CASE AUTH/2143/7/08

NURSE v SYNER-MED

Promotion of Ferinject

A nurse complained about what she had been told about Ferinject (ferric carboxymaltose), an injectable iron preparation, at a Syner-Med exhibition stand. She also referred to a detail aid.

The complainant had been told that Ferinject was an IV iron and 1,000mg could be given in a single dose over 15 minutes. The complainant asked about safety concerns worldwide and was informed that Ferinject was safe.

The complainant had since discovered that the maximum dose was 1,000mg iron per week, but should not exceed 15mg/kg of body weight. This was included on page 9 of the detail aid 'The next generation of intravenous iron'. The complainant alleged that the detail aid was misleading as patients might need more than one dose.

The Food and Drug Administration (FDA) had refused to approve Ferinject in the US because of safety issues; 10 deaths occurred during trials. The complainant was concerned that as a nurse she had been misled over safety issues and the single dosage of Ferinject.

The detailed response from Syner-Med is given below.

On the basis of the parties' submissions the Panel did not consider that there was sufficient evidence to show that on the balance of probabilities any of the representatives on Syner-Med's stand had described Ferinject as safe. The Panel ruled no breach of the Code.

With regard to the maximum infusible 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 had to be calculated for each patient individually according to a formula in the SPC 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 the Code was ruled.

A nurse complained about what she had been told about Ferinject (ferric carboxymaltose), an injectable iron preparation from Syner-Med (Pharmaceutical Products) Limited, when she visited the company's stand at a meeting in May 2008. The complainant also referred to a detail aid.

COMPLAINT

The complainant explained that she had enquired at the Syner-Med stand about Ferinject and was told that it was an IV iron and 1,000mg could be given in single dose over 15 minutes. The complainant asked about safety concerns worldwide and was informed that Ferinject was safe.

The complainant had since discovered that the maximum dose was 1,000mg iron per week, but should not exceed 15mg/kg of body weight. This was written in smaller print on page 9 of the detail aid 'The next generation of intravenous iron' (ref F07/01-05-08-039). The complainant considered the detail aid and the representation of the usage of Ferinject was misleading as patients might need more than one dose.

The complainant had since discovered that the Food and Drug Administration (FDA) had refused to approve Ferinject in the US because of safety issues; 10 deaths occurred during trials.

The complainant was concerned that as a nurse she had been misled over safety issues and the single dosage of Ferinject.

When writing to Syner-Med, the Authority asked it to respond in relation to Clauses 7.2, 7.9 and 7.10 of the 2006 Code which were the same as the 2008 Code. This case was considered under the 2008 Constitution and Procedure.

RESPONSE

Syner-Med submitted that it was very difficult to investigate the circumstances surrounding the conversation about safety as there were very few details given and the complaint was made more than two months after the incident. There was no precise date, no specified time and no named company employee with whom to verify this conversation. The exhibition spanned three days, with more than a thousand delegates and fourteen Syner-Med employees on the stand at different times. None of them recalled a conversation as described by the complainant. From the information provided it was unclear as to how long the conversation lasted, whether other people were involved and the circumstances (eg whether the exhibition stand was crowded and there were distractions, whether everything was audible to both parties).

There was no information as to what was said by either party and therefore no context in which Syner-Med could make specific comments. The complainant's phrase 'Ferinject was safe' appeared to be a summary statement. Given the complainant's open question ie 'I asked about safety concerns worldwide' the answer given had to be a summary; if the answer was taken as a verbatim statement, then it neither answered the question nor made sense.

Syner-Med knew that it was inappropriate to imply that a product had no side-effects or to use the word 'safe' in the promotion of medicines under both guidance from the Medicines and Healthcare products Regulatory Agency (MHRA) and Clause 7.9 of the Code. All the company's sales representatives had successfully passed the ABPI examination and equally knew that the use of the term was inappropriate. The Ferinject detail aid, to which the complainant referred, made no such statement, and, in line with the requirements to encourage rational use of a medicine by presenting it objectively and without exaggeration (Clause 7.10), the company had conveyed the 'benefit/risk' profile clearly in the text. Syner-Med noted that a whole A4 page was devoted to the issue of adverse events with Ferinject. Thirteen specific adverse events were reported with their relative frequency. Reference was also made to the frequency of life threatening anaphylactic reactions. On Page 9 reproduced, in bold print, a warning/precaution from the summary of product characteristics (SPC): 'Parenterally administered iron preparations can cause hypersensitivity reactions. Therefore facilities for cardio-pulmonary resuscitation must be available'.

