dose iron in just one visit' was readable. The next question to consider was whether the visible claims promoted Monofer or whether the page at issue was in line with the Code.

The Panel noted Pharmacosmos' submission that readers accessed the site because they were already seeking information regarding Monofer. The Panel noted that members of the public would be able to access the Monofer SPC on the eMC which would include the product's indication. The Code made it clear that a number of materials including the SPC could be made available as a resource for the public/patients. The Panel considered that the pop-up window in combination with promotional claims for Monofer intended for health professionals which were visible to members of the public meant that a prescription only medicine had been promoted to the public who would also be encouraged to ask their health professionals to prescribe it and breaches of the Code were ruled. The Panel considered that high standards had not been maintained. A breach of the Code was ruled.

The complainant alleged that the Monofer SPC on the website was out of date. The Panel noted Pharmacosmos' submission that after the European Medicines Agency had reviewed all IV iron products in September 2013, an update of all the SPCs was

recommended. The Panel noted Pharmacosmos' submission that the updated Monofer SPC was currently under review by the regulatory authorities and, as yet, no formal changes had been approved. Pharmacosmos also submitted that the SPC on Monofer.com was the current version. The Panel did not consider that the complainant had established that the Monofer SPC on the website was out of date. Thus the Panel ruled no breaches of the Code including no breach of Clause 2.

The Panel noted Pharmacosmos' submission that that the word 'new' should no longer have appeared as Monofer had been available for several years. A breach of the Code was ruled as acknowledged by the company.

Prior to being advised of the Panel's rulings, Pharmacosmos indicated that it no longer wished to accept the jurisdiction of the Authority and did not complete and return the form of undertaking and assurance. The Authority was bound by Paragraph 11.4 of the Constitution and Procedure to report the company to the Code of Practice Appeal Board.

In relation to the report from the Authority the Appeal Board noted that Pharmacosmos A/S had previously agreed to abide by the Code as a non member company. The complaint in this case was the first one which involved Pharmacosmos UK so that company had been invited to join the list of non member companies that agreed to comply with the Code and accept the jurisdiction of the PMCPA.

The Appeal Board noted the reasons given by Pharmacosmos for its decision not to join the list of non member companies that had agreed to comply with the Code and accept the jurisdiction of the PMCPA.

The Appeal Board noted Pharmacosmos' submission that it had changed the material at issue. However, the Appeal Board noted that by failing to provide the requisite undertaking and assurance Pharmacosmos had failed to comply with the procedure set out in Paragraph 7 of the Constitution and Procedure and thus the Appeal Board decided, in accordance with Paragraph 11.4 of the Constitution and Procedure, to remove Pharmacosmos from the list of non member companies which had agreed to comply with the Code*. Responsibility for Pharmacosmos under the Code could no longer be accepted. The Medicines and Healthcare Products Regulatory Agency (MHRA) and the ABPI Board of Management were subsequently advised of the Appeal Board's decision.

****Pharmacosmos UK submitted that it could not be removed from the non-members list as it had never formally agreed to join it. Pharmacosmos A/S and Pharmacosmos UK had, however, between 2010 and April 2014, each demonstrated their willingness to voluntarily comply with the Code and accept the jurisdiction of the Authority both in terms of complaints received and complaints submitted and in that regard both appeared to consider themselves effectively, if not formally, on the non members list.***

An anonymous, contactable complainant complained about the advertising of Monofer (iron (III) isomaltoside 1000), by Pharmacosmos UK Ltd on its website (www.pharmacosmos.co.uk).

Monofer was indicated for the treatment of iron deficiency anaemia when oral iron preparations were ineffective or could not be used and where there was a clinical need to deliver iron rapidly

COMPLAINT

The complainant referred to two linked websites. The complainant explained that he/she used www.pharmacosmos.co.uk to review Pharmacosmos' two intravenous (IV) iron products. The complainant assumed that black triangles needed to be black and noted that the one here was blue. The complainant followed the link from the Pharmacosmos website to the www.monofer.com site. The complainant stated that he/she had previously visited this site and although it described itself as an international site it was linked from the UK website so appeared to be intended for his/her viewing. The complainant noted that Monofer had a black triangle and had had this for some time prior to all IV irons requiring one in Europe which indicated that the site was aimed at the UK. Although browsers had to state that they were a health professional, the website stated that 'This medical website focuses on Monofer (iron isomaltoside 1000), a treatment for iron deficiency anemia'. Most other sites the complainant had used did not specify the medicines' uses before visitors had indicated whether they were health professionals. The complainant submitted that a lot of the health professional site was visible behind the initial box, something that could easily be seen by the general public. The complainant was most concerned that the summary of product characteristics (SPC) on the website was out of date which was concerning as the European Medicines Agency (EMA) / Medicines Healthcare Products Regulatory Agency (MHRA) had raised concerns over IV irons safety last year. The complainant alleged that if this SPC was used patients would potentially be discharged without monitoring for 30 minutes and Monofer could be used in contraindicated patients. The Monofer website described the iron matrix technology as new which was not so; Monofer had been available for several years.

