CASE AUTH/3134/12/18

COMPLAINANT v SHIELD

Information about Feraccru

A complainant who described him/herself as a concerned UK health professional, complained about the answers to frequently asked questions (FAQs) on the Feraccru (ferric maltol) website. Feraccru, was indicated for the treatment of iron deficiency in adults.

The complainant noted the following FAQ and answer:

> **'Can Feraccru be used in patients with Hb<9.5g/dL?**
>
> **Feraccru should not be used in IBD [inflammatory bowel disease] patients with haemoglobin <9.5g/dL. We have not studied the use of Feraccru in these patients. However, our phase 3 CKD study included patients with haemoglobin levels as low as 8g/dL.'**

The complainant stated that the first line was correct. The second line appeared to reassure - especially the use of the word 'however' - data in Phase 3 trials did not mean one could advocate use beyond the data in the summary of product characteristics (SPC).

The complainant was even more worried about a FAQ on pregnancy:

> **'Is Feraccru suitable for patients that are pregnant or breastfeeding?**
>
> **We do not have any clinical data in this population. A benefit/risk assessment should be made before prescribing Feraccru.'**

The complainant referred to the SPC which used much stronger language:

> **'Pregnancy**
> **There are no data from the use of Feraccru in pregnant women. Ferric maltol is not systemically available.**
>
> **Definitive animal studies are not available for maltol with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of Feraccru during pregnancy.**
>
> **Breastfeeding**
> **Ferric maltol is not available systemically and is therefore unlikely to pass into the mother's milk. No clinical studies are available to date. As a precautionary measure, it is preferable to avoid the use of Feraccru during breast-feeding.'**

The complainant was concerned that Shield had many flaws on its other website and it appeared that the company was encouraging the use of its product in several groups which was against the licensed indication.

The detailed response from Shield is given below.

The Panel noted that Feraccru was indicated in adults for the treatment of iron deficiency. Section 4.4 of the SPC, special warnings and precautions for use, stated that Feraccru should not be used in patients with IBD flare or in IBD patients with haemoglobin (Hb) <9.5g/dL. Section 5.1 of the SPC referred to data from IBD studies which included IBD patients with the lower limit of haemoglobin. The SPC did not mention a lower limit for haemoglobin in other groups of patients.

The Panel noted the answer to the question on the Shield website referred to data in patients with chronic kidney disease (CKD) with haemoglobin as low as 8g/dl. The Panel noted that the SPC made no specific mention of CKD. The Panel was unsure of the impact of the statement in the SPC that Feraccru had not been studied in patients with impaired renal and/or hepatic function.

The Panel did not consider that the response on the Shield website advocated use of the medicine beyond the SPC given the broad indication for Feraccru and no breach of the Code was ruled. The response could have been better worded but, in the Panel's view, it was not misleading and the Panel therefore ruled no breaches of the Code.

The Panel noted that the response to the question on the Shield website in relation to use in pregnancy or breast feeding, did not include all the relevant information from the SPC. It was made clear that there was no clinical data in this population. The response was referenced to the SPC and PIL; readers were not specifically referred to the statements in the SPC and PIL for further information as stated by Shield.

The Panel noted that health professionals would make a benefit/risk assessment before prescribing any medicine, particularly so in patients who were pregnant or breastfeeding. The Panel considered that to omit from the answer very relevant additional information from the SPC that as a precautionary measure it was preferable to avoid the use of Feraccru during pregnancy and breastfeeding was misleading. Full information had not been provided. The Panel also considered that the answer to the FAQ on the Shield website was inconsistent with information in the SPC. The Panel therefore ruled breaches of the Code which were upheld on appeal by Shield. It was important that health professionals could rely upon the industry for accurate, complete information about its medicines. The Panel did not consider that high standards had

been maintained and ruled a breach of the Code which was upheld on appeal by Shield. The Panel did not consider that the particular circumstances of this case warranted a ruling of a breach of Clause 2 which was reserved as a sign of particular censure.

A complainant who described him/herself as a concerned UK health professional, complained about the answers to frequently asked questions (FAQs) on the Feraccru (ferric maltol) website. Feraccru, was indicated for the treatment of iron deficiency in adults.

COMPLAINT

The complainant noted the following FAQ and answer:

> 'Can Feraccru be used in patients with Hb<9.5g/dL?
>
> Feraccru should not be used in IBD [inflammatory bowel disease] patients with haemoglobin <9.5g/dL. We have not studied the use of Feraccru in these patients. However, our phase 3 CKD study included patients with haemoglobin levels as low as 8g/dL.'

