PHARMACOSMOS v VIFOR

Competitor dosing information

Pharmacosmos explained that it and Vifor differed in their interpretation of the dosing information given in the Monofer (iron isomaltoside, marketed by Pharmacosmos) summary of product characteristics (SPC). Monofer was for the parenteral treatment of iron deficiency anaemia; Vifor marketed a competitor product. Pharmacosmos alleged that Vifor representatives had told health professionals that a total dose infusion of Monofer was subject to a maximum total dose of 1,000mg which was not so. Pharmacosmos was concerned that training and briefing material encouraged the Vifor representatives to breach the Code in that regard.

The detailed response from Vifor is given below.

The Panel noted that, in support of its allegation, Pharmacosmos had reproduced part of an anonymised undated email from a health professional. It did not provide the original email. No other evidence was provided. The Panel noted that the complainant had to establish its case on the balance of probabilities.

The Panel noted that according to its SPC, Monofer could be administered as a total dose infusion given as a single dose of up to 20mg iron/kg body weight as an intravenous drip infusion. If the total iron dose exceeded 20mg iron/kg body weight, the dose must be split into two administrations with an interval of at least one week. No upper dose limit was explicitly stated.

The Panel noted Vifor's submission that it had not instructed its staff to discuss a maximum dose of Monofer. All materials that referred to Monofer dosing were withdrawn between October and December 2011. According to Vifor, discussions by its representatives on Monofer dosing were restricted to the Monofer SPC; in April 2012 representatives were advised by email to refer queries about Monofer dosing to Pharmacosmos or to the Monofer SPC. They were told that they must not offer any interpretation of the Monofer SPC or advice on dosing or administration of any competitor product. A slide for the May sales conference gave similar guidance. The Panel was concerned that given Vifor had stated its position during inter-company dialogue in December 2011, the earliest written guidance to its representatives was in April 2011, some 2 days before Pharmacosmos' complaint was received by the Authority. However, taking into account its concerns and comments above the Panel did not consider that Pharmacosmos had established that Vifor representatives had, on the balance of probabilities, commented on Monofer dosing as alleged or had been briefed to do so. No breach of the Code was ruled.

Pharmacosmos A/S complained about information given by Vifor Pharma UK Limited about the dosing of Pharmacosmos' product, Monofer (iron isomaltoside). Monofer was indicated for the treatment of iron deficiency anaemia when oral iron preparations were ineffective or could not be used or where there was a clinical need to deliver iron rapidly. Vifor marketed Ferinject (iron as ferric carboxymaltose) for the treatment of iron deficiency when oral preparations were ineffective or could not be used.

Inter-company dialogue had been unsuccessful.

COMPLAINT

Pharmacosmos stated that it and Vifor had different interpretations in respect of the dose of Monofer.

Pharmacosmos explained that Monofer could be administered as an intravenous bolus injection, a total dose infusion in which the total iron dose was given in a single administration or an intravenous infusion of a fixed 200-1000mg dose weekly until the total iron dose had been administered. The calculation of the correct dose was important for patient safety and the summary of product characteristics (SPC) identified a specific calculation. The dose required might determine the manner of administration:

Bolus injection
A 100mg-200mg slow injection given over a minimum of 2-4 minutes (up to 50mg/min), repeated up to three times a week.

Intravenous infusion of a 200-1,000mg fixed dose
This involved the product being given via an infusion (drip). The infusion time depended on the dose being administered and body weight. The dose per infusion was 200mg-1,000mg, repeated once a week until the total iron dose had been administered.

Total dose infusion (hospital only)
The entire required iron dose was given in one infusion up to 20mg/kg. If the required dose exceeded 20mg/kg the dose must be split in two infusions given at least one week apart. The infusion time depended on the dose being administered and body weight.

Pharmacosmos submitted that the description of Monofer dosing was also part of the Scottish Medicines Consortium evaluation of Monofer which was provided.

