Ferrous Sulphate 200mg Coated Tablets BP

PL 15894/0004

UKPAR

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Ferrous Sulphate 200mg Coated Tablets BP

PL 15894/0004

LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Quantum Generics a Marketing Authorisation (licence) for the medicinal product Ferrous Sulphate 200mg Coated Tablets BP (PL 15894/0004) on 10th June 2011. This is a prescription-only medicine (POM) used to treat iron deficiency anaemia.

These tablets contain the active ingredient ferrous sulphate, which is a form of iron. Ferrous Sulphate 200mg Coated Tablets BP belong to a group of medicines called iron supplements.

Iron is needed by the body to maintain good health, particularly for making red blood cells that carry oxygen around the body. A shortage of iron may mean that the body cannot produce enough normal red blood cells to keep you healthy. This is known as iron deficiency anaemia. This can cause tiredness, breathlessness, palpitations, dizziness and headache.

Iron is found naturally in certain foods but for some people, who do not get enough iron from their diet, an iron supplement can be necessary. Some conditions can also cause iron deficiency anaemia, such as pregnancy or heavy periods.

No new or unexpected safety concerns arose from this application and it was therefore judged that the benefits of Ferrous Sulphate 200mg Coated Tablets BP outweigh the risks; hence a Marketing Authorisation has been granted.

Ferrous Sulphate 200mg Coated Tablets BP

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SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the MHRA granted Quantum Generics a Marketing Authorisation for the medicinal product Ferrous Sulphate 200mg Coated Tablets BP (PL 15894/0004) on 10th June 2011. The product is a prescription-only medicine (POM).

This is an abridged, bibliographic application for Ferrous Sulphate 200mg Coated Tablets BP, submitted under Article 10a (well-established use) of Directive 2001/83/EC, as amended.

Ferrous Sulphate 200mg Coated Tablets BP are indicated for the treatment of iron-deficiency anaemia.

Ferrous sulphate belongs to the pharmacotherapeutic group, anti-anaemic preparations, iron preparations (ATC code: R03A A07). Administration of iron preparations corrects erythropoietic abnormalities caused by a deficiency of iron. Iron is an essential component in cells and has several vital functions. Ionic iron is a component of a number of enzymes necessary for energy transfer (e.g., cytochrome oxidase, xanthine oxidase, succinic dehydrogenase) and is also present in compounds necessary for transport and utilisation of oxygen (e.g., haemoglobin, myoglobin). Iron deficiency can interfere with these vital functions and lead to morbidity and mortality.

No new non-clinical or clinical efficacy studies were necessary for this application, which is acceptable given that this was a bibliographic application for a product containing an active of well-established use. Bioequivalence studies are not necessary to support this bibliographic application.

The MHRA considers that the pharmacovigilance system as described by the Marketing Authorisation Holder (MAH) fulfils the requirements and provides adequate evidence that the MAH has the services of a Qualified Person (QP) responsible for pharmacovigilance and has the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

The Marketing Authorisation Holder has provided adequate justification for not submitting a detailed Environmental Risk Assessment (ERA). The ubiquity of iron and its salts in the environment does not present an environmental hazard and the incremental environmental burden likely to arise from use of ferrous sulphate tablets as a medicinal product is negligible. There are no environmental concerns associated with the method of manufacture or formulation of the product.

PHARMACEUTICAL ASSESSMENT

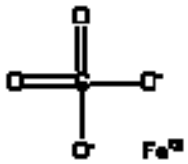
ACTIVE SUBSTANCE

Ferrous Sulphate

Nomenclature:

INN: Ferrous Sulphate

Structure:



Molecular formula:	$FeSO_4$, H_2O
Molecular weight:	151.9 g/mol (anhydrous)
CAS No:	13463-43-9
Physical form:	Greyish-white powder
Solubility:	Slowly but freely soluble in water, very soluble in boiling water, practically insoluble in ethanol (96 percent). It oxidises in air, becoming brown.

The active substance, ferrous sulphate, is the subject of a European Pharmacopeia (Ph. Eur.) monograph.

All aspects of the manufacture and control of ferrous sulphate are supported by a European Directorate for the Quality of Medicines (EDQM) Certificate of Suitability (CEP). The certificate is accepted as confirmation of the suitability of ferrous sulphate for inclusion in this medicinal product.

MEDICINAL PRODUCT

Description & Composition

Ferrous Sulphate 200mg Coated Tablets BP are presented as red, circular, slightly convex, coated tablets. Each tablet contains 200mg Ferrous Sulphate dried Ph. Eur. equivalent to 65mg elemental iron.

Other ingredients consist of pharmaceutical excipients, namely maize starch, maltodextrin, calcium stearate, lactose monohydrate, powdered cellulose, copovidone, sucrose, macrogol 4000, talc, sodium starch glycolate and sodium dodecyl sulphate making up the tablet core; and sucrose, colorant ponceau 4R (E124), red lacquer colour ponceau 4R Lake (E124), povidone K-25, talc, calcium carbonate, titanium dioxide E171, magnesium stearate, macrogol 4000, theobroma oil and shellac constituting the coating. Appropriate justification for the inclusion of each excipient has been provided.

All excipients of the tablet cores comply with their respective European Pharmacopoeia monographs. The coating is constituted from Ph. Eur. ingredients apart from the colourants, colorant ponceau 4R (E124) and red lacquer colour ponceau 4R Lake (E124), which comply with the EU colouring regulation 95/45/EC. The excipient, theobroma oil is controlled by the German pharmacopeia (DAB). Satisfactory Certificates of Analysis have been provided for all excipients.

The calcium stearate and magnesium stearate have been confirmed as being of vegetable origin. The only excipient used that contains material of animal or human origin is lactose monohydrate. The applicant has provided a declaration that milk used in the production of lactose monohydrate is sourced from healthy animals under the same conditions as that for human consumption. None of the excipients are sourced from genetically modified organisms.

There were no novel excipients used and no overages.

Pharmaceutical development

Details of the pharmaceutical development of the medicinal product have been supplied and are satisfactory. The objective was to develop a highly stable, coated tablet formulation that provides a good availability of the active ingredient, ferrous sulphate.

Satisfactory dissolution data were provided.

Manufacture

A description and flow-chart of the manufacturing method has been provided.

In-process controls are appropriate considering the nature of the product and the method of manufacture. Process validation studies were conducted and the results were satisfactory. The validation data demonstrated consistency of the manufacturing process.

Finished product specification

Finished product specifications are provided for both release and shelf-life and are satisfactory. Acceptance limits have been justified with respect to conventional pharmaceutical requirements and, where appropriate, safety. Test methods have been described and have been adequately validated, as appropriate. Satisfactory batch analysis data are provided and accepted. The data demonstrate that the batches are compliant with the proposed specifications. Certificates of Analysis have been provided for any reference standards used.

Container Closure System

Ferrous Sulphate 200mg Coated Tablets BP are licensed for marketing in polyvinylchloride (PVC)/polyvinylidene chloride (PVdC) - aluminium foil blister strips, which are placed with the Patient Information Leaflet (PIL) into cardboard outer cartons in pack sizes of 28 coated tablets.