The complainant stated that the first line was correct. The second line appeared to reassure - especially the use of the word 'however' - data in Phase 3 trials did not mean one could advocate use beyond the data in the summary of product characteristics (SPC).

> The complainant was even more worried about a FAQ on pregnancy:
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> 'Is Feraccru suitable for patients that are pregnant or breastfeeding?
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> We do not have any clinical data in this population. A benefit/risk assessment should be made before prescribing Feraccru.'
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> The complainant referred to the SPC which used much stronger language:
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> 'Pregnancy
> There are no data from the use of Feraccru in pregnant women. Ferric maltol is not systemically available.
>
> Definitive animal studies are not available for maltol with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of Feraccru during pregnancy.
>
> Breastfeeding
> Ferric maltol is not available systemically and is therefore unlikely to pass into the mother's milk. No clinical studies are available to date. As a precautionary measure, it is preferable to avoid the use of Feraccru during breast-feeding.'

The complainant stated that it was quite concerning that Shield had many flaws on its other website and it appeared that the company was encouraging the use of its product in several groups which was against the licensed indication.

In writing to Shield the Authority drew attention to Clauses 2, 3.2, 7.2 and 9.1.

RESPONSE

Shield stated that as the complainant was anonymous, it was not possible to assess if he/she was a health professional and therefore whether access to the health professional section of the website was appropriate.

With regard to the FAQ about use of the medicine in patients with haemoglobin levels below 9.5g/dl, Shield submitted that Feraccru was indicated in adults for the treatment of iron deficiency. There was no specific lower level of haemoglobin specified, however Section 4.4 of the SPC provided information that limited the use of Feraccru in patients with Inflammatory Bowel Disease (IBD) to those with a Hb level >9.5g/dl. This limit reflected the study population from the original studies of Feraccru. A subsequent study in CKD patients included those with a Hb level as low as 8g/dl. The information reflected the full body of data available for Feraccru, was entirely consistent with the licensed indication and provided additional information to allow rational and appropriate use of Feraccru. Shield denied a breach of Clauses 3.2, 7.2 or 9.1.

With regard to the second issue raised by the complainant, the FAQ referring to the use of Feraccru in patients who were pregnant or breastfeeding, Shield referred to the answer on the website and that the response referred readers to the SPC and PIL for further information. Shield also referred to the relevant sections in the SPC and submitted that the SPC did not prohibit the use of Feraccru in either pregnancy or breast feeding. As was the case for most new medicines, there was no data available in these populations and therefore it was preferable to avoid use unless the benefit outweighed any risk as judged by the treating physician.

Ferric maltol was not systemically available and iron was a physiological substance required by mother and infants.

Shield submitted that the response to the FAQ was not misleading, it was consistent with the SPC, referred the reader to the SPC and PIL to provide further information and did not encourage off label use. Shield denied a breach of Clause 3.2 or 7.2.

In light of the above, Shield submitted that there was also no evidence of a breach of Clause 2.

PANEL RULING

The Panel noted that Feraccru was indicated in adults for the treatment of iron deficiency. Section 4.4 of the SPC, special warnings and precautions for use, stated that Feraccru should not be used in patients with IBD flare or in IBD patients with haemoglobin (Hb) <9.5g/dL. Section 5.1 of the SPC referred to data from IBD studies which included IBD patients with the lower limit of haemoglobin. The SPC did not mention a lower limit for haemoglobin in other groups of patients.

The Panel noted the answer to the question on the Shield website referred to data in patients with chronic kidney disease (CKD) with haemoglobin as low as 8g/dl. The Panel noted that the SPC made no specific mention of CKD. The Panel was unsure of the impact of the statement in the SPC that Feraccru had not been studied in patients with impaired renal and/or hepatic function. The Panel noted that Clause 3.2 stated that the promotion of a medicine must be in accordance with the particulars listed in its SPC. This clause did not prohibit companies from providing information not included in a SPC if that information was not inconsistent with the particulars listed in the SPC.

The Panel did not consider that the response on the Shield website advocated use of the medicine beyond the SPC given the broad indication for Feraccru and no breach of Clause 3.2 was ruled. The response could have been better worded but, in the Panel's view, it was not misleading and the Panel therefore ruled no breach of Clause 7.2. The Panel consequently ruled no breach of Clauses 9.1 and 2.

