CASE AUTH/2173/10/08

NURSE v SYNER-MED

Ferinject detail aid

A nurse alleged that the revised edition of a Ferinject (ferric carboxymaltose) detail aid entitled 'The next generation of intravenous iron' issued by Syner-Med was inaccurate.

Page 1 of the detail aid, headed 'What is required of the next generation intravenous iron?', listed five features, the second of which was 'Single dose delivery'. The list was followed by a chart detailing administration details of, *inter alia*, iv iron dextran (Vitaline Pharma UK's product CosmoFer). It was stated that [CosmoFer] could be given in a 200mg bolus which was not true. It took 35 minutes to give 200mg iron dextran. It was not accurate to state that the 1000mg infusion time for iv iron dextran was 4-6 hours when a patient with a body weight of 75kg could receive 1500mg of iron dextran, a much larger dose, as a total dose infusion over four hours. Page 1 also referred to single dose delivery. This was misleading as a patient had to weigh over 67kg to receive 1000mg of Ferinject.

The detailed response from Syner-Med is set out below.

The Panel noted that the CosmoFer summary of product characteristics (SPC) required a test dose of 25mg to be administered before the first dose could be given to a new patient. If no adverse reactions were seen after 60 minutes, the remaining dose could be given. The dose and dosage schedule must be individually estimated for each patient. The dosage schedule normally recommended was 100-200mg iron corresponding to 2-4ml two or three times a week depending on the haemoglobin level. In certain circumstances CosmoFer could be administered as a total dose infusion up to a total replacement dose corresponding to 20mg iron/kg body weight. Subsequent doses depended on the method of administration. If given via an intravenous drip 100-200mg of iron could be diluted in 100ml of normal saline or 5% glucose solution. On each occasion the first 25mg should be infused over a period of 15 minutes. If there were no adverse reactions the remaining portion should be given at a rate of not more than 100ml in 30 minutes. If CosmoFer was being given as an iv injection 25mg of iron should be injected slowly over a period of 1 to 2 minutes. If no adverse reactions occurred within 15 minutes the remaining portion could be given. The product could also be given as a total dose infusion up to 20mg/kg body weight iv over 4-6 hours. The first 25mg of iron to be infused over 15 minutes. The SPC stated that this method of administration should be restricted to hospital use only. The SPC stated that the iv drip infusion was the preferred route of administration. However it could be administered as undiluted solution intramuscularly.

The Panel did not consider that the chart detailing, *inter alia*, the administration of CosmoFer was sufficiently clear as to the route of administration and dosing schedule being referred to. There was no mention that each patient's dose had to be calculated individually according to haemoglobin levels. It appeared that for CosmoFer there was a choice of two doses; 200mg or 1000mg. It appeared that the 200mg bolus dose could be administered over 10 minutes which was not so; there was no indication that the total injection time was comprised of the time taken to administer the test dose plus the time needed to administer the rest of the dose. The Panel considered that the chart was too simple given the complex dosing instructions for CosmoFer. The chart was misleading in this regard and a breach of the Code was ruled.

The Panel did not consider that it was incorrect to state that the infusion time for a 1000mg dose of CosmoFer would be 4-6 hours. It would have been helpful to state that this was not a fixed dose but was dependent upon a patient's body weight and haemoglobin level. Nonetheless, if a dose of 1000mg was required it could be infused over 4-6 hours. The Panel thus considered that the material was not misleading as alleged and no breach was ruled.

With regard to the statement 'Single dose delivery' the Panel noted that this was one response to the question 'What is required of the next generation intravenous iron?'. The Panel noted that the front cover of the brochure was headed 'Ferinject' followed by 'The next generation intravenous iron'. Page 3, facing page 2, was headed 'Ferinject the next generation intravenous iron' and thus the features listed on page 1 would be read as applying to Ferinject. According to its SPC Ferinject could be administered as 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 per week. The Panel noted that the administration of Ferinject was not straightforward but page 1 implied that it was. The list featured on page 1 was repeated on page 10 but with a comment about Ferinject next to each feature. On page 10 the claim 'Single dose delivery' was followed by 'Up to 1000mg* but not exceeding 15mg/kg/wk'. The asterisked footnote stated that the iron deficit should be calculated (see SPC) and that a single dose should not exceed 15mg/kg/wk. The Panel considered that page 1 was misleading as alleged and a breach of the Code was ruled.

A nurse complained about the revised edition of a Ferinject (ferric carboxymaltose) detail aid entitled 'The next generation of intravenous iron' (ref F17) issued by Syner-Med (Pharmaceutical Products) Limited.

Page 1 of the detail aid, headed 'What is required of the next generation intravenous iron?', listed five features, the second of which was 'Single dose delivery'. The list was followed by a chart detailing administration details of, *inter alia*, iv iron (iii) hydroxide dextran complex (Vitaline Pharma UK's product CosmoFer).

The complainant had complained previously about the promotion of Ferinject (Cases AUTH/2143/7/08 and AUTH/2144/7/08).

COMPLAINT

The complainant alleged that the updated version of the detail aid was unfortunately still inaccurate.

Page 1 stated that iron dextran [CosmoFer] could be given in a 200mg bolus which was not true. It took 35 minutes to give 200mg iron dextran. It was not accurate to state that the 1000mg infusion time for iv iron dextran was 4-6 hours when a patient with a body weight of 75kg could receive 1500mg of iron dextran, a much larger dose, as a total dose infusion over four hours.