Satisfactory specifications and Certificates of Analysis for all packaging components used have been provided. All primary product packaging complies with EU legislation, Directive 2002/72/EC (as amended), and is suitable for contact with foodstuffs.

Stability

Finished product stability studies have been conducted in accordance with current guidelines, using product stored in the packaging proposed for marketing. These data support a shelf-life of 36 months, with the storage instructions ‘Store in the original packaging’.

Quality Overall Summary

A satisfactory quality overview is provided, and has been prepared by an appropriately qualified expert. The CV of the expert has been supplied.

PRODUCT INFORMATION:

The approved Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling are satisfactory. Mock-ups of the PIL and labelling have been provided. The user-testing of the PIL has been evaluated and is accepted. The labelling fulfils the statutory requirements for Braille.

Conclusion

All pharmaceutical issues have been resolved and the quality grounds for this application are considered adequate. There are no objections to approval of Ferrous Sulphate 200mg Coated Tablets BP from a pharmaceutical point of view.

NON-CLINICAL ASSESSMENT

This is an abridged, bibliographic application for Ferrous Sulphate 200mg Coated Tablets BP, submitted under Article 10a of Directive 2001/83/EC, as amended.

Specific non-clinical studies have not been performed, which is acceptable considering that this was a bibliographic application for a product containing an active of well-established use.

As ferrous sulphate has been in clinical use for an extensive period of time, the non-clinical information has become of secondary relevance in the assessment of the risk/benefit of iron compared to the vast clinical experience in man. In view of the well-established use of iron salts in medical practice, together with the substantial body of data supporting the safety of iron salts, additional non-clinical studies are unnecessary. Therefore, the non-clinical overview is based on information derived from standard texts and a review of the more recent literature. The non-clinical overview provides a satisfactory review of the pharmacodynamic, pharmacokinetic, and toxicological properties of ferrous sulphate. The CV of the non-clinical expert has been supplied.

The Marketing Authorisation Holder has provided adequate justification for not submitting an Environmental Risk Assessment (ERA).

There are no objections to approval of Ferrous Sulphate 200mg Coated Tablets BP from a non-clinical point of view.

CLINICAL ASSESSMENT

1. INTRODUCTION AND BACKGROUND

This is an abridged, bibliographic application for Ferrous Sulphate 200mg Coated Tablets BP, submitted under Article 10a (well-established use) of Directive 2001/83/EC, as amended.

Iron preparations have been widely used in medicinal practice for decades, or even centuries, in the treatment of iron deficiency and related diseases. Numerous dosage forms containing ferrous sulphate have been authorised for a number of different indications in the European Community and are currently marketed in Member States.

Iron is an essential trace element needed for the synthesis of haemoglobin and other iron-containing proteins. Ferrous sulphate is used as a source of iron for patients with iron-deficiency anaemia. It is given by mouth and the dried form is frequently used in solid dosage forms. Usual doses of ferrous sulphate are up to 600 mg daily.

1.1 Indications

Ferrous Sulphate 200mg Coated Tablets BP are indicated for the treatment of iron-deficiency anaemia.

1.2 Dose and Dose Regimen

Full details concerning the posology are provided in the SmPC. The posology is satisfactory.

2. CLINICAL PHARMACOLOGY

2.1 Pharmacokinetics

Iron is irregularly and incompletely absorbed from the GI tract, the main sites of absorption being the duodenum and jejunum. Absorption is aided by the acid secretion of the stomach and by some dietary acids (such as ascorbic acid) and is more readily affected when the iron is in the ferrous state or is part of the haem complex (haem iron). Absorption is also increased in conditions of iron deficiency or in the fasting state but is decreased if the body stores are overloaded.

Ferrous iron passes through the GI mucosal cells directly into the blood and is immediately bound to transferrin. Transferrin, a glycoprotein beta1-globulin, transports iron to the bone marrow where it is incorporated into haemoglobin. Total body iron is determined by intake, loss, and storage of the mineral. Small excesses of iron within the villous epithelial cells are oxidized to the ferric state. Ferric iron combines with the protein apoferritin to yield ferritin and is stored in mucosal cells, which are exfoliated at the end of their life span and excreted in the faeces. Ferritin, a soluble protein complex, is the principal storage form of iron (about 70% in men and 80% in women), with smaller amounts being stored in haemosiderin, an insoluble protein complex. Ferritin and haemosiderin are present principally in the liver, reticuloendothelial system, bone marrow, spleen, and skeletal muscle; small amounts of ferritin also circulate in plasma.

Iron metabolism occurs in a virtually closed system. Most of the iron liberated by breakdown of haemoglobin is conserved and reused by the body. Daily excretion of iron in healthy men amounts to only 0.5 - 2 mg. This excretion occurs principally through faeces and via desquamation of cells in the skin, GI mucosa, nails, and hair; only trace amounts of iron are excreted in bile and sweat. Blood loss greatly increases iron loss. The average monthly loss of iron in normal menstruation is 12 - 30 mg, increasing the average iron requirements by 0.3 - 0.5 mg daily to compensate for this loss. The increased requirement secondary to pregnancy-associated tissue growth and blood loss at delivery and postpartum averages 3 mg daily over 280 days of gestation. In healthy individuals, trace amounts of blood are lost through physiological GI loss secondary to the normal turnover in the intestinal mucosa. Pathological GI blood loss occurs in infants and children sensitive to cow's milk and in adults secondary to peptic ulcer disease (including non-steroidal anti-inflammatory use), inflammatory bowel syndrome, and GI cancer. Parasitic infections also are associated with blood loss.

Assessor's comment:
An adequate description of the pharmacokinetics of oral iron has been presented.

3. CLINICAL EFFICACY

This section is based on a literature review provided by the applicant and does not contain any new clinical data. Summaries of clinical trials on ferrous iron salts have been presented by the applicant to illustrate the clinical benefits of treatment or prevention of iron deficiency states; most studies have been conducted in recent years. These clinical studies are largely confirmatory of the clinical efficacy of this product for use in the indication claimed by the applicant.

3.1 Treatment of Anaemia

Paediatric

The objective of the study of de Silva *et al* (2004) was to evaluate the effects of iron supplementation on iron status and morbidity in Sri Lankan children with or without infection. Children aged 5-10 years were recruited from outpatients for a randomised, controlled, double-blind study. Children with a history of recurrent upper respiratory tract infections (URTIs) and with laboratory and clinical evidence of a current URTI constituted the infection group (n = 179), and children without infection constituted the control group (n = 184). Subjects in both groups were supplemented with ferrous sulphate (60 mg elemental iron) or placebo once daily for 8 weeks. The overall prevalence of anaemia in the study population was 52.6% at baseline. Iron supplementation significantly improved iron status by increasing haemoglobin ($p < 0.001$) and serum ferritin ($p < 0.001$) concentrations from baseline values in the children with or without infection. There was no significant improvement in iron status in the children who received placebo. In both the infection group and the control group, the mean number of URTI episodes and the total number of days sick with an URTI during the period of intervention were significantly lower ($p < 0.005$ and $p < 0.001$, respectively) in the children who received iron supplements than in those who received placebo. It was concluded that iron supplementation significantly improved iron status and reduced morbidity from URTIs in children with or without infection.