The Panel noted that the response to the question on the Shield website in relation to use in pregnancy or breast feeding, did not include all the relevant information from the SPC. It was made clear that there was no clinical data in this population. The response was referenced to the SPC and PIL; readers were not specifically referred to the statements in the SPC and PIL for further information as stated by Shield.

The Panel noted that health professionals would make a benefit/risk assessment before prescribing any medicine, particularly so in patients who were pregnant or breastfeeding. The Panel considered that to omit from the answer very relevant additional information from the SPC that as a precautionary measure it was preferable to avoid the use of Feraccru during pregnancy and breastfeeding was misleading. Full information had not been provided. The Panel also considered that the answer to the FAQ on the Shield website was inconsistent with information in the SPC. The Panel therefore ruled breaches of Clauses 7.2 and 3.2 of the Code. It was important that health professionals could rely upon the industry for accurate, complete information about its medicines. The Panel did not consider that high standards had been maintained and ruled a breach of Clause 9.1. The Panel did not consider that the particular circumstances of this case warranted a ruling of a breach of Clause 2 which was reserved as a sign of particular censure.

APPEAL BY SHIELD

Shield noted that the Panel's ruling of breaches of Clauses 3.2, 7.2 and 9.1 of the Code related to the information it had provided on the FAQ section of its website regarding Feraccru, specifically in relation to the suitability of Feraccru for patients who were pregnant or breast-feeding. This information was set out below:

'FAQ:

Is Feraccru suitable for patients that are pregnant or breastfeeding?

Response:

We do not have any clinical data in this population. A benefit/risk assessment should be made before prescribing Feraccru'

Shield noted that its response to the question was accompanied by a footnote, which directed the reader to the SPC and the PIL. The Panel had concluded that Shield's website did not include all the relevant information from the SPC and was therefore misleading in breach of Clause 7.2. In doing so, the Panel appeared to have placed significant reliance on the fact that the following text from the SPC was not repeated in the FAQ section on the website: 'As a precautionary measure, it is preferable to avoid the use of Feraccru during pregnancy [and] breast-feeding.' The Panel had also concluded that the response was inconsistent with information in the SPC, in breach of Clause 3.2. Further, in view of the rulings above, the Panel had ruled a breach of Clause 9.1.

Shield stated that iron deficiency was a significant health issue in pregnancy and when breast-feeding. Oral iron salts were commonly used but had poor bioavailability and were often poorly tolerated. Women were therefore frequently left iron deficient throughout their pregnancy leading to increased complication during partus and the puerperium. Given the challenges of iron replacement faced by health professionals, Shield had received many questions around the potential use of Feraccru in pregnancy and breastfeeding.

Shield submitted that it promoted Feraccru as a second line therapy and as an alternative to IV iron and it was also positioned as such on formularies in the NHS.

In Shield's view that it was reasonable to assume that a health professional accessing Shield's website to search for a question as to whether Feraccru could be used in pregnancy had a reason to do so, such as they had found other preparations to be ineffective or the patient was intolerant.

Shield submitted that the information provided for Feraccru through Shield's FAQ section was in accordance with the terms of its marketing authorisation and was consistent with the particulars listed in its SPC. The information provided was balanced, fair, objective, unambiguous and conveyed meaning of the wording in the SPC.

Shield submitted that it was important to place the use of the 'precautionary measure' in the appropriate context. The words 'as a precautionary measure' were reasonably understood to mean that, in the absence of an appropriate medical assessment, it was preferable to avoid use of Feraccru during breast-feeding. Information was provided to ensure the health professional recognised the lack of data for patients who were pregnant or who were breast feeding. It was Shield's belief that a

reasonable health professional would interpret the fact that there was no data from the use of pregnant women or in breast feeding to mean, inherently, that alternative products should be used if possible. However, the additional statement 'A benefit/risk assessment should be made before prescribing Feraccru', easily directed the attention of the health professional to the SPC and PIL and ensured that any decision on prescribing was made after a full benefit/risk assessment was carried out to consider the patient's individual circumstances, and any decision was made having considered the full contents of the SPC and PIL. For these reasons, Shield did not accept that its response was inconsistent with the information in the SPC and could not be found in breach of Clause 3.2.

Shield noted that the Panel ruled that omitting the precautionary statement from its response to the FAQ rendered it misleading (Clause 7.2) and inconsistent with the information in the SPC (Clause 3.2). To do so was to place disproportionate importance on the precautionary statement and ignored other essential information in the SPC which was necessary to consider when carrying out a balanced assessment. Indeed, had Shield chosen, for example, only to use some of the language around lack of ferric maltol systemically, or the fact that it was unlikely to be found in breast milk in its response, then Shield could have been accused of 'cherry picking' from the SPC and could rightly have been found to be in breach of Clause 7.2 for this reason.