When writing to Pharmacosmos, the Authority asked it to respond in relation to Clauses 2, 4.11, 7.2, 7.11, 9.1, 23.1 and 23.2 of the Code. It appeared that the case preparation manager was referring to the 2014 Code.

RESPONSE

Pharmacosmos submitted that it was fully committed to compliance with the Code and welcomed the opportunity to comment on the concerns raised by the complainant. As part of its investigation, it undertook a thorough review of the Pharmacosmos websites. Pharmacosmos addressed each point in turn.

Pharmacosmos submitted that www.pharmacosmos.co.uk was the publicly visible UK corporate

website. It was non-promotional and intended as a public 'face' for the company in the manner of a typical company website. The site included a link to a section which listed the products that Pharmacosmos made available in the UK.

Within this section, the company decided to include the black triangle symbol even though there was no requirement under the Code for it to do so. The website was non-promotional in nature and acted as a window to the corporate aspects of its business, including providing contact information.

As the complainant correctly highlighted, the standard colour for the black triangle should, indeed be black. The text used in this area of the website was a very dark blue. This was an oversight; Pharmacosmos was grateful to the complainant for pointing this out and it had changed the colour of the triangle to black.

However, Pharmacosmos denied a breach of Clause 4.11 as that aspect of the Code related specifically to the presence of the triangle on promotional material. The section of the website referred to by the complainant was not promotional (by virtue of the fact it was intended for public viewing) and therefore the colour of the triangle was not subject to the specific clause. While Pharmacosmos recognized that it was a fine point, it was, nevertheless an important distinction.

As stated in the complainant's letter, www.monofer.com could be accessed via a link from the pharmacosmos.co.uk site. Pharmacosmos submitted that it could be seen from a screenshot provided that the source page on pharmcosmos.co.uk clearly indicated that the products were for health professionals. A link allowed the reader to visit monofer.com. Access was also provided to the eMC website.

On first reaching monofer.com, the reader was presented with a pop-up window that asked the reader to click to indicate the most relevant area of the site for them: health professional or public. This pop-up window to Monofer.com as stated by the complainant included the indication for Monofer. The intention of this pop-up was to explain briefly the purpose of the site so that the user could select the most appropriate route of entry (health professional/public).

Pharmacosmos submitted that it was appropriate for readers to understand the purpose of the site before they selected a route of entry so they could be sure what the correct action was for them to take. This was an informative message presented in response to the user accessing a medicine-specific website. Pharmacosmos was not aware of any ban on stating the indication, *per se*, in this context and accordingly denied a breach of Clauses 23.1 and 23.2.

Pharmacosmos reviewed the pop-up window again in light of the complainant's comments. The window background was transparent. Pharmacosmos agreed that some of the background screen was therefore visible, albeit much less prominently than the pop-up itself, as could be seen from the screen shot provided.

Pharmacosmos submitted that it had already taken steps to amend the construct of the website such that users now entered a totally separate landing page before being redirected to the appropriate area of the website. A copy of the revised screenshot was provided.

Pharmacosmos provided a screenshot that accurately showed the visible text and submitted that complete phrases were *not* visible.

Specifically the phrases: 'High dose Infusi' 'up to 20', and 'High dose iron' and the top third of the letters that formed the words 'in just one visit ' were readable on a photograph showing a hand holding a vial of Monofer.

Whilst there was no intention to advertise medicines to the public, Pharmacosmos accepted that these statements and the photograph together could be regarded as communicating limited product information to the public.

However, Pharmacosmos did not consider that the visible wording (primarily 'high dose iron') constituted any form of benefit that would be relevant to the patient. It merely reflected the actual licensed indication. As such Pharmacosmos did not consider this should constitute advertising to the public and denied a breach of Clauses 23.1 and 23.2.