Given that the complainant made detailed reference to the specifics contained in the detail aid it seemed unreasonable to ignore all the safety information contained therein, and claim that the company had misrepresented the safety issue.

At the exhibition stand there was other information relating to safety contained in the Ferinject SPC. The medical information department was also represented on the stand and many written questions were left for follow up. All these opportunities were available to the complainant yet they were not taken up. Syner-Med considered that they were all important considerations in the context of the complaint.

Regarding the supply of safety information on Ferinject, Syner-Med noted that the product was licensed in eighteen European countries but had only been launched in Germany, the UK and Switzerland. The time period from launch in each country was such that Periodic Safety Data had only been submitted from one country to date. In the context of the discussion between the complainant and the representative this information would not be known to the representative.

In conclusion, the company had thoroughly investigated the complainant's comments and was unable to identify anyone who remembered being involved in a conversation of this nature. In line with the regulations, the company did not allow staff to use the word 'safe' in the promotion of any medicine, either verbally or written.

With regard to the dosing of Ferinject, Syner-Med was again unable to identify anyone who remembered the specific details of the conversation described. However, the verbal statement that Ferinject was an IV iron preparation and 1,000mg could be given in a single dose over 15 minutes was correct and in line with the product licence.

Page 5 of the detail aid cited by the complainant stated:

'Ferinject
Up to 1000mg
Single Infusion
Dose in 15 mins.'

This statement complied with the product licence as a dose of 'Ferinject may be administered by intravenous infusion up to a maximum single dose of 20ml (1000mg) of iron …' (ref SPC).

As identified by the complainant, page 9 of the detail aid stated: 'The maximum single dose by infusion is 1000mg iron per week, but should not exceed '15mg/Kg'.

This also complied with the licence and occurred at a very relevant place in the brochure. This came under the heading 'Administration by drip infusion'. This section contained information about vial sizes, volumes of saline to be used, and administration time. To include detailed information about maximum doses and the frequency of dosing was highly relevant to this section. Thus, the company refuted the suggestion that there was some attempt to be misleading in the layout of the information in the detail aid.

Syner-Med submitted that the complainant made a

different point when she stated that the information was 'misleading as patients might need more than one dose'. The detail aid did not claim that the total dose required could be administered in any one visit (for example, the phrase 'total dose infusion' was not used). The wording used was 'Up to 1000mg Single Infusion' which simply meant that there was flexibility in dosing from 100mg up to 1,000mg. This was not a statement about frequency of dosing.

Syner-Med strenuously refuted the allegation that it had breached Clauses 7.2, 7.9 and 7.10.

PANEL RULING

The provisions of Clauses 7.2, 7.9 and 7.10 of the 2008 Code were considered. These clauses were the same in the 2006 Code.

With regard to the question about the safety of Ferinject, the Panel noted that the parties' accounts differed; it was difficult in such cases to know what had transpired. A judgement had to be made on the available evidence bearing in mind the extreme dissatisfaction usually necessary on the part of an individual before he or she was moved to actually submit a complaint.

The complainant had submitted that she was told that Ferinject was safe. Syner-Med had been unable to find anyone who had been on the company stand who remembered the alleged conversation. The company had submitted that it knew it could not describe Ferinject as safe; the detail aid did not describe Ferinject as safe.

On the basis of the parties' submissions the Panel did not consider that there was sufficient evidence to show that on the balance of probabilities any of the representatives on Syner-Med's stand had described Ferinject as safe. The Panel ruled no breach of Clauses 7.9 and 7.10.

With regard to the maximum infusible dose of Ferinject 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.

Complaint received **17 July 2008**

Case completed **28 August 2008**