Shield submitted that if the only additional statement in the SPC were to be that it was preferable to avoid the use of Feraccru at all in pregnancy and breastfeeding then a health professional could consider that they ought never to use Feraccru in such a situation. As was clear from the rest of the contents of the SPC, it would be erroneous to make a blanket decision not to prescribe Feraccru to women who were pregnant or breast-feeding. Such an error in judgement could lead to a failure to prescribe in the appropriate circumstances and might lead to women not receiving a treatment that could provide benefit to them and their infant.

Shield submitted that it followed that to take the precautionary statement out of context, and to misinterpret it so as to find Shield in breach of the Code, was unreasonable and perverse in the context of Clause 7.2.

Shield submitted that there was nothing in the response that conflicted with the full SPC in the sense that there could reasonably be said to be any 'encouraging' (to quote the complainant) of the use of Feraccru. Instead, the response to the question ensured that the fact that no data was available in pregnancy and breast-feeding was clear and directed the health professional to read the full SPC and assess the individual patient circumstances before making a prescribing decision. Shield did not accept that ensuring rational prescribing was in any way failing to maintain high standards and therefore there should be no finding of breach of Clause 9.1.

Shield submitted that it had acted in accordance with industry standards and promoted its products in a consistent manner and in accordance with the marketing authorisations. On no reasonable interpretation could it be said to have failed in respect of its accuracy, fairness and objectivity in the way in which it had provided information to the relevant health professional. No element of this case involved Shield preventing the information which would permit a health professional to make a fair, complete and accurate assessment of each individual patient from being readily available.

Shield submitted that the basis of the complaint was premised on a disagreement about the way certain information was provided to health professionals. This appeal set out the good reasons for the approach adopted in its response to the FAQ and the way in which that interacted with the SPC. It also highlighted why the position adopted by the Panel was flawed and if upheld could put patients at risk of not receiving medicines that could benefit them. Shield stood by the approach it had adopted, which ensured that patient safety was paramount and allowed health professionals to make a fully informed decision when prescribing Feraccru.

COMMENTS FROM THE COMPLAINANT

The complainant noted that given that this matter had already been viewed by industry experts he/she would not add any further value.

APPEAL BOARD RULING

The Appeal Board noted that the FAQ on Shield's Feraccru website for health professionals stated, 'Is Feraccru suitable for patients that are pregnant or breastfeeding?' and the drop-down response stated 'We do not have any clinical data in this population. A benefit/risk assessment should be made before prescribing Feraccru [1,4]'. The superscript 1 and 4 were linked to a separate page that contained a list of references including the SPC (at position 1) and PIL (at position 4) for Feraccru. There was no mention on the page containing the FAQ to indicate what the superscript 1 and 4 were referring to. The SPC and PIL were included as unnumbered links at the bottom of the page along with other documents.

The Appeal Board noted Section 4.6 of the Feraccru SPC referred to the absence of data from the use of Feraccru in pregnant women and that ferric maltol was not systemically available. It also stated that 'Definitive animal studies are not available for maltol with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of Feraccru during pregnancy', and 'As a precautionary measure, it is preferable to avoid the use of Feraccru during breast-feeding'. The Appeal Board noted there was a difference between the absence of data and the absence of definitive data.

The Appeal Board noted the company's submission at the appeal that a risk/benefit assessment would include a detailed examination of the entire SPC and consideration of each patient's particular circumstances.

The Appeal Board considered that in terms of a health professional making a prescribing decision, the response to the FAQ was neutral; whereas the SPC included a specific precautionary measure that it was preferable to avoid the use of Feraccru during pregnancy [and] breast-feeding. The Appeal Board noted that the warning would be included in the SPC for a reason and failure to include it in the FAQ response was misleading. Consequently, the Appeal Board considered that the response to the FAQ at issue was misleading and inconsistent with the SPC and it upheld the Panel's rulings of breaches of Clauses 7.2 and 3.2. A prescriber reading the response to the FAQ might not be aware of the precautionary measure in the SPC. It was important that health professionals could rely upon the industry for accurate and complete information about its medicines. The Appeal Board upheld the Panel's ruling of a breach of Clause 9.1. The appeal was unsuccessful.

Complaint received **17 December 2018**

Case completed **2 April 2019**