CASE AUTH/2149/8/08

FREELANCE MEDICAL WRITER v SYNER-MED

Promotion of Ferinject

A freelance medical writer complained about the promotion of Ferinject (ferric carboxymaltose) by Syner-Med at the British Renal Society meeting in May 2008. The materials at issue were a detail aid, a two page brochure and a leavepiece.

The detailed response from Syner-Med is given below.

In relation to the detail aid, the complainant was mainly concerned about the claim in small print at the foot of page 9 that 'The maximum dose by infusion is 1000mg iron per week, but should not exceed 15mg/kg'. This was essential information because it meant that the maximum dose by infusion (1000mg) should not be given to a patient with a body weight of less than 67kg. However, the statement did not appear with the dosage information earlier in the brochure and might easily be missed. In the interests of patient safety, and to provide a clear and accurate statement of the dosage of Ferinject by infusion, the complainant thought that this information should be incorporated in context, on pages 5/6, for example.

The Panel noted that the summary of product characteristics (SPC) stated 'Ferinject may be administered by intravenous infusion up to a maximum single dose of 20ml of Ferinject (1000mg of iron) but not exceeding 0.3ml of Ferinject (15mg of iron) per kg body weight or the calculated cumulative dose. Do not administer 20ml (1000mg of iron) as an infusion more than once a week'. The adequate cumulative dose required by a patient could be calculated according to a formula given in the SPC; the dose must be calculated for each patient individually and must not be exceeded. The dosing of Ferinject was thus not straightforward.

Page 5 of the detail aid stated simply 'Ferinject, Up to 1000mg, Single Infusion, Dose in 15 mins'. The headline to page 6 (which faced page 5) stated 'Ferinject… the only intravenous iron that allows for 1000mg to be given in 15 mins'. Page 9, in a footnote to a table detailing administration by drip infusion, stated 'The maximum dose by infusion is 1000mg iron per week, but should not exceed 15mg/kg'.

The Panel considered that it was not acceptable to refer to the maximum permitted single dose by infusion on one page but give the qualifying information (ie the dose should not exceed 15mg/kg) on another. It was only in the prescribing information that it was stated that the cumulative dose must be calculated for each patient individually and must not be exceeded. The Panel considered that the detail aid was misleading with regard to the dosage particulars for Ferinject and a breach of the Code was ruled.

The complainant alleged that the claim 'reduces infusion time… 6hrs to 15mins' referenced to a competitor product's SPC (CosmoFer) was unreasonable given that the infusion time stated in the CosmoFer SPC was 4-6 hours.

The Panel considered that the claim 'Reduces infusion time … 6 hours to 15 minutes was misleading as it only referred to the maximum length of time over which a total dose infusion of CosmoFer could be given. A breach of the Code was ruled. The Panel considered that, for similar reasons, its ruling in this regard also applied to claims made in the brochure and the leavepiece.

The complainant alleged that in the detail aid there was no reference as to where the prescribing information appeared. It did not include a statement that prescribers should consult the SPC in relation to other side-effects. The line length of the prescribing information was much longer than the 100 characters recommended in the Code. There was no date of preparation.

The Panel noted that the detail aid was 12 pages in total and did not include a reference as to where the prescribing information could be found. A breach of the Code was ruled as acknowledged by Syner-Med. This ruling also applied to the leavepiece, again as acknowledged by Syner-Med.

The Panel noted that the side effects listed in the prescribing information were the complete list from the SPC. Thus there was no need for the prescribing information to include a statement that prescribers should consult the SPC in relation to other side effects. No breach of the Code was ruled in this regard. This ruling also applied to the brochure and the leavepiece.

The Panel noted that with regard to prescribing information the Code's supplementary information gave recommendations to assist legibility. The Panel considered that although the line length of the prescribing information at issue (around 150 characters) was more than the recommended 100 characters, this did not necessarily mean that it was not legible. The spacing between the lines and emboldening of the headings were helpful. The Panel decided that although on the limits of acceptability the prescribing information was legible and no breach of the Code was ruled. This ruling also applied to the brochure.