Serum ferritin and haemoglobin levels were increased by daily and intermittent iron supplementation in both anaemic and non-anaemic high school girls in a study by Kianfar (2000). Subjects were randomised to receive either a daily dose of iron as 150 mg ferrous sulphate (50 mg elemental iron; n=92), the same dose twice weekly (n=112), the same dose once weekly (n=171), or no supplementation as a control (n=148) for a period of 3 months. After 3 months, haemoglobin and serum ferritin concentrations had increased in all treated groups ($p < 0.007$). Increases in the haemoglobin levels of anaemic girls were no different between the supplemented groups, but were all significantly greater than control ($p < 0.00001$). The rise in serum ferritin concentration was higher in the subjects receiving daily iron than in those in the other two treatment groups ($p < 0.00001$). During the study, the prevalence of anaemia dropped by 35% in the daily and twice-weekly groups and by 29% in the once-weekly group ($p < 0.0005$). Iron deficiency in all subjects decreased by 56.5% in the daily treated group, 26% in the twice-weekly group, and 24% with once-weekly supplementation. The investigators concluded that intermittent supplementation was as effective for the treatment of mild anaemia as daily administration.

Shobha and Sharada (2003) found that twice weekly dosing and daily dosing of iron were equally effective in raising the haemoglobin levels of adolescent Indian girls who had mild, moderate, or severe anaemia. In a randomised study, 203 anaemic adolescent girls, 13 to 15 years of age, were stratified into 3 groups according to haemoglobin level. Within the stratified groups, the girls were randomised to receive iron 60 mg and folic acid 0.5 mg either daily or twice weekly for 12 weeks. Haemoglobin levels rose steadily in all groups. By 9 weeks, the mildly anaemic subjects in the daily dosing group had achieved normal haemoglobin levels (12 g/dl), while those on twice-weekly dosing had near-normal levels. By 12 weeks, both mildly and severely anaemic girls had reached near-normal haemoglobin levels. During the study, abdominal pain was experienced by 41% of the girls in the daily dosing group and 5% of those in the twice-weekly group. Respective values for nausea were 11% vs 1%, and for vomiting 6% vs 0%. In view of the responsiveness of haemoglobin to twice-weekly iron supplementation at the expense of far fewer side-effects, which had been reported by others, the twice-weekly regimen was advocated on the likelihood of better compliance being achieved.

Beasley (2000) evaluated the effect of administering weekly doses of 400 mg of ferrous sulphate for 4 months on the iron status of adolescent girls in a controlled trial in Tanzania. Supplementation led to a significantly greater increase in serum ferritin compared with the control group (+ 15.6 µg/l vs. 8.6 µg/l; $p = 0.002$) but there was no significant difference in change in haemoglobin concentrations.

To assess the efficacy and acceptability of daily and intermittent iron supplementation, a double-blind, placebo-controlled trial was conducted in a public school in Peru (Zavaleta 2000). Adolescent girls (n = 312), 12-18 years old, were randomly assigned to one of the following three groups:

1) 60 mg iron as ferrous sulphate daily 5 days/week
2) 60 mg iron as ferrous sulphate 2 days/week and placebo 3 days (intermittent)
3) placebo from Monday to Friday.

Field-workers administered the supplements during school hours for 17 weeks. During the post-interventional period, haemoglobin, serum ferritin and free erythrocyte protoporphyrin were improved significantly in the iron-supplemented groups compared with the placebo group ($p < 0.05$). Daily supplements led to higher haemoglobin increases than intermittent supplements ($p < 0.05$). Serum ferritin and free erythrocyte protoporphyrin did not change in the two active groups, but fell in the placebo group. The proportion of anaemic subjects was similar in the three groups at entry to the trial. At the end of the trial the proportion of anaemic subjects in the daily treatment group (10.9%) was lower compared with the intermittent treatment (17.3%) and the placebo (22.7%) groups ($p < 0.05$).

Adult

Studies presented to support the efficacy of ferrous sulphate for the treatment of IDA in adults mainly focus on IDA in pregnancy.

Casparis *et al*, 1996 conducted a study in 40 women aged 20-35 presenting with iron-deficiency anaemia during or immediately after pregnancy. The women were divided into four treatment groups of 10 patients each and were treated as follows for 30 days: Group A with oral liquid ferrous gluconate (75 mg per day in 2 vials a day); Group B with solid ferrous gluconate (80 mg per day in a single effervescent tablet); Group C with solid ferrous sulphate (105 mg per day in a single tablet); and Group D with ferric protein succinylate (80 mg per day in 2 vials a day). Analysis of the therapeutic efficacy parameters (red blood cells, haemoglobin, haematocrit and serum iron) showed significant improvements but there were no statistically significant differences between the groups.

De Souza *et al*, 2004 conducted a randomised clinical trial with blinded laboratory analysis in order to evaluate the effectiveness of three regimens employing ferrous sulphate to treat pregnant women with anaemia. Iron (60 mg) was administered as 300 mg ferrous sulphate tablets. The women were allocated to three treatment groups according to the frequency of taking the tablets: once a week (48 women), twice a week (53 women), and daily (49 women). The groups were compared for values of haemoglobin concentration, mean corpuscular volume, and ferritin before and after treatment. The response rate (Hb > 11 g/dl) was 27% in the patients treated once a week, 34% in those treated twice a week, and 47% in the women treated daily. Treatment failure (Hb < 10 g/dl) was seen in 41.6%, 13.2%, and 2.0% of the patients in the respective groups.

In a study by Bayoumen *et al* (2002) oral ferrous sulphate 240 mg daily was given for 4 weeks, and was compared with IV iron sucrose in patients with iron deficiency detected at 6 months of pregnancy. After 4 weeks the requirement of each group for continued oral iron was determined. The effect of treatment on haemoglobin and reticulocytes was determined after 8, 15, 21 and 30 days and at delivery, and of ferritin on day 30 and at delivery. The baby's birth weight and iron stores were noted. An increase in haemoglobin was observed rising from 9.6 ± 0.79 g/dL to 11.11 ± 1.30 g/dL on day 30 in the IV group and from 9.7 ± 0.5 g/dL to 11.0 ± 1.25 g/dL on day 30 in the oral group (NS). There were no differences in haemoglobin between the two treatment groups at any time. Ferritin was higher in the IV group on days 30 and at delivery ($p < 0.0001$ and $p < 0.01$ respectively). Babies in the IV group were heavier but the difference between groups was not significant.

Kumar *et al* (2005) compared the effectiveness of oral iron supplementation (100 mg elemental iron) with two high dose (250 mg) intramuscular (IM) injections of iron sorbitol in 220 pregnant women with a singleton pregnancy with haemoglobin concentrations between 8 and 11 g/dL at 16 – 24 weeks. Blood indices were evaluated on enrolment and at 36 weeks of gestation. There were definitive and comparable improvements in haemoglobin and all blood indices in the two groups. Serum ferritin showed a significant but less than 1 μg/dL difference in favour of parenteral iron. Obstetric outcome was comparable in the two groups.