Page 1 also referred to single dose delivery. This was misleading as a patient had to weigh over 67kg to receive 1000mg of Ferinject.

When writing to Syner-Med, the Authority asked it to respond in relation to Clause 7.2 of the Code which was the same in the 2008 Code as the 2006 Code.

RESPONSE

Syner-Med explained that iron dextran was licensed to be administered intramuscularly, intravenously or via the venous limb of a dialyser. The intravenous route permitted the product to be administered either as an infusion or injection. The definition of a bolus injection was (medical online dictionary) 'The injection of a drug (or drugs) in a high quantity (called a bolus) at once, the opposite of gradual administration (as in intravenous infusion)'. The CosmoFer summary of product characteristics (SPC) stated 100 – 200mg iron (2-4mls) by slow intravenous injection. The statement was thus correct and in line with the CosmoFer SPC.

The complainant was correct that it took 35 minutes to give 200mg iron dextran. However the complainant had not noted that the information on page 1 broke down the administration time of iron dextran into the time it took to administer a test dose and the time it took to administer the remaining portion of the dose.

Syner-Med submitted that the time that it might take to administer 1000mg of iron dextran was correctly stated in the detail aid. There was no attempt to provide specific prescribing information regarding the minimum or maximum dosage of iron dextran and no attempt to provide specific prescribing information for individual patients. The statement that the 1000mg infusion time was 4-6 hours was correct and in line with the CosmoFer SPC.

Syner-Med noted that the statement 'Single dose delivery' appeared under the question 'What is required of the next generation intravenous iron?' and referred to potential product characteristics which health professionals might find beneficial when treating patients with parenteral iron. There was no reference on this page to the prescribing of Ferinject. The company did not believe that the information or statements were misleading.

PANEL RULING

The Panel noted that the CosmoFer SPC required a test dose of 25mg to be administered before the first dose could be given to a new patient. If no adverse reactions were seen after 60 minutes, the remaining dose could be given. The dose and dosage schedule must be individually estimated for each patient. The dosage schedule normally recommended was 100-200mg iron corresponding to 2-4ml two or three times a week depending on the haemoglobin level. In certain circumstances CosmoFer could be administered as a total dose infusion up to a total replacement dose corresponding to 20mg iron/kg body weight. Subsequent doses depended on the method of administration. If given via an intravenous drip 100-200mg of iron could be diluted in 100ml of normal saline or 5% glucose solution. On each occasion the first 25mg should be infused over a period of 15 minutes. If there were no adverse reactions the remaining portion should be given at a rate of not more than 100ml in 30 minutes. If CosmoFer was being given as an iv injection 25mg of iron should be injected slowly over a period of 1 to 2 minutes. If no adverse reactions occurred within 15 minutes the remaining portion could be given. The product could also be given as a total dose infusion up to 20mg/kg body weight iv over 4-6 hours. The first 25mg of iron to be infused over 15 minutes. The SPC stated that this method of administration should be restricted to hospital use only. The SPC stated that the iv drip infusion was the preferred route of administration. However it could be administered as undiluted solution intramuscularly.

The Panel did not consider that the chart on page 2 of the detail aid, detailing, *inter alia*, the administration of CosmoFer was sufficiently clear as to the route of administration and dosing schedule being referred to. There was no mention that each patient's dose had to be calculated individually according to haemoglobin levels. It appeared that for CosmoFer there was a choice of two doses;

200mg or 1000mg. It appeared that the 200mg bolus dose could be administered over 10 minutes which was not so; there was no indication that the total injection time was comprised of the time taken to administer the test dose plus the time needed to administer the rest of the dose. The Panel considered that the chart was too simple given the complex dosing instructions for CosmoFer. The chart was misleading in this regard and a breach of Clause 7.2 was ruled.

The Panel did not consider that it was incorrect to state that the infusion time for a 1000mg dose of CosmoFer would be 4-6 hours. It would have been helpful to state that this was not a fixed dose but was dependent upon a patient's body weight and haemoglobin level. Nonetheless, if a dose of 1000mg was required it could be infused over 4-6 hours. The Panel thus considered that the material was not misleading as alleged and no breach of Clause 7.2 was ruled.

With regard to the statement 'Single dose delivery' the Panel noted that this was one response to the question 'What is required of the next generation intravenous iron?'. The Panel noted that the front cover of the brochure was headed 'Ferinject' followed by 'The next generation intravenous iron'. Page 3, facing page 2, was headed 'Ferinject the next generation intravenous iron' and thus the features listed on page 1 would be read as applying to Ferinject. According to its SPC Ferinject could be administered as 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 per week. The Panel noted that the administration of Ferinject was not straightforward but page 1 implied that it was. The list featured on page 1 was repeated on page 10 but with a comment about Ferinject next to each feature. On page 10 the claim 'Single dose delivery' was followed by 'Up to 1000mg* but not exceeding 15mg/kg/wk'. The asterisked footnote stated that the iron deficit should be calculated (see SPC) and that a single dose should not exceed 15mg/kg/wk. The Panel considered that page 1 was misleading as alleged and a breach of Clause 7.2 was ruled.

Complaint received **10 October 2008**

Case completed **25 November 2008**