The Code required that the date that the prescribing information was drawn up or last revised was given. This was given as December 2007. In addition promotional material other than advertisements appearing in professional publications must include the date on which the promotional material was drawn up or last revised. The company submitted that the reference code for the detail aid included the date of preparation. However, as this was not obvious or understandable to the reader the Panel ruled a breach of the Code. This ruling also applied to the brochure and the leavepiece.

A freelance medical writer complained about promotional material for Ferinject (ferric carboxymaltose) distributed by Syner-Med (Pharmaceutical Products) Limited at the British Renal Society (BRS) meeting in Glasgow, 13/14 May 2008.

The materials at issue were a detail aid, 'The next generation intravenous iron' (ref F07/01-05-08-039), a two page brochure 'Anaemia Service… Redesigning Provision' (ref F09/07-05-08-045) and a leavepiece, 'The next generation intravenous iron' (ref F08/06-05-08-044).

When writing to Syner-Med, the Authority asked it to respond in relation to Clauses 4.1, 4.8, 4.9 and 7.2 which were the same in the 2008 Code as in the 2006 Code.

A Detail aid 'The next generation intravenous iron'

1 Dosage information

COMPLAINT

The complainant was mainly concerned about the claim in small print at the foot of page 9 that 'The maximum dose by infusion is 1000mg iron per week, but should not exceed 15mg/kg'. Clearly this information was absolutely essential for the safe prescribing of Ferinject because it meant that the maximum dose by infusion (1000mg) should not be given to a patient with a body weight of less than 67kg. However, the statement did not appear where the dosage information was boldly displayed earlier in the brochure and might easily be missed by the reader. In the interests of patient safety, and to provide a clear and accurate statement of the dosage of Ferinject by infusion, the complainant thought that this information should be incorporated in context, on pages 5/6, for example.

RESPONSE

Syner-Med submitted that pages 5/6 of the brochure complied with the Ferinject summary of product characteristics (SPC) Section 4.2 Posology and Method of Administration: a maximum single dose of Ferinject up to 1000mg might be administered over 15 minutes once a week. There was no reference to variable dosing or individual patient dosing, the two statements referred to nothing other than the maximum weekly dose and the convenience to patients of a short infusion time. No other claims about specific product dosing had been made.

Page 9 of the detail aid headed 'Ferinject Administration' clearly contained information about vial sizes, volumes of saline to be used, administration time and different methods of administration. The statement regarding the maximum single dose by infusion of 1000mg iron per week, stated that this should not exceed 15mg/kg and was correctly documented on the relevantly titled page.

PANEL RULING

With regard to the dosing information the Panel considered its ruling in another case, Case AUTH/2143/7/08 also applied here.

The Panel noted that the SPC stated 'Ferinject may be administered by intravenous infusion up to a maximum single dose of 20ml of Ferinject (1000mg of iron) but not exceeding 0.3ml of Ferinject (15mg of iron) per kg body weight or the calculated cumulative dose. Do not administer 20ml (1000mg of iron) as an infusion more than once a week'. The adequate cumulative dose required by a patient could be calculated according to a formula given in the SPC; the dose must be calculated for each patient individually and must not be exceeded. The dosing of Ferinject was thus not straightforward.

Page 5 of the detail aid stated simply 'Ferinject, Up to 1000mg, Single Infusion, Dose in 15 mins'. The headline to page 6 (which faced page 5) stated 'Ferinject… the only intravenous iron that allows for 1000mg to be given in 15 mins'. Page 9, in a footnote to a table detailing administration by drip infusion, stated 'The maximum dose by infusion is 1000mg iron per week, but should not exceed 15mg/kg'.

The Panel considered that, given the details regarding dosage in the SPC, the dosage statements in the detail aid were too simple and important information was omitted. It was not acceptable to refer to the maximum permitted single dose by infusion on one page but give the qualifying information (ie the dose should not exceed 15mg/kg) on another. It was only in the prescribing information that it was stated that the cumulative dose must be calculated for each patient individually and must not be exceeded. The Panel considered that the detail aid was misleading with regard to the dosage particulars for Ferinject and a breach of Clause 7.2 was ruled.