Bhandal and Russell (2006) undertook a prospective randomised trial to compare the effect of treatment with oral ferrous sulphate and IV ferrous sucrose on postpartum iron deficiency anaemia. Forty four women with haemoglobin of <9 g/dL and ferritin of <15 μg/L at 24 – 48 h post-delivery were randomised to receive either oral ferrous sulphate 200 mg twice daily for 6 weeks (group O) or IV ferrous sucrose 200 mg, two doses given on days 2 and 4 post enrolment (group I). By day 5, the haemoglobin level in women treated with IV iron had risen from 7.3 ± 0.9 to 9.9 ± 0.7 g/dL, while there was no change in those treated with oral iron. Women treated with IV iron had significantly higher haemoglobin levels on days 5 and 14 ($p < 0.01$) than women on oral iron, although by day 40, there was no significant difference between the two groups. Throughout the study ferritin levels rose rapidly in those treated with IV iron and remained significantly higher than in those treated with oral iron ($p < 0.01$). The study was not large enough to address the safety of the IV strategy. Although the clinical response was much slower with oral ferrous sulphate, this remains by far the most cost-effective treatment.

A Cochrane review by Reveiz in 2007 identified 17 trials involving 2578 women to assess the effects of different treatments for iron-deficiency anaemia in pregnancy on maternal and neonatal morbidity and mortality. The trials were small and generally methodologically poor. They covered a very wide range of differing drugs, doses and routes of administration, making it difficult to pool data. Oral iron in pregnancy showed a reduction in the incidence of anaemia. The conclusion of the authors was that although daily oral iron treatment improves haematological indices (but causes frequent gastrointestinal adverse effects), there was insufficient evidence to say when or how iron-deficiency anaemia in pregnancy needs to or should be treated.

Iron supplementation is required in virtually all patients with chronic renal failure who are receiving erythropoietin. It is generally accepted that oral iron is insufficient to meet the requirements of these patients, and that IV supplementation is necessary.

Rimon *et al* (2005) undertook a study in patients aged over 80 years to determine whether low-dose iron therapy could reverse iron-deficiency anaemia in this population. Ninety hospitalised patients with iron-deficiency anaemia were randomised to receive daily doses of 15 mg or 50 mg iron as liquid ferrous gluconate or 150 mg elemental iron as ferrous calcium citrate tablets, for 60 days. Thirty control patients without anaemia were given 15 mg of iron for 60 days. By day 60, iron treatment had significantly increased haemoglobin and ferritin concentrations to a similar extent in all three groups of anaemic patients (for example Hb levels rose from 10.0 g/dL to 11.3 g/dL with 15 mg/day of iron therapy and from 10.2 g/dL to 11.6 g/dL with 150 mg/day. The corresponding increases in ferritin were 40.4 and

44.1 ng/mL). In contrast, no significant changes occurred in the control group in either parameter. Abdominal discomfort, nausea, vomiting, changes in bowel habit and black stools were significantly more common at higher iron doses. The investigators therefore considered that low-dose iron treatment could replace the commonly used higher doses in octagenarians with iron deficiency anaemia, and significantly reduce adverse effects.

The clinical overview includes further evidence to demonstrate efficacy of ferrous sulphate in the treatment of iron deficiency anaemia in non-pregnant adults. Evidence has been provided for the use of ferrous sulphate in the treatment of iron-deficiency anaemia associated with the following conditions in adults:

- blood donation
- childbirth
- uterine haemorrhage
- following gastro-intestinal surgery
- colorectal carcinoma
- inflammatory bowel disease
- idiopathic viz. in the absence of overt blood loss, other deficiency states, malabsorption, or pregnancy

A further 15 clinical studies have been presented covering a range of aetiologies of IDA, and showing efficacy of oral ferrous sulphate in the treatment of IDA in adults.

Assessor's comment:
Adequate evidence has been provided to demonstrate efficacy of ferrous sulphate in prevention and treatment of IDA in children, and treatment of IDA in adults.

Dosage

The dosing instructions in adults and children, as proposed by the applicant in the SmPC, are supported by the literature presented in the clinical overview.

4. CLINICAL SAFETY

Serious and life-threatening hypersensitivity reactions have, until recently, been limited to the IV administration of iron salts, especially iron dextran and thus may be of limited relevance to the coated oral tablet formulation. A few cases of eruptive dermatoses have been reported as adverse reactions to oral iron salts and more serious reactions can also occur, as detailed in case reports (Ortega, 2000 - pruritus and erthyematous maculopapular eruptions in response to oral iron; de Barrio, 2000 – anaphylaxis in response to oral iron salts).

GI intolerance of iron preparations is mainly a function of the total amount of elemental iron per dose. The usual oral therapeutic doses of iron preparations including ferrous sulphate induce constipation, diarrhoea, dark stools, nausea, and/or epigastric pain in approximately 5 - 20% of patients (AHFS, 2009). GI symptoms are common with ferrous sulphate preparations, occurring in 10% of patients. Nausea and epigastric pain or discomfort usually subside within a few minutes to hours, whereas constipation and diarrhoea may not subside for several days (Brock *et al*, 1985); dark stools tend to persist throughout dosing.

Tablets should be taken with an amount of water adequate to ascertain that the tablet reaches the stomach, as the extended contact of the undissolved tablet with the oropharyngeal or laryngeal mucosae may cause irritation, ulceration or swallowing difficulties (Laine *et al*, 1988; Fernandez-Viadero *et al*, 1998; Jones *et al,* 2006; Abbarah *et al*, 1976). This is reflected in Section 4.2 of the SmPC.

The long-term administration of large amounts of iron may cause haemosiderosis clinically resembling haemochromatosis, a genetic condition characterised by excessive iron absorption, excess tissue iron stores, and potential tissue injury.

There has been concern about the potential consequences of iron supplementation in individuals and groups who are not actually iron-deficient. Apart from the suggestion that certain populations may be at increased risk of microbial infection following supplementation, there is some evidence that supplementation in non-iron-deficient children may retard their growth (Idjradinata *et al,* 1994). It has also been proposed that iron may be associated with ischaemic heart disease by modifying low-density lipoprotein in ways that increase its atherogenic potential, and by sensitising the myocardium to ischaemic injury (Burt *et al,* 1993; Sullivan, 1993). However, the conclusions of the important NHANES II mortality cohort study (Sempos *et al*, 2000) and a systematic review by meta-analysis (Danesh and Appleby, 1999) failed to support any correlation between iron status and coronary heart disease.

Assessor's comment:
The evidence presented to support the clinical safety of oral ferrous sulphate is adequate. The applicant has provided supportive evidence for the frequencies of each of the adverse events listed in Section 4.8 of the SmPC.

5. CLINICAL OVERVIEW

A satisfactory clinical overview is provided and has been prepared by an appropriately qualified expert. The CV of the clinical expert has been supplied.

6. PRODUCT INFORMATION:

Summary of Product Characteristics (SmPC)

The approved SmPC is satisfactory.