Pharmacosmos asked the PMCPA to bear in mind that readers accessed the site because they were already seeking information regarding Monofer. In that respect, there was no intention that the visible statements should encourage members of the public to ask their health professional to prescribe Monofer. The visible information was factual and presented in a balanced way; it needed to be in order to comply with the health professional aspects of the Code. It was not misleading regarding safety as no safety claims were made. The statements did not raise unfounded hopes of successful treatment, not least because the only visible statements were in respect of dosage (high dose), not outcome. The other statement that was not fully readable concerned convenience (one visit) but the average reader would have to study the text to even work out what the phrase was because approximately only the top third of the letters in the words were visible.

Clause 9.1 related to the maintenance of high standards. Pharmacosmos acknowledged that some aspects of the site were visible behind the pop-up, however there was clearly no intention to promote; the pop-up box was designed to direct readers to the appropriate area of the website. On selecting 'patient or relative', readers were shown the non-promotional area of the website that had been specifically designed for access by the public. The monofer.com link was accessible from the product page on the corporate website; this page clearly indicated that the products were for use by health professionals and readers were required to confirm their status as a health professional before they directly accessed the health professional area of the site.

Pharmacosmos had already taken steps to amend the construct of the website such that the user now

entered a totally separate landing page before being redirected to the appropriate area of the website.

Whilst one promotional area of the health professional text was indeed visible, there was no visibility of a complete claim. The average reader was unlikely to even take notice of the background as the focus would be on the pop-up, which automatically appeared. Pharmacosmos did not consider that this constituted a failure to maintain high standards as alleged.

Pharmacosmos submitted that it acted quickly to address the concerns raised and wished to reassure the PMCPA of its best intentions in this and all matters of compliance. Pharmacosmos had immediately undertaken discussions with its international business and the website was corrected immediately. Accordingly, it denied a breach of Clause 9.1.

Pharmacosmos submitted that the SPC as listed on the website was correct and current.

After a review of all intravenous (IV) iron products in Europe by the EMA in Septemebr 2013, an update of the SPC for all IV irons was recommended. Many of the intended changes to the SPC had been the subject of public discussions. The update of the Monofer SPC was currently under review by the regulatory authorities and, as yet, no formal changes had been approved. Therefore the SPC displayed on Monofer.com was the correct version. When it was approved, the SPC on the website would be changed.

Accordingly Pharmacosmos denied breaches of Clauses 7.2, 9.1 and 2.

Having reviewed the page identified by the complaint and the entire Monofer.com website, Pharmacosmos was able to find only a single use of the word 'new' at the very foot of the page:

> 'Based on Pharmacosmos' new iron Matrix technology, Monofer is the only treatment for iron deficiency anaemia that combines the advantages of 1) a dose range up to 20mg/kg with no upper dose limit, 2) a fast high dose iron correction in one visit, and 3) no test dose requirement'.

Pharmacosmos accepted that the word 'new' should no longer appear; it had been removed from the website, but accordingly, Pharmacosmos acknowledged a breach of Clause 7.11. A screenshot of the revised website was provided.

PANEL RULING

The Panel noted the clauses of the 2014 Code cited by the case preparation manager. The transition period for newly introduced requirements applied from 1 January 2014 until 30 April 2014. There had been no changes to Clauses 2, 4.11, 7.2 and 9.1. Clause 23.1 and 23.2 had been renumbered (previously Clauses 22.1 and Clause 23.2). Thus the Panel decided to use the 2014 edition as in relation to the complaint being considered; the relevant requirements were the same as in the Second 2012 Edition (as amended).

The Panel noted that Clause 4.11 of the Code stated that when required by the licensing authority, all promotional material must show an inverted black triangle to denote that special reporting was required in relation to adverse reactions. The Panel noted Pharmacosmos' submission that the website, www.pharmacosmos.co.uk, was the publicly visible UK corporate website and was non-promotional. It also considered that Pharmacosmos had changed the relevant part of the website so that the black triangle was now black. The Panel noted that Clause 4.11 only required a black triangle to be included on promotional material and considered that the complainant had not proved his/her complaint on the balance of probabilities that the website was promotional and thus no breach of Clause 4.11 of the Code was ruled. During its consideration of this matter, the Panel noted that the 2014 Code included new requirements about the use of the black triangle in materials for patients, Clause 23.3. It requested that this was drawn to the attention of Pharmacosmos.