Pharmacosmos stated that at the heart of the matter was the dose that could be administered by total dose infusion. Vifor had alleged that this technique

was subject to a maximum total dose of 1,000mg. Pharmacosmos had assured Vifor that this was not so and that its reading of the SPC was incorrect. Despite this, Pharmacosmos submitted that it had anecdotal evidence that Vifor representatives continued to advise health professionals that total dose infusion was subject to a maximum dose of 1,000mg.

One email from a health professional stated:

> 'Vifor are saying that the SPC states that you can only give 1,000mg as a drip infusion which is the same thing as a total dose and the total dose states that the most you can is 20mg/per kg I just need this to be cleared up. What is the right answer a max of 1,000mg or is it 20mg/per kg'.

Pharmacosmos stated that it was not appropriate for competitors to communicate incorrect dosing information to health professionals in obvious and deliberate contradiction to what the manufacturers of that product had clearly stated was the correct interpretation of the licence.

Pharmacosmos requested in writing in November and 6 December 2011 clarification that Vifor's information to health professionals or its representative training did not include information about a dosing maximum of 1,000mg for Monofer when administered in a hospital setting.

Vifor acknowledged in December, that representatives would restrict discussions to the Monofer SPC. However, Pharmacosmos contended that this was an attempt to deflect its legitimate concerns – as Vifor had previously stated that its interpretation differed from that of Pharmacosmos, therefore Vifor had effectively stated that it would not change its position. As Vifor's interpretation of the licence differed from that of Pharmacosmos, Pharmacosmos considered that the information given to and by the Vifor representatives was incorrect and thus misleading.

In February, Pharmacosmos sought specific confirmation of the information given to Vifor employees in relation to the dose: 'Please clearly confirm that Vifor UK acknowledges the possibility to give Monofer in doses up to 20mg/kg without an absolute dose limit of 1,000mg or any other absolute dose limit. Please also confirm that you have instructed your sales force and other relevant staff accordingly'.

In its response in March Vifor repeated that it would restrict discussions to the Monofer SPC. The company did not respond specifically to the question raised about an absolute dose limit of 1,000mg. Pharmacosmos therefore considered that inter-company dialogue had not resolved this matter.

Specifically Pharmacosmos was concerned that training and briefing material provided by representatives had encouraged them to breach the Code, in breach of Clause 15.9. While Pharmacosmos did not have copies of the training material, the inter-company responses were such that it believed that Vifor had either communicated the incorrect dosing of Monofer to its representatives, or had failed to communicate the correct dose following written clarification from Pharmacosmos. To fail to provide the correct information would result in incorrect and therefore misleading information about a competitor product (Monofer).

Pharmacosmos stated that it was clearly concerned about the communication by [Vifor] representatives to health professionals. Pharmacosmos was reluctant to approach customers to ask them to get involved in an inter-company dispute. Hence it had restricted its comments on this occasion to the briefing material (or the failure to issue briefing material) by Vifor and the anonymised quotation from a physician's email to its UK medical information service.

While it understood that its interpretation of the licence differed from Vifor's, Pharmacosmos could not allow Vifor to provide prescribers with incorrect information about Pharmacosmos products. As the licence holder, Pharmacosmos was responsible for ensuring that health professionals appreciated the correct dose of its products. When other companies communicated a different position this caused confusion and therefore risked patient safety and good medical practice.

RESPONSE

Vifor submitted that it took all matters related to the Code very seriously. It recognised that it and Pharmacosmos had a difference of opinion regarding the Monofer dosing wording contained within the current SPC and as such Vifor had requested clarity from Pharmacosmos. The information provided by Pharmacosmos did not clarify the position. Discussions about gaining clarity were contained within inter-company dialogue and thus did not transfer to any briefings to representatives or within material.

In the absence of clarification from Pharmacosmos, Vifor had not briefed or trained staff to discuss a maximum dose of Monofer. To avoid confusing health professionals Vifor restricted any discussions on Monofer dosing to the product's SPC as stated in letters sent to Pharmacosmos in December 2011 and March 2012 and thus considered that inter-company dialogue had been successful.

