ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Velphoro 500 mg chewable tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each chewable tablet contains sucroferric oxyhydroxide corresponding to 500 mg iron.

The sucroferric oxyhydroxide contained in one tablet is comprised of polynuclear iron (III)-oxyhydroxide (containing 500 mg iron), 750 mg sucrose and 700 mg starches (potato starch and pregelatinised maize starch).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Chewable tablet.
Brown, circular tablets embossed with PA500 on one side. Tablets have a 20 mm diameter and a thickness of 6.5 mm.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Velphoro is indicated for the control of serum phosphorus levels in adult chronic kidney disease (CKD) patients on haemodialysis (HD) or peritoneal dialysis (PD).

Velphoro is indicated for the control of serum phosphorus levels in paediatric patients 2 years of age and older with CKD stages 4-5 (defined by a glomerular filtration rate <30 mL/min/1.73 m²) or with CKD on dialysis.

Velphoro should be used within the context of a multiple therapeutic approach, which could include calcium supplement, 1,25-dihydroxy vitamin D_3 or one of its analogues, or calcimimetics to control the development of renal bone disease.

4.2 Posology and method of administration

Posology

Starting dose for adults and adolescents (⩾12 years of age)
The recommended starting dose is 1,500 mg iron (3 tablets) per day, divided across the meals of the day.

Titration and maintenance for adults and adolescents (⩾12 years of age)
Serum phosphorus levels must be monitored and the dose of sucroferric oxyhydroxide up or down titrated in increments of 500 mg iron (1 tablet) per day every 2 – 4 weeks until an acceptable serum phosphorus level is reached, with regular monitoring afterwards.

In clinical practice, treatment will be based on the need to control serum phosphorus levels, though patients who respond to Velphoro therapy usually achieve optimal serum phosphorus levels at doses of 1,500 – 2,000 mg iron per day (3 to 4 tablets).

If one or more doses are missed, the normal dose of the medicinal product should be resumed with the next meal.

Maximum tolerated daily dose for adults and adolescents (≥12 years of age)
The maximum recommended dose is 3,000 mg iron (6 tablets).

Starting dose, titration and maintenance for paediatric patients (2 to <12 years of age)
Velphoro is also available as 125 mg oral powder in sachet for use in paediatric patients 2 to <12 years of age. The choice of the formulation depends on patient's age, preference, characteristics and compliance. When transitioning between formulations, the same recommended dose should be used. Recommended starting doses and dose titrations of Velphoro for paediatric patients 2 to <12 years of age are shown in the Table 1.

Table 1 Recommended starting doses and dose titrations for paediatric patients 2 to <12 years of age

Patient age (years)	Daily starting dose	Dose increases or decreases	Maximum recommended daily dose
≥2 to <6	500 mg	125 or 250 mg	1,250 mg
≥6 to <9	750 mg	125, 250 or 375 mg	2,500 mg
≥9 to <12	1,000 mg	250 or 500 mg	3,000 mg

For patients 2 to <6 years of age oral powder should be administered, as the chewable tablet formulation is not appropriate for this age group.

For patients 6 to <12 years of age Velphoro chewable tablets may be prescribed instead of or in combination with Velphoro oral powder in case the daily dose is 1,000 mg iron (2 chewable tablets) or more.

Serum phosphorus levels must be monitored and the dose of sucroferric oxyhydroxide up or down titrated in increments per day every 2 – 4 weeks until an acceptable serum phosphorus level is reached, with regular monitoring afterwards.

Paediatric population <2 years of age
The safety and efficacy of Velphoro in children below the age of 2 years has not been established. No data are available.

Renal impairment
Velphoro is indicated for the control of serum phosphorus levels in adult CKD patients on HD or PD. There is no clinical data available in patients with earlier stages of renal impairment.

Hepatic impairment
Patients with severe hepatic impairment were excluded from participating in clinical studies with sucroferric oxyhydroxide. However, no evidence of hepatic impairment or significant alteration of hepatic enzymes were observed in the clinical studies with sucroferric oxyhydroxide. See further information in section 4.4.