Patient Information Leaflet (PIL)

The final PIL is in line with the approved SmPC and is satisfactory.

Labelling

The labelling is satisfactory.

7. CONCLUSION

This application has been submitted as a so called “bibliographic application”; the applicant has submitted no new data. The pharmacodynamics and pharmacokinetics of ferrous sulphate are well-documented in the literature and the clinical use is established. Sufficient clinical information has been submitted to support this application. The product literature is approved. The grant of a Marketing Authorisation was, therefore, recommended.

OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

QUALITY

The important quality characteristics of Ferrous Sulphate 200mg Coated Tablets BP are well defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

NON-CLINICAL

No new non-clinical data were submitted and none are required for an application of this type.

CLINICAL

No new data are submitted and none are required for this type of application.

The published literature supports the efficacy of this product in the proposed indication, treatment of iron-deficiency anaemia. The safety and efficacy of ferrous sulphate is well-known. The presented evidence for well-established use of the active substance is sufficient.

The literature review identifies no new safety issues or concerns. The safety profile of ferrous sulphate is well-known.

PRODUCT LITERATURE

The approved SmPC is satisfactory.

The PIL is in line with the SmPC and is satisfactory. The package leaflet has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC, as amended. The results show that the package leaflet meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

The approved labelling artwork complies with statutory requirements. In line with current legislation, the name of the product in Braille appears on the outer packaging and sufficient space has been included for a standard UK pharmacy dispensing label.

BENEFIT-RISK ASSESSMENT

The quality of the product is acceptable and no new non-clinical or clinical safety concerns have been identified. Ferrous sulphate is an active substance of well-known safety and efficacy. It has been used for a number of decades in the EC. Extensive clinical experience with ferrous sulphate is considered to have demonstrated the therapeutic value of the active substance. The benefit: risk ratio is considered to be positive.

Ferrous Sulphate 200mg Coated Tablets BP

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STEPS TAKEN FOR ASSESSMENT

1 The MHRA received the Marketing Authorisation application on 15th April 2010

2 Following standard checks and communication with the applicant the MHRA considered the application valid on 4th May 2010

3 Following assessment of the application the MHRA requested further information relating to the quality dossier on 2nd September 2010 and 16th December 2010; and further information relating to the clinical dossier on 2nd July 2010 and 3rd November 2010

4 The applicant responded to the MHRA's requests, providing further information for the quality sections on 13th December 2010 and 1st March 2011 respectively; and further information for the clinical sections on 14th October 2010 and 13th January 2011 respectively

5 The application was determined 10th June 2011

Ferrous Sulphate 200mg Coated Tablets BP

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STEPS TAKEN AFTER AUTHORISATION

Date submitted	Application type	Scope	Outcome
21/06/2011	Pharmaceutical Type 1B	To add Kent Pharmaceuticals Limited, Wotton Road, Ashford, Kent, TN23 6LL as an own label supplier of the finished product. Consequentially, additional label and leaflet artworks have been provided.	Granted 18/07/2011

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Ferrous Sulphate 200mg Coated Tablets BP

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 200mg Ferrous Sulphate dried Ph Eur equivalent to 65mg elemental iron.

Also contains sucrose, lactose and Ponceau 4R colorant (E124).

For full list of excipients see Section 6.1.

3 PHARMACEUTICAL FORM

Coated tablets

Ferrous sulphate 200mg tablets are red, circular, slightly convex coated tablets.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of iron-deficiency anaemia

4.2 Posology and method of administration

Posology

Adults: one tablet 2-3 times daily
Paediatric population: Not recommended for children weighing less than 44kg. For children weighing over 44kg: one tablet twice daily. For children and adolescents weighing over 66kg: same as the adult dose.

The haemoglobin concentration should rise by about 2g/dL over 3-4 weeks. When the haemoglobin is in the reference range treatment should be continued for a further 3 months to replenish iron stores.

Special populations

Elderly (> 65 years): The usual adult dose can be administered.
Renal impairment: The usual adult dose can be administered. However, patients with chronic renal failure on haemodialysis may require iv iron therapy.

Method of administration

For oral use.

The tablets should be swallowed whole with a glass of water before food (see section 4.5)

The tablets should not be crushed or chewed.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients

Patients receiving repeated blood transfusions

Concomitant parenteral iron therapy

Haemochromatosis and other iron overload syndromes

4.4 Special warnings and precautions for use

General: before starting treatment, it is important to exclude any underlying cause of the anaemia (e.g. gastric erosion, colonic carcinoma).

Administer with caution in patients with haemolytic anaemia, haemoglobinopathies, iron-storage or iron-absorption diseases, existing gastrointestinal disease.

This product contains lactose and sucrose. Patients with rare hereditary problems of galactose intolerance or fructose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

This product also contains Ponceau 4R colorant (E124) which may cause allergic reactions. Iron preparations are a common cause of accidental overdose in children. The label will state "Important warning: Contains iron. Keep out of the reach and sight of children, as overdose may be fatal". This will appear on the front of the pack within a rectangle in which there is no other information.

4.5 Interaction with other medicinal products and other forms of interaction

The absorption of iron salts is decreased in the presence of antacids, preparations containing zinc, calcium, phosphorus, trientine, or when taken with tea, coffee, milk, eggs and whole grain foods. Iron supplements should not be taken within one hour before or two hours after ingestion of these products.

Cholestyramine may bind to iron in the gastrointestinal tract, thus preventing its absorption.

Chloramphenicol can reduce the response to iron therapy in iron deficiency anaemia.

Absorption of iron salts is enhanced by ascorbic acid and meat.

Concurrent administration with tetracyclines may impair absorption of both agents.

The absorption of quinolones (e.g. ciprofloxacin, norfloxacin, levofloxacin and ofloxacin) is reduced by oral iron. Iron salts may reduce the bioavailability of methyldopa, levodopa, entacapone, penicillamine, levothyroxine and bisphosphonates the effectiveness of which might be reduced.

Dimercaprol forms a toxic complex with iron and should not be given concomitantly.

4.6 Pregnancy and lactation

Ferrous salts are recommended for use in pregnancy and lactation, and no contraindications to such are known. No special requirements are to be anticipated.

Iron supplementation should not be routinely offered to all pregnant women in the absence of a diagnosis of iron deficiency anaemia.

4.7 Effects on ability to drive and use machines

None known

4.8 Undesirable effects

The most frequent adverse reactions to treatment with ferrous sulphate are gastrointestinal in origin. Although iron preparations are best absorbed on an empty stomach, they may be taken after food to reduce gastrointestinal side-effects.

The following terms and frequencies are applied: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000), not known (cannot be estimated from the available data).

Gastrointestinal disorders:
Very common: nausea, epigastric or abdominal pain, constipation
Common; diarrhoea, faeces discoloured, vomiting

Immune system disorders:
Not known: hypersensitivity reaction

Skin and subcutaneous tissue disorders:
Common: rash
Nausea and epigastric pain are dose-related but the relationship between dose and altered bowel habit (constipation, diarrhoea) is less clear. Iron preparations taken orally may have a constipating effect, particularly in older patients, occasionally leading to faecal impaction.

Hypersensitivity reactions have been reported with parenteral iron administration, but the frequency of occurrence is not known with ferrous sulphate taken orally. Hypersensitivity reactions to parenteral iron range from rash, sometimes severe, to anaphylactic reaction.

4.9 Overdose

Symptoms
Ingestion of 20 mg/kg elemental iron is potentially toxic and 200-250 mg/kg is potentially fatal. No single method of assessment is entirely satisfactory; clinical features as well as laboratory analysis must be taken into account. Peak serum levels in overdose are reached 4 to 6 hours following ingestion. Serum iron taken at about 4 hours after ingestion is the best laboratory measure of severity: less than 3 mg/L (55 micromol/L) means mild toxicity; 3-5 mg/L (55-90 micromol/L) means moderate toxicity; more than 5 mg/L (90 micromol/L) means severe toxicity.

Early features (less than 6 hours after ingestion) include nausea, vomiting, abdominal pain and diarrhoea; the vomit and stools may be grey or black.

In mild cases early features improve 6-12 hours after ingestion but in more serious cases there may be evidence of hypoperfusion (cool peripheries and hypotension), metabolic acidosis and systemic toxicity. There is often a latent phase with minimal symptoms which may last up to 24 hours and may be misinterpreted as an apparent recovery. In serious cases there can be recurrence of vomiting and gastrointestinal bleeding, 12 or more hours after ingestion. Shock can result from hypovolaemia or direct cardiotoxicity. Evidence of hepatocellular necrosis appears at this stage with jaundice, bleeding, hypoglycaemia, encephalopathy and positive anion gap metabolic acidosis. Poor tissue perfusion may lead to renal failure. Rarely, gastric scarring causing stricture or pyloric stenosis (alone or in combination) may lead to partial or complete bowel obstruction 2-5 weeks after ingestion.

Management
Management depends on clinical findings, dose and time from ingestion. Supportive and symptomatic measures include ensuring a clear airway and adequate ventilation, monitoring cardiac rhythm, BP and urine output, establishing intravenous access and administering sufficient fluids to ensure adequate hydration. Routine urea, electrolytes, liver function tests and blood counts, glucose and gases should be checked. Whole bowel irrigation should be considered.

If metabolic acidosis persists despite correction of hypoxia and adequate fluid resuscitation, for adults an initial dose of 50 mmol sodium bicarbonate may be given and repeated as necessary, guided by arterial blood gas monitoring (aim for pH of 7.4)

Administration of deferrioxamine should be considered if the patient is symptomatic (other than nausea) and serum iron concentration is between 3-5 mg/L (55-90 micromol/L) or higher and still rising. Haemodialysis does not remove iron effectively but should be considered on supportive basis for acute renal failure as this will facilitate removal of the iron-desferrioxamine complex.

Paediatric population
Iron preparations are an important cause of accidental overdose in children. As little as 20 mg/kg elemental iron is enough to lead to symptoms of toxicity.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: anti-anaemic preparations, iron preparations
ATC Code: B03A A07

Mechanism of action
Administration of iron preparations corrects erythropoietic abnormalities caused by a deficiency of iron. Iron is an essential component in cells and has several vital functions. Ionic iron is a component of a number of enzymes necessary for energy transfer (e.g.,

cytochrome oxidase, xanthine oxidase, succinic dehydrogenase) and is also present in compounds necessary for transport and utilisation of oxygen (e.g., haemoglobin, myoglobin). Iron deficiency can interfere with these vital functions and lead to morbidity and mortality.

5.2 Pharmacokinetic properties

Absoption
Absorption of iron from a 200mg ferrous sulphate tablet is evident within 0.5 hours and reaches a peak concentration in plasma after 2-3 hours. Absorption occurs principally in the duodenum and proximal jejunum and is most efficient when iron is ingested in its ferrous rather than its ferric form, on an empty stomach. Gastric acid increases absorption by maintaining ferric iron in a soluble form.

Absorption of iron is influenced by many factors including the form in which it is administered, the dose, iron stores, the degree of erythropoiesis, and diet. The principal factor controlling absorption is the amount of iron stored in the body. Absorption increases when body iron stores are low and decreases when stores are sufficient or large. Increased erythrocyte production also can stimulate absorption. In iron-deficient individuals, 10 to 30% is absorbed, the amount being approximately proportional to the degree of deficiency, compared to 5 to 15% in non-iron deficient individuals.

Distribution
When taken orally, in food or as a supplement, iron passes through the mucosal cells in the ferrous state and is bound with the protein transferrin.

Elimination
No physiological system of elimination exists for iron, and it can accumulate in the body to toxic amounts. Most of the iron liberated by destruction of haemoglobin is conserved and reused by the body. Excretion occurs principally through faeces and as desquamation of cells such as skin, GI mucosa, nails, and hair. Blood loss greatly increases iron loss.

5.3 Preclinical safety data

The long-established use of iron salts, including ferrous sulphate, in clinical practice, and the consequential abundance of data on the human effects of iron, renders the animal data on iron toxicity of secondary importance.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core:

Maize starch
Maltodextrin
Calcium stearate
Lactose monohydrate
Cellulose powdered
Copovidone
Sucrose
Macrogol 4000
Talc
Sodium starch glycolate
Sodium dodecyl sulphate

Coating:

Sucrose
Colorant Ponceau 4R E124
Red lacquer Colour Ponceau 4R Lake E124
Povidone K-25
Talc
Calcium carbonate

Titanium dioxide E171
Magnesium stearate
Macrogol 4000
Theobroma oil
Shellac

6.2 Incompatibilities

None known

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store in the original packaging

6.5 Nature and contents of container

PVC-PVDC/Aluminium blister pack

Pack size: 28 tablets

6.6 Special precautions for disposal

Not applicable

7 MARKETING AUTHORISATION HOLDER

Quantum Generics
57-65 Station Road
Redhill
Surrey
RH1 1DL

8 MARKETING AUTHORISATION NUMBER(S)

PL 15894/0004

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10/06/2011

10 DATE OF REVISION OF THE TEXT

10/06/2011

PRODUCT INFORMATION LEAFLET

PACKAGE LEAFLET

FERROUS SULPHATE
200 MG COATED TABLETS BP

The name of your medicine is Ferrous Sulphate 200 mg coated tablets BP, referred to as Ferrous Sulphate tablets or ferrous sulphate throughout this leaflet.

Read all of this leaflet carefully before you start taking this medicine

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT FERROUS SULPHATE TABLETS ARE AND WHAT THEY ARE USED FOR

Ferrous Sulphate tablets contain the active ingredient ferrous sulphate which is a form of iron. They belong to the group of medicines called iron supplements.

Iron is needed by the body to maintain good health, particularly for making red blood cells that carry oxygen around the body.

A shortage of iron may mean that the body cannot produce enough normal red blood cells to keep you healthy. This is known as iron deficiency anaemia. This can cause tiredness, breathlessness, palpitations, dizziness and headache.

Iron is found naturally in certain foods, but for some people who do not get enough iron from their diet an iron supplement can be necessary. Some conditions can also cause iron deficiency anaemia, such as pregnancy or heavy periods.