The Panel noted that the website www.monofer.com was described by Pharmacosmos UK as the international Monofer website, however the SPC page appeared to feature the UK prescribing information as the NHS cost was given in £ sterling. This page also referred to www.mhra.gov.uk/yellowcard for how to report side effects in the UK. The prescribing information and monitoring details were not provided for any other country. The Panel noted that the website made specific reference to the availability or use of the medicine in the UK which was one of the factors listed in Clause 25.2 as bringing such material placed on the internet by a UK company or its affiliate within the scope of the Code. In addition the site was linked from the Pharmacosmos UK website. The Panel considered that although the website stated that 'Monofer.com is a resource for healthcare professionals outside US only. The information on this site is not country-specific and may contain product information otherwise not accessible or valid in your country', the emphasis on the UK was such that on balance the UK Code applied.

The Panel noted that Clause 23.1 prohibited the advertising of prescription only medicines to the public. Clause 23.2 permitted information to be supplied directly or indirectly to the public but such information had to be factual and presented in a balanced way. It must not raise unfounded hopes of successful treatment or be misleading with respect to the safety of the product. Statements must not be made for the purpose of encouraging members of the public to ask their doctor to prescribe a specific prescription only medicine.

The Panel noted that when entering the www.monofer.com site, a pop-up window appeared which stated 'Welcome to Pharmacosmos' international Monofer website. This medical website focuses om [sic] Monofer (iron isomaltoside 1000), a treatment for iron deficiency anemia'. The health professional site was visible behind the pop-up window. The Panel noted from the screenshot that the phrases: 'High dose Infusi', 'up to 20', and 'High dose iron' were entirely visible and part of the letters that formed the words 'in just one visit' were visible

on a photograph showing a hand holding a vial of Monofer. The Panel considered that even though only part of the letters that formed the words 'in just one visit' were visible, the claim 'High dose iron in just one visit' was readable. The next question for the Panel to consider was whether the visible claims were promotional for Monofer or whether the page at issue was in line with the requirements of Clause 23.2.

The Panel noted Pharmacosmos' submission that readers accessed the site because they were already seeking information about Monofer. The Panel noted that members of the public would be able to access the Monofer SPC on the eMC which would include the product's indication. The supplementary information to Clause 23.2 made it clear that a number of materials including the SPC could be made available as a resource for the public/patients. The Panel considered that the pop-up window in combination with promotional claims for Monofer intended for health professionals which were visible to members of the public meant that a prescription only medicine had been promoted to the public who would also be encouraged to ask their health professionals to prescribe it. Breaches of Clauses 23.1 and 23.2 were ruled. The Panel considered that high standards had not been maintained. A breach of Clause 9.1 was ruled.

The complainant alleged that the Monofer SPC on the website was out of date. The Panel noted Pharmacosmos' submission that after a review of all IV iron products in Europe by the EMA in September 2013, an update of the SPCs for all of these products was recommended. The Panel noted Pharmacosmos' submission that the update of the Monofer SPC was currently under review by the regulatory authorities and, as yet, no formal changes had been approved. Pharmacosmos also submitted that the SPC on Monofer.com was the correct and current version. The Panel did not consider that the complainant had established that the Monofer SPC on the website was out of date. Thus the Panel ruled no breach of Clause 7.2 and consequently ruled no breach of Clauses 9.1 and 2.

The Panel noted that Clause 7.11 stated that the word 'new' must not be used to describe any product or presentation which has been generally available, or any therapeutic indication which has been generally promoted, for more than twelve months in the UK. The Panel noted Pharmacosmos' submission that that the word 'new' should no longer have appeared when referring to Monofer's iron matrix technology. Monofer had been available for several years. A breach of Clause 7.11 was ruled as acknowledged by the company. The website had been updated in this regard.

COMMENTS FROM PHARMACOSMOS

At the same time as it was advised of the complaint, Pharmacosmos UK was invited to join the PMCPA list of non-member companies which had agreed to comply with the Code. In response, and before it was advised of the Panel's rulings above, Pharmacosmos submitted that it had given this invitation serious consideration and it was fully committed to ethical promotion of its products; however, it found the current approach to dealing with complaints within the PMCPA Constitution and Procedure increasingly challenging to manage. As a result, it declined the offer to join the PMCPA list of non-member companies.