Elderly population (≥65 years of age)
Velphoro has been administered to over 248 seniors (≥65 years of age) according to the approved dosing regimen. Of the total number of subjects in clinical studies of sucroferric oxyhydroxide, 29.7% were aged 65 years and over, while 8.7% were aged 75 years and over. No special dose and administration guidelines were applied to seniors in these studies and the dosing schedules were not associated with any significant concerns.

Method of administration

Oral use.
Velphoro is a chewable tablet that must be taken with meals. In order to maximise the adsorption of dietary phosphate, the total daily dose should be divided across the meals of the day. Patients are not required to drink more fluid than they normally would and should adhere to their prescribed diets. Tablets must be chewed or crushed; tablets must not be swallowed whole.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Haemochromatosis and any other iron accumulation disorders.

4.4 Special warnings and precautions for use

Peritonitis, gastric and hepatic disorders and gastrointestinal surgery

Patients with a recent history of peritonitis (within the last 3 months), significant gastric or hepatic disorders and patients with major gastrointestinal surgery have not been included in clinical studies with Velphoro. Velphoro treatment should only be used in these patients following careful assessment of benefit/risk.

Discoloured stool

Sucroferric oxyhydroxide can cause discoloured (black) stool. Discoloured (black) stool may visually mask gastrointestinal bleeding (see section 4.5).

Information about sucrose and starches (carbohydrates)

Velphoro contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicinal product. It may be harmful to the teeth.

Velphoro contains potato starch and pregelatinised maize starch. Patients with diabetes should take notice that one tablet of Velphoro is equivalent to approximately 1.4 g of carbohydrates (equivalent to 0.116 bread units).

4.5 Interaction with other medicinal products and other forms of interaction

Velphoro is almost not absorbed from the gastrointestinal tract. Although the potential for interactions with medicinal products seems low, for concomitant treatment with medicinal products with a narrow therapeutic window, the clinical effect and adverse events should be monitored, on initiation or dose-adjustment of either Velphoro or the concomitant medicinal product, or the physician should consider measuring blood levels. When administering any medicinal product that is already known to interact with iron (like alendronate and doxycycline) or has the potential to interact with sucroferric oxyhydroxide based only on *in vitro* studies like levothyroxine, the medicinal product should be administered at least one hour before or two hours after Velphoro.

In vitro studies with the following active substances did not show any relevant interaction: acetylsalicylic acid, cephalexin, cinacalcet, ciprofloxacin, clopidogrel, enalapril, hydrochlorothiazide, metformin, metoprolol, nifedipine, pioglitazone and quinidine.

Interaction studies have only been performed in healthy volunteers. They have been conducted in healthy human male and female subjects with losartan, furosemide, digoxin, warfarin, and omeprazole. Concomitant administration of Velphoro did not affect the bioavailability of these medicinal products as measured by the area under the curve (AUC).

Data from clinical studies have shown that sucroferric oxyhydroxide does not affect the lipid lowering effects of HMG-CoA reductase inhibitors (e.g., atorvastatin and simvastatin). In addition, post-hoc analyses from clinical studies demonstrated no impact of Velphoro on iPTH lowering effect of oral Vitamin D analogues. Vitamin D and 1,25-dihydroxy Vitamin D levels remained unchanged.

Velphoro does not affect guaiac based (Haemoccult) or immunological based (iColo Rectal and Hexagon Obti) faecal occult blood tests.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no available clinical data from the use of sucroferric oxyhydroxide on exposed human pregnancies.

Reproductive and developmental toxicity studies in animals revealed no risk with respect to pregnancy, embryonic/foetal development, parturition or postnatal development (see section 5.3). Sucroferric oxyhydroxide should only be used by pregnant women if clearly needed following careful assessment of benefit/risk.

Breast-feeding

There are no available clinical data from the use of Velphoro in breast-feeding women. Since absorption of iron from this medicinal product is minimal (see section 5.2), excretion of iron from sucroferric oxyhydroxide in breast milk is unlikely. A decision on whether to continue breast-feeding or to continue therapy with sucroferric oxyhydroxide should be made taking into account the benefit of breast-feeding to the child and the benefit of Velphoro therapy to the mother.