2 Comparison with CosmoFer

CosmoFer (iron (III)) was marketed by Vitaline Pharma UK.

COMPLAINT

The complainant alleged that the claim 'reduces infusion time… 6hrs to 15mins' on page 6, referenced to the CosmoFer SPC was unreasonable, in that it compared the maximum infusion time for CosmoFer, whereas the infusion time given in the CosmoFer SPC was 4-6 hours.

RESPONSE

Syner-Med submitted that the claim about reducing the infusion time from 6 hours to 15 minutes was made in the context of reducing the maximum amount of time a patient would spend in a clinic receiving an iron infusion. Including the impact on a patient's travel and waiting time and the overall convenience that reducing the infusion time would confer to the patient. The maximum infusion rate of Cosmofer was 6 hours.

Syner-Med strenuously refuted that it had breached Clause 7.2.

PANEL RULING

The Panel noted that the CosmoFer SPC gave two options for administration by infusion, iv drip infusion or total dose infusion. The dosage instructions for the iv drip infusion (100mg-200mg) were similar to those of the iv bolus injection (up to 200mg) detailed in the Ferinject SPC whilst the total dose infusion (up to 20mg/kg bodyweight) referred to in the CosmoFer SPC was the equivalent of the iv drip infusion (maximum 1000mg not to exceed 15mg/kg) of the Ferinject SPC. The Panel considered that the use of iv drip infusion by two companies to describe two different methods of administration was confusing and as such, given the very different doses involved, any comparison of the different methods of administration for the two products should make it abundantly clear as to which method and dose was being cited for each.

The claim at issue simply stated 'Reduces infusion time … 6 hrs to 15 mins' which was referenced to the CosmoFer SPC. The page was headed 'Ferinject … the only iv iron that allows for 1000mg to be given in 15 mins'. Given the reference to a 1000mg dose the Panel assumed that the claim at issue was about the total dose infusion for CosmoFer which could be administered over 4-6 hours.

The Panel considered that the claim 'Reduces infusion time … 6 hours to 15 minutes was misleading as it only referred to the maximum length of time over which a total dose infusion of CosmoFer could be given. A breach of Clause 7.2 was ruled.

3 Prescribing information

COMPLAINT

The complainant alleged that there was no reference as to where the prescribing information appeared. It did not include a statement that prescribers should consult the SPC in relation to other side-effects. The line length of the prescribing information was much longer than the 100 characters recommended in the Code. There was no date of preparation.

RESPONSE

Syner-Med agreed that there was no reference as to where the prescribing information appeared. The company acknowledged a technical breach of Clause 4.8 which would be corrected.

The prescribing information contained all the currently known side-effects of Ferinject and the incidence of frequency. There were no other side effects referred to in the SPC and therefore no requirement to include a statement referring prescribers to the SPC. The prescribing information was not in breach of Clause 4.2.

Each line of the prescribing information was longer than the recommended 100 characters. However every effort had been made to ensure that the prescribing information was legible. The font was Arial which was clearly legible with black type on a very light background and each section title in bold. The Code required prescribing information to be clear and legible; the 100 characters per line was a recommendation, and not a requirement. The prescribing information met the requirements for clarity and legibility. The company refuted the alleged breach of Clause 4.1.

The detail aid included a company identifiable code, date of preparation and company job number found on the back cover above the box containing the prescribing information. This code F07/01-05-08-039, denoted the code relevant to identify the item (F07), date of preparation (01-05-08) of the brochure and the print code (039). The company refuted a breach of Clause 4.9.

PANEL RULING

The Panel noted that the detail aid was 12 pages in total and did not include a reference as to where the prescribing information could be found. A breach of Clause 4.8 of the Code was ruled as acknowledged by Syner-Med.

The Panel noted that the side effects listed in the prescribing information were the complete list from the SPC. Thus there was no need for the prescribing information to include a statement that prescribers should consult the SPC in relation to other side effects. No breach of Clause 4.1 was ruled in this regard as it was this clause that required the prescribing information to be present

whereas Clause 4.2 set out the elements of the prescribing information.