Vifor recognised that the briefing of staff could have occurred in January 2012, however all promotional material that referred to Monofer dosing was withdrawn from use during October and December 2011. Vifor stated that current materials did not refer to Monofer dosing and staff were instructed to directly refer any questions about Monofer dosing to the product SPC or to the Pharmacosmos medical information department.

Vifor submitted that the sales force had been briefed by email in April 2012 and instruction had been

incorporated into the company initial training course. The same direction was further emphasised at the sales conference in May 2012; the relevant slide was provided.

Pharmacosmos referred to an email from a health professional requesting clarity on the dosing regimen for Monofer after a statement that Vifor had referred to the product SPC. Vifor could not verify or investigate this as no details of date or location were provided or any indication that this was given verbally or in writing to the health professional. Vifor therefore submitted that the use of such anecdotal reference was inappropriate particularly when followed with the allegation that Vifor had communicated incorrect dosing information to customers when this was neither substantiated nor verified. All staff had been instructed to refer any query regarding dosing to the Monofer SPC or Pharmacosmos medical information.

Vifor submitted that Pharmacosmos had highlighted specific concerns regarding training and briefing materials to representatives which was alleged to encourage breaches of the Code; Clause 15.9 was referred to. Vifor noted that Pharmacosmos did not have specific copies of the training material and as such had produced no evidence to support the allegation. Vifor repeated that no representative training material or briefing documents had been produced or supplied that communicated incorrect dose information for Monofer and as such Vifor had not and did not encourage staff to breach the Code in letter or spirit.

PANEL RULING

The Panel noted Vifor's submission that inter-company dialogue had been successful. The Panel noted Vifor's submission in inter-company dialogue that it would restrict any discussions on Monofer to its SPC. Vifor however, despite being asked to do so, did not clarify what its interpretation of the Monofer SPC was with regard to the subject of the complaint, ie the maximum total dose that could be administered via the total dose infusion method. This was not helpful and in this regard inter-company dialogue had been unsuccessful. The case preparation manager had referred the complaint to the Panel for consideration.

The Panel noted that Pharmacosmos had alleged that Vifor representatives had advised health professionals that the Monofer total dose infusion was subject to a maximum dose of 1000mg and that it had anecdotal evidence in this regard. In support it reproduced part of an anonymised undated email from a customer. It did not provide the original email. No other evidence in relation to activities in the UK was provided. The Panel noted that the complainant had to establish its case on the balance of probabilities.

The Panel noted that according to its SPC, Section 4.2 Posology and method of administration, Monofer could be administered as a total dose infusion given as a single dose of up to 20mg iron/kg body weight as an intravenous drip infusion. If the total iron dose exceeded 20mg iron/kg body weight, the dose must be split into two administrations with an interval of at least one week. The Panel noted that in relation to the intravenous drip infusion Monofer could be administered in doses of 200-1000mg once a week. The Panel noted that no upper dose limit was explicitly stated in the subsection which discussed total dose infusion.

The Panel noted Vifor's submission that it had not briefed or trained staff to discuss a maximum dose of Monofer. All materials that referred to Monofer dosing were withdrawn between October and December 2011. According to Vifor, discussions by its representatives on Monofer dosing were restricted to the Monofer SPC and it referred to its comments in this regard in inter-company dialogue in December 2011 and March 2012. The Panel noted that representatives were advised by an email dated 11 April 2012, and flagged as high importance, to refer queries about Monofer dosing to Pharmacosmos or to the Monofer SPC. They were told that they must not offer any interpretation of the Monofer SPC or advice on dosing or administration of any competitor product. A slide for the May sales conference made a similar comment and advised representatives not to provide any opinion or advice on Monofer dosing. The Panel was concerned that given Vifor had stated its position during inter-company dialogue in December 2011, the earliest written guidance to its representatives was in April 2011, some 2 days before Pharmacosmos' complaint was received by the Authority. However, taking into account its concerns and comments above the Panel did not consider that Pharmacosmos had established, on the balance of probabilities, that Vifor representatives had commented on Monofer dosing as alleged or had been briefed accordingly. No breach of Clause 15.9 was ruled.

Complaint received **13 April 2012**

Case completed **28 June 2012**