Fertility

There are no data on the effect of Velphoro on fertility in humans. In animal studies, there were no adverse effects on mating performance, fertility, and litter parameters following treatment with sucroferric oxyhydroxide (see section 5.3).

4.7 Effects on ability to drive and use machines

Velphoro has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

The current safety profile of Velphoro is based on a total of 778 patients on haemodialysis and 57 patients on peritoneal dialysis, who received sucroferric oxyhydroxide treatment of up to 55 weeks.

In these clinical trials, approximately 43% of the patients experienced at least one adverse reaction during Velphoro treatment, and 0.36% of the adverse reactions were reported as serious. The majority of the adverse reactions reported from trials were gastrointestinal disorders, with the most frequently reported adverse reactions being diarrhoea and discoloured faeces (very common). The vast majority of these gastrointestinal disorders occurred early during treatment and abated with time with continued dosing. No dose-dependent trends were observed in the adverse reaction profile of Velphoro.

Tabulated list of adverse reactions

Adverse reactions reported from the use of Velphoro at doses from 250 mg iron/day to 3,000 mg iron/day in these patients (n=835) are listed in Table 2.

The reporting rate is classified as very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100).

Table 2 Adverse reactions detected in clinical trials

System organ class	Very common	Common	Uncommon
Metabolism and nutrition disorders			Hypercalcaemia Hypocalcaemia
Nervous system disorders			Headache
Respiratory, thoracic and mediastinal disorders			Dyspnoea
Gastrointestinal disorders	Diarrhoea* Faeces discoloured	Nausea Constipation Vomiting Dyspepsia Abdominal pain Flatulence Tooth discolouration	Abdominal distension Gastritis Abdominal discomfort Dysphagia Gastro-oesophageal reflux disease (GORD) Tongue discolouration
Skin and subcutaneous tissue disorders			Pruritus Rash
General disorders and administration site conditions		Product taste abnormal	Fatigue

Description of selected adverse reactions

**Diarrhoea*

Diarrhoea occurred in 11.6% of patients in clinical trials. In the 55 weeks long term studies, the majority of these diarrhoea adverse reactions were transient, occurred early during treatment initiation and led to treatment discontinuation in 3.1% of the patients.

Paediatric population

In general, the safety profile of Velphoro in paediatric (2 to <18 years of age) and adult patients was comparable. The adverse reactions most frequently reported were gastrointestinal disorders including diarrhoea (very common, 16.7%), vomiting (common, 6.1%), gastritis (common, 3.0%) and discoloured faeces (common, 3.0%).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Any instances of overdose of Velphoro (e.g. hypophosphataemia) should be treated by standard clinical practice.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: All other therapeutic products; drugs for treatment of hyperkalaemia and hyperphosphataemia; ATC code: V03AE05

Mechanism of action

Velphoro contains sucroferric oxyhydroxide which is comprised of polynuclear iron(III)-oxyhydroxide (pn-FeOOH), sucrose and starches. Phosphate binding takes place by ligand exchange between hydroxyl groups and/or water and the phosphate ions throughout the physiological pH range of the gastrointestinal tract.

Serum phosphorus levels are reduced as a consequence of the reduced dietary phosphate absorption.

Clinical efficacy

One phase 3 clinical study has been performed in patients with CKD on dialysis to investigate the efficacy and safety of Velphoro in this population. This study was an open-label, randomised, active-controlled (sevelamer carbonate), parallel group study for up to 55 weeks. Adult patients with hyperphosphataemia (serum phosphorus levels ≥1.94 mmol/L) were treated with sucroferric oxyhydroxide at a starting dose of 1,000 mg iron/day followed by an 8-week dose titration period. Non-inferiority to sevelamer carbonate was determined at week 12. Subjects were continued on their study medication from week 12 to week 55. From week 12 to 24, dose titrations were allowed for both tolerability and efficacy reasons. Treatment of patient sub-populations from week 24 to week 27 with maintenance dose of sucroferric oxyhydroxide (1,000 to 3,000 mg iron/day) or low dose (250 mg iron/day) of sucroferric oxyhydroxide demonstrated superiority of the maintenance dose.