Ferrous Sulphate tablets are used to treat iron deficiency anaemia.

2. BEFORE YOU TAKE FERROUS SULPHATE TABLETS

Do not take Ferrous Sulphate Tablets:

- If you are **allergic** (hypersensitive) to ferrous sulphate or any of the other ingredients in the tablets (see section 6 of this leaflet).
- If you are receiving repeated **blood transfusions**
- If you are receiving **iron intravenously**
- If you have a disorder in which there is **too much iron in your blood.**

Tell your doctor before taking Ferrous Sulphate tablets if you think any of the above applies to you.

Take special care with Ferrous Sulphate Tablets and tell your doctor or pharmacist:

- If you suffer from any disease which affects your stomach and intestines (gastro-intestinal tract),
- If you suffer from any form of anaemia other than iron deficiency anaemia or from any other condition which affects your body's iron levels.

Before starting treatment with Ferrous Sulphate tablets it is important to exclude any underlying cause of the anaemia such as heavy periods, or blood loss in the stool or urine.

If you are not sure if any of the above applies to you, talk to your doctor or pharmacist before taking Ferrous Sulphate tablets.

Taking other medicines

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without prescription.

Especially if you are taking any of the following, as ferrous sulphate can reduce the effect of these medicines:

- Tetracycline antibiotics (to treat infections), such as tetracycline or doxycyline
- Ciprofloxacin, norfloxacin, levofloxacin or ofloxacin (antibiotics to treat infections)
- Methyldopa (to treat high blood pressure)
- Levodopa or entacapone (for Parkinson's disease)
- Penicillamine (for rheumatoid arthritis)
- Levothyroxine (to treat thyroid problems)
- Bisphosphonates such as alendronate or clodronate (to prevent loss of bone mass or to treat osteoporosis)

Please also tell your doctor or pharmacist if you are taking:

- Chloramphenicol by mouth or injection (to treat an infection), as this can reduce the response to treatment with ferrous sulphate
- Dimercaprol (to treat poisoning with certain metals), as this causes a toxic (harmful) complex with ferrous sulphate
- Colestyramine (to reduce blood cholesterol), as this can prevent the absorption of iron

Some other medications can also affect the absorption of iron. Do not take Ferrous Sulphate tablets within one hour before or two hours after taking antacids (for indigestion), trientine (for Wilson's disease) or medicines containing zinc, calcium, phosphorus.

Taking Ferrous Sulphate tablets with food and drink

Some foods can affect the absorption of iron. It is advisable not to take your medicine within one hour before or two hours after eating wholegrain foods or eggs or drinking tea, coffee or milk, as this may reduce the effect of the tablets.

Pregnancy and Breast-feeding

Ask your doctor or pharmacist for advice before taking any medicine. You should let your doctor know if you are pregnant, think you are pregnant, are planning to become pregnant or if you are breast-feeding.

Important information about some of the ingredients of Ferrous Sulphate tablets

Ferrous Sulphate tablets contain the colour E124 which may cause allergic reactions.

This product contains lactose and sucrose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. HOW TO TAKE FERROUS SULPHATE TABLETS

Method of administration

Swallow the tablets whole with a glass of water.

Do not break, crush or chew the tablets, or put them in water before swallowing.

It is best to take Ferrous Sulphate tablets on an empty stomach, but they may be taken after food to reduce gastro-intestinal side effects.

Dosage

Always take Ferrous Sulphate tablets exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure. Your doctor will tell you how much you should take and how often.

Adults including the elderly:

The usual dose is one tablet two or three times a day.

Children:

Children weighing over 44kg: one tablet twice a day.

Children and adolescents weighing over 66kg: one tablet three times a day.

Ferrous Sulphate tablets should not be given to children weighing less than 44kg.

Your doctor will advise you on how long you should take the tablets.

If you have taken more Ferrous Sulphate Tablets than you should

If you take too many tablets or you think a child may have swallowed any, go to your nearest hospital casualty department or contact your doctor immediately even if you feel well, because of the risk of serious side effects. Take the tablet pack with you so that the medical staff know exactly what you have taken.

The initial symptoms of an overdose may include being sick, diarrhoea, a racing heart (tachycardia) and tiredness.

If you forget to take Ferrous Sulphate Tablets

If you forget to take a dose, take it as soon as you remember. However, if it is nearly time for the next dose, skip the missed dose. Do not take a double dose (two doses at the same time) to make up for a forgotten dose.

If you have any further questions about these tablets, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Ferrous Sulphate tablets can cause side effects, although not everybody gets them.

If you experience any of the following side effects, **stop taking Ferrous Sulphate tablets and tell your doctor immediately:**

An allergic reaction which may occur as

- Swollen face or tongue
- Shortness of breath or difficulty breathing
- Itchy skin rashes

Tell your doctor as soon as possible if you notice any of the following side effects:

- Stomach discomfort
- Feeling sick or being sick
- Constipation
- Diarrhoea

Also, you might find your stools are darker in colour after you have taken this medicine. This is quite commonly seen with all iron preparations and is normal.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE FERROUS SULPHATE TABLETS

IMPORTANT WARNING: Contains iron

KEEP OUT OF THE REACH AND SIGHT OF CHILDREN, as overdose may be fatal.

Do not use Ferrous Sulphate tablets after the expiry date which is stated on the carton. The expiry date refers to the last day of the month.

Store the tablets in the original packaging.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer needed. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Ferrous Sulphate Tablets contain

The active substance is dried ferrous sulphate BP. Each tablet contains 200 mg dried ferrous sulphate BP equivalent to 65 mg ferrous iron (the ingredient that makes the tablets work).

The other ingredients are maize starch, maltodextrin, calcium stearate, lactose monohydrate, cellulose powdered, co-povidone, sucrose, Macrogol 4000, talc, sodium starch glycollate, sodium dodecyl sulphate, Ponceau 4R red colour and red lacquer (E124), povidone, calcium carbonate, titanium dioxide (E171), magnesium stearate, shellac, theobroma oil.

What Ferrous Sulphate Tablets look like and contents of the pack

The tablets are red circular biconvex coated tablets. The tablets come in packs of 28 tablets.

Marketing authorisation holder

Quantum Generics Limited
57-65 Station Road, Redhill, Surrey RH1 1DL

Manufacturer

Lomapharm – Rudolf Lohmann GmbH KG
Langes Feld 5, D – 31860 Emmerthal, Germany

This leaflet was last approved in June 2011

Alternative Patient Information Leaflet

CP.FES.200T.V1P1

PACKAGE LEAFLET

FERROUS SULPHATE

200 MG COATED TABLETS BP

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- If you suffer from any form of anaemia other than iron deficiency anaemia or from any other condition which affects your body's iron levels.

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57-65 Station Road, Redhill, Surrey RH1 1DL

Manufacturer

Lomapharm – Rudolf Lohmann GmbH KG
Langes Feld 5, D – 31860 Emmerthal, Germany

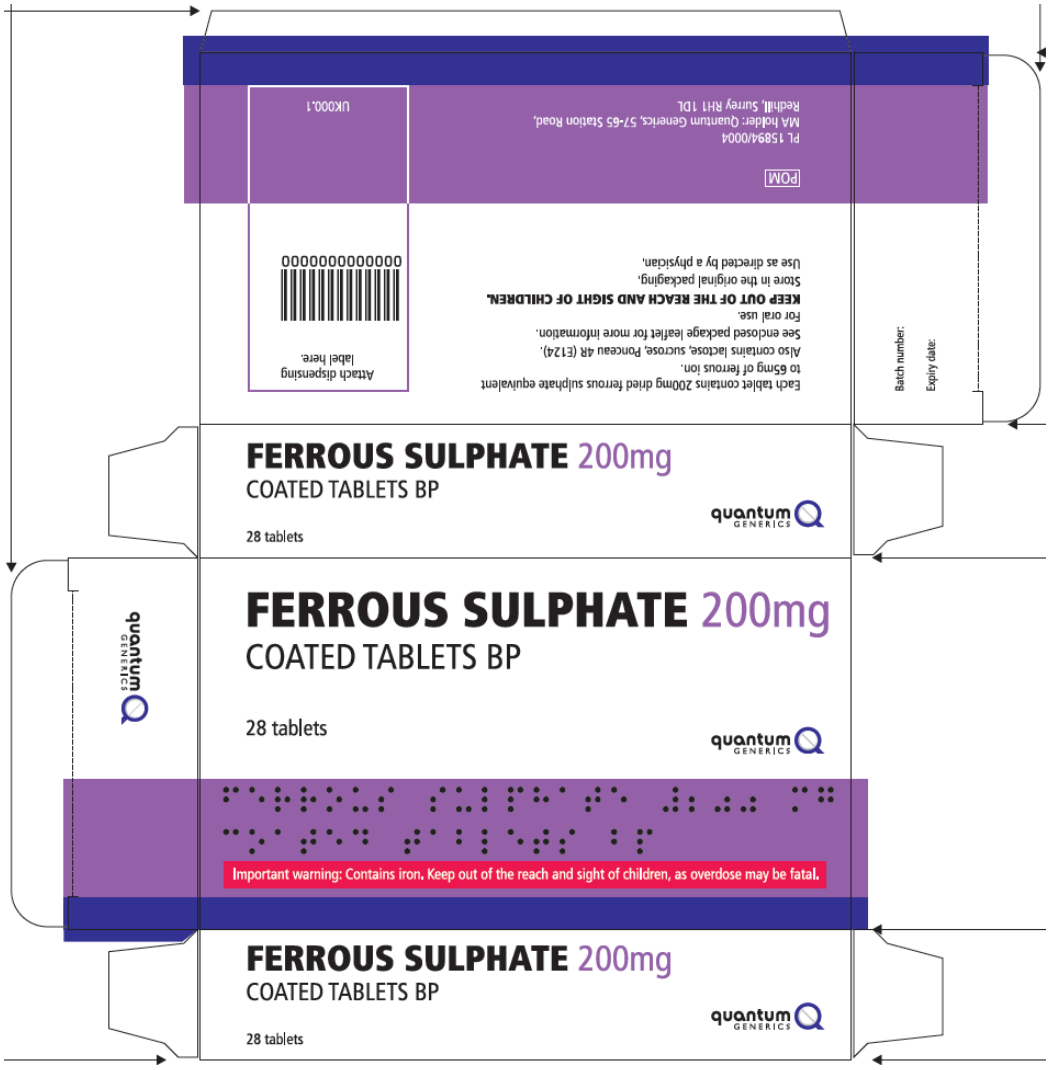
Distributor

Kent Pharmaceuticals Limited,
Repton Road, Measham, DE12 7DT, U.K.

This leaflet was last approved in June 2011

LABELLING

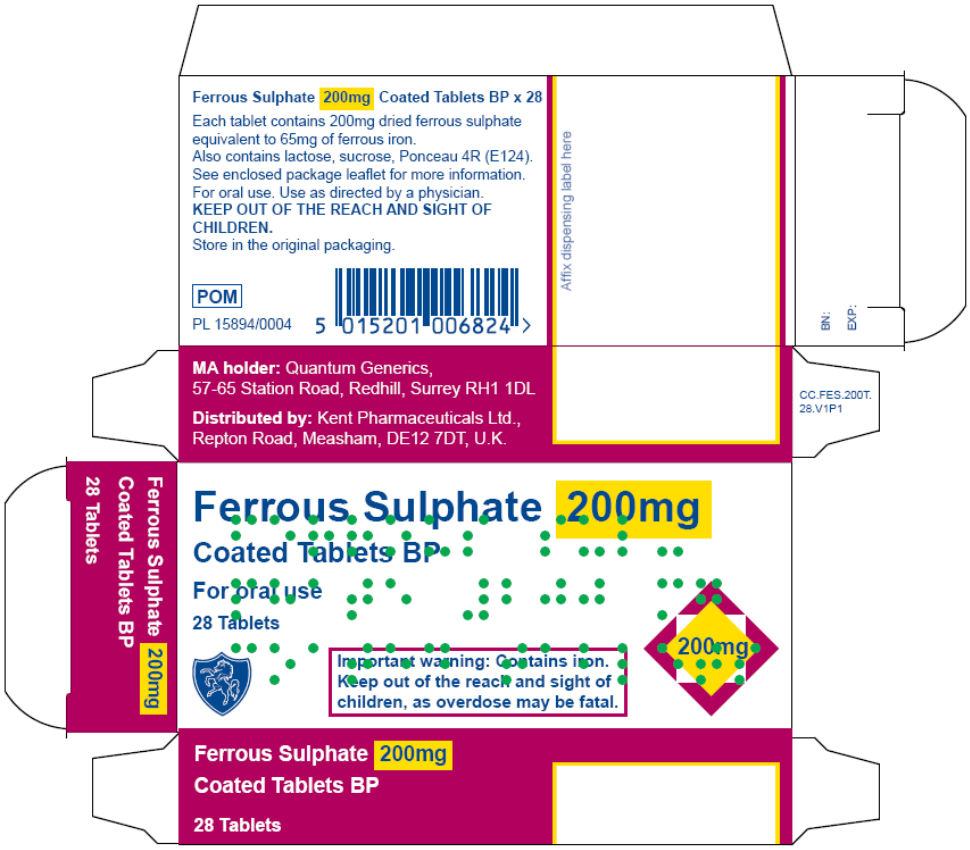
Carton



Blister foil

Alternative Labelling

Carton



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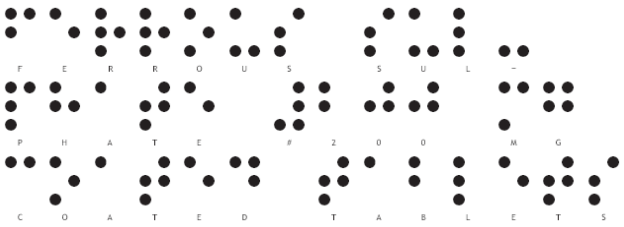

Blister foil