Pharmacosmos submitted that there were a number of reasons for this decision and it highlighted a couple. Pharmacosmos found anonymous complaints highly problematic, it had over the last year or so, received a number of anonymous complaints. These complaints had clearly been submitted by individuals with an intimate knowledge of the Code and the IV iron market. One of Pharmacosmos' competitors, Takeda, had also received an anonymous complaint recently.

Pharmacosmos submitted that processing such cases to provide an adequate response for the PMCPA was very time consuming. By submitting the complaint anonymously the complainant bypassed inter-company dialogue and had no risk of penal fees for unsubstantiated complaints, mechanisms that would normally serve to keep the number of PMCPA cases to a relevant minimum.

In addition, Pharmacosmos found it highly problematic that the PMCPA made rulings concerning products without consulting the relevant marketing authorisation holders to ensure the correctness of the information provided by the different parties.

Pharmacosmos submitted that the recently published case, Case AUTH/2623/7/13 Anonymous v Takeda, contained several incorrect statements on its product Monofer made by the anonymous complainant, Takeda, and the Panel.

Pharmacosmos considered this was another example of how a complainant was abusing the Panel and the Code to influence market perception incorrectly – this time with regard to stipulating incorrect dosing limitations on the use of Monofer in haemodialysis patients (albeit not in a complaint about Pharmacosmos itself).

Given these numerous examples of misuse of the self-regulatory system and after careful consideration, Pharmacosmos had decided not to join the list of non-member companies neither as Pharmacosmos A/S or Pharmacosmos UK. Pharmacosmos stated that it had been involved in a number of inter-company complaints via the PMCPA over the last four years. The clear majority of rulings had been in favour of Pharmacosmos which showed its commitment to ethical promotion of its products in the past. Although Pharmacosmos' association with the PMCPA was now ended, it welcomed the constructive nature of its historical interactions. Pharmacosmos stated that it would continue to be fully committed to the ethical promotion of its products moving forward.

Pharmacosmos advised that it had already changed the material at issue. It referred to the letter it had sent to the PMCPA before it received the Panel's decision.

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The Authority noted that Pharmacosmos no longer wished to accept the jurisdiction of the Authority and did not complete and return the form of undertaking and assurance. The Authority was bound by Paragraph 11.4 of the Constitution and Procedure to report the company to the Code of Practice Appeal Board.

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COMMENTS FROM PHARMACOSMOS ON THE REPORT

Pharmacosmos did not attend the Appeal Board meeting for the consideration of the report and had no further comments on the case.

APPEAL BOARD CONSIDERATION OF THE REPORT FROM THE AUTHORITY

The Appeal Board noted that Pharmacosmos A/S had previously agreed to abide by the Code as a non member company. The complaint in this case was the first one which involved Pharmacosmos UK so that company had been invited to join the list of non member companies that agreed to comply with the Code and accept the jurisdiction of the PMCPA.

The Appeal Board noted the reasons given by Pharmacosmos for its decision not to join the list of non member companies that had agreed to comply with the Code and accept the jurisdiction of the PMCPA, in particular its views about anonymous complaints. The Appeal Board noted that the PMCPA had always dealt with anonymous complaints, regardless of whether the complainant was contactable or not, and although it was preferable that complainants were not anonymous consideration of such complaints by the PMCPA was an important element of robust self regulation.

The Appeal Board noted Pharmacosmos' submission that it had changed the material at issue. However, the Appeal Board noted that by failing to provide the requisite undertaking and assurance Pharmacosmos had failed to comply with the procedure set out in Paragraph 7 of the Constitution and Procedure and thus the Appeal Board decided, in accordance with Paragraph 11.4 of the Constitution and Procedure, to remove Pharmacosmos from the list of non member companies which had agreed to comply with the Code*. Responsibility for Pharmacosmos under the Code could no longer be accepted. The Medicines and Healthcare Products Regulatory Agency (MHRA) and the ABPI Board of Management were subsequently advised of the Appeal Board's decision.

Pharmacosmos UK submitted that it could not be removed from the non-members list as it had never formally agreed to join it. Pharmacosmos A/S and Pharmacosmos UK had, however, between 2010 and April 2014, each demonstrated their willingness to voluntarily comply with the Code and accept the jurisdiction of the Authority both in terms of complaints received and complaints submitted and in that regard both appeared to consider themselves effectively, if not formally, on the non members list.

Complaint received	**16 January 2014**
Report to Appeal Board	**24 July 2014**
MHRA informed	**24 June 2014 and 4 August 2014**
ABPI Board informed	**4 August 2014**