In Study-05A, 1,055 patients on haemodialysis (N=968) or peritoneal dialysis (N=87) with serum phosphorus ≥1.94 mmol/L following a 2 – 4-week phosphate binder washout period, were randomised and treated with either sucroferric oxyhydroxide, at a starting dose of 1,000 mg iron/day (N=707), or active-control (sevelamer carbonate, N=348) for 24 weeks. At the end of week 24, 93 patients on haemodialysis whose serum phosphorus levels were controlled (<1.78 mmol/L) with sucroferric oxyhydroxide in the first part of the study, were re-randomised to continue treatment with either their week 24 maintenance dose (N=44 or a non-effective low dose control 250 mg iron/day, N=49) of sucroferric oxyhydroxide for a further 3 weeks.

Following completion of Study-05A, 658 patients (597 on haemodialysis and 61 on peritoneal dialysis) were treated in the 28-week extension study (Study-05B) with either sucroferric oxyhydroxide (N=391) or sevelamer carbonate (N=267) according to their original randomization.

Mean serum phosphorus levels were 2.5 mmol/L at baseline and 1.8 mmol/L at week 12 for sucroferric oxyhydroxide (reduction by 0.7 mmol/L). Corresponding levels for sevelamer carbonate at baseline were 2.4 mmol/L and 1.7 mmol/L at week 12 (reduction by 0.7 mmol/L), respectively.

The serum phosphorus reduction was maintained over 55 weeks. Serum phosphorus levels and calcium-phosphorus product levels were reduced as a consequence of the reduced dietary phosphate absorption.

The response rates, defined as the proportion of subjects achieving serum phosphorus levels within the Kidney Disease Outcomes Quality Initiative (KDOQI) recommended range were 45.3% and 59.1% at week 12 and 51.9% and 55.2% at week 52, for sucroferric oxyhydroxide and sevelamer carbonate, respectively.

The mean daily dose of Velphoro over 55 weeks of treatment was 1,650 mg iron and the mean daily dose of sevelamer carbonate was 6,960 mg.

Post-authorisation data

A prospective, non-interventional, post-authorisation safety study (VERIFIE) has been conducted, evaluating the short- and long-term (up to 36 months) safety and effectiveness of Velphoro in adult patients on haemodialysis (N=1,198) or peritoneal dialysis (N=160), who were followed in routine clinical practice for 12 to 36 months (safety analysis set, N=1,365). During the study, 45% (N=618) of these patients were concomitantly treated with phosphate binder(s) other than Velphoro.

In the safety analysis set, the most common ADRs were diarrhoea and discoloured faeces, reported by 14% (N=194) and 9% (N=128) of patients, respectively. The incidence of diarrhoea was highest in the first week and decreased with duration of use. Diarrhoea was of mild to moderate intensity in most patients and resolved in the majority of patients within 2 weeks. Discoloured (black) faeces is expected for an oral iron-based compound, and may visually mask gastrointestinal bleeding. For 4 of the 40 documented concomitant gastrointestinal bleeding events, Velphoro-related stool discolouration was reported as causing an insignificant delay in diagnosis of gastrointestinal bleeding, without affecting patient health. In the remaining cases, no delay in diagnosis of gastrointestinal bleeding has been reported.

The results from this study showed that the effectiveness of Velphoro in a real-life setting (including concomitant use of other phosphate binders in 45% of patients), was in line with that observed in the phase 3 clinical study.

Paediatric population

An open label clinical study investigated the efficacy and safety of Velphoro in paediatric patients 2 years of age and older with CKD, and hyperphosphatemia (CKD stages 4-5 (defined by a glomerular filtration rate <30 mL/min/l .73 m²) or with CKD on dialysis). Eighty-five subjects were randomised to Velphoro (N=66) or active control calcium acetate arm (N=19) for a 10-week dose titration (Stage 1), followed by a 24-week safety extension (Stage 2). Most patients were ≥12 years of age (66%). Eighty percent of patients were CKD patients on dialysis (67% on haemodialysis and 13% on peritoneal dialysis) and 20% were CKD patients not on dialysis.