The Panel noted that Clause 4.2 required prescribing information to include a succinct statement of common side effects, serious side effects and precautions and contra-indications relevant to the indications in the advertisement giving in an abbreviated form the substance of the relevant information in the SPC. The Code did not require all the information in the SPC to be given.

The Panel noted the line length used in the prescribing information was longer than 100 characters. The supplementary information to Clause 4.1, Legibility of Prescribing Information gave recommendations to assist legibility. The Panel considered that although line length at around 150 characters was more than recommended this did not necessarily mean the prescribing information was not legible. The spacing between the lines and emboldening of the headings were helpful. The Panel decided that although on the limits of acceptability the prescribing information was legible and no breach of Clause 4.1 was ruled.

The Code required that the date that the prescribing information was drawn up or last revised was given (Clause 4.2). This was given as December 2007. In addition promotional material other than advertisements appearing in professional publications must include the date on which the promotional material was drawn up or last revised. The Panel noted Syner-Med's submission that the reference code for the item included the date of preparation. However this was not obvious or understandable to the reader. Thus the Panel ruled a breach of Clause 4.9.

B Brochure 'Anaemia Service… Redesigning Provision'

Page 2 of the brochure included a section headed 'Time to Deliver i.v. Iron Dose (incl 10min setup time/visit)'. This was followed by a bar chart which showed that CosmoFer 1000mg took 370 minutes to deliver including 10 minutes to set up. The key beside the barchart stated that CosmoFer was a 6 hour iv infusion.

1 Comparison with CosmoFer

COMPLAINT

The complainant alleged that, as in point A2 above, the 'Time to Deliver' data compared the maximum infusion time for CosmoFer, whereas the infusion time given in the CosmoFer SPC was 4-6 hours.

RESPONSE

Syner-Med referred to its response in point A2 above.

PANEL RULING

The Panel considered that although the brochure was different to the detail aid it was nonetheless misleading for similar reasons stated in point A2 above. A breach of Clause 7.2 was ruled.

2 Prescribing information

COMPLAINT

The complainant alleged that the prescribing information did not include a statement that prescribers should consult the SPC in relation to other side-effects. The lines of the prescribing information were very much longer than the 100 characters recommended in the Code. There was no date of preparation.

RESPONSE

Syner-Med referred to the relevant part of its response in point A3 above.

PANEL RULING

The Panel considered that the relevant part of its rulings in point A3 above applied here ie no breach of the Code regarding the statement to consult the SPC in relation to side-effects and the line length of the prescribing information and a breach of Clause 4.9 with regard to the date of preparation.

C Leavepiece 'The next generation intravenous iron'

1 Comparison with CosmoFer

COMPLAINT

The complainant alleged that, as in point A2 above, the claim 'reduces infusion time… 6hrs to 15mins' compared the maximum infusion time for CosmoFer, whereas the infusion time given in the CosmoFer SPC was 4-6 hours.

RESPONSE

Syner-Med referred to its response in point A2 above.

PANEL RULING

The Panel noted that the leavepiece was very similar to the detail aid and that it was misleading for similar reasons to those stated in point A2 above. A breach of Clause 7.2 was ruled.

2 Prescribing information

COMPLAINT

The complainant alleged that there was no reference as to where the prescribing information appeared. The prescribing information did not include a statement that prescribers should consult the SPC in relation to other side-effects. There was no date of preparation.

RESPONSE

Syner-Med referred to its response in point A3 above.

PANEL RULING

The Panel noted that the leavepiece was 6 pages in total and did not include a reference as to where the prescribing information could be found. A breach of Clause 4.8 was ruled as acknowledged by Syner-Med.

The Panel considered that the relevant part of its rulings in point A3 above applied here ie no breach of the Code regarding the statement to consult the SPC in relation to other side effects and a breach of Clause 4.9 with regard to the date of preparation.

Complaint received	**24 July 2008**
Case completed	**21 August 2008**