The limited difference in reduction in mean serum phosphorus level from baseline to the end of Stage 1 in the Velphoro group (N=65) was not statistically significant with -0.120 (0.081) mmol/L (95% CI: -0.282, 0.043) based on the mixed model calculations with actual data showing a mean of 2.08 mmol/L at baseline and 1.91 mmol/L at the end of Stage 1 (reduction by 0.17 mmol/L). The effect was maintained during Stage 2, although some fluctuations in mean effect over time were noticed (0.099 (0.198) mmol/L (95% CI: -0.306, 0.504)).

The percentage of subjects with serum phosphorus levels within normal ranges increased from 37% at baseline to 61% at the end of Stage 1, and was 58% at the end of Stage 2, showing the sustainable phosphorus lowering effect of sucroferric oxyhydroxide. Among subjects whose serum phosphorus was above age-related normal ranges at baseline (N=40), serum phosphorus levels showed statistically significant decrease from baseline to the end of Stage 1, with the LS mean (SE) change -0.87 (0.30) mg/dL (95% CI: -1.47, -0.27; p=0.006).

The safety profile of Velphoro in paediatric patients was generally comparable to that previously observed in adult patients.

5.2 Pharmacokinetic properties

Velphoro works by binding phosphate in the gastrointestinal tract and thus the serum concentration is not relevant for its efficacy. Due to the insolubility and degradation characteristics of Velphoro, no classical pharmacokinetic studies can be carried out, e.g., determination of the distribution volume, area under the curve, mean residence time, etc.

In 2 Phase 1 studies, it was concluded that the potential for iron overload is minimal and no dose dependent effects were observed in healthy volunteers.

Absorption

The active moiety of Velphoro, pn-FeOOH, is practically insoluble and therefore not absorbed. Its degradation product, mononuclear iron species, can however be released from the surface of pn-FeOOH and be absorbed.

The absolute absorption studies in humans were not performed. Non-clinical studies in several species (rats and dogs) showed that systemic absorption was very low (≤1% of the administered dose).

The iron uptake from radiolabelled Velphoro active substance, 2,000 mg iron in 1 day was investigated in 16 CKD patients (8 pre-dialysis and 8 haemodialysis patients) and 8 healthy volunteers with low iron stores (serum ferritin <100 mcg/L). In healthy subjects, the median uptake of radiolabelled iron in the blood was estimated to be 0.43% (range 0.16 – 1.25%) on day 21, in pre-dialysis patients 0.06% (range 0.008 – 0.44%) and in haemodialysis patients 0.02% (range 0 – 0.04%). Blood levels of radiolabelled iron were very low and confined to the erythrocytes.

Distribution

The distribution studies in humans were not performed. Non-clinical studies in several species (rats and dogs) showed that pn-FeOOH is distributed from the plasma to the liver, spleen and bone marrow, and utilized by incorporation into red blood cells.

In patients, absorbed iron is expected to be also distributed to the target organs, i.e. liver, spleen and bone marrow, and utilized by incorporation into red blood cells.

Biotransformation

The active moiety of Velphoro, pn-FeOOH, is not metabolised. However, the degradation product of Velphoro, mononuclear iron species, can be released from the surface of polynuclear iron(III)-oxyhydroxide and be absorbed. Clinical studies have demonstrated that the systemic absorption of iron from Velphoro is low.

In vitro data suggest that the sucrose and starch components of the active substance can be digested to glucose and fructose, and maltose and glucose, respectively. These compounds can be absorbed in the blood.

Elimination

In animal studies with rats and dogs administered ^{59}Fe-Velphoro active substance orally, radiolabelled iron was recovered in the faeces but not the urine.

5.3 Preclinical safety data

Nonclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity and genotoxicity.

Effects seen in the rabbit embryo-foetal development toxicity study (skeletal variations and incomplete ossificaton) are related to exaggerated pharmacology, and likely not relevant for patients. Other reproduction toxicity studies showed no adverse effects.

Carcinogenicity studies were performed in mice and rats. There was no clear evidence of a carcinogenic effect in mice. Mucosal hyperplasia, with diverticulum/cyst formation was observed in the colon and caecum of mice after 2-years treatment, but this was considered a species-specific effect

with no diverticula/cysts seen in long term studies in rats or dogs. In rats, there was a slightly increased incidence of benign C-cell adenoma in the thyroid of male rats given the highest dose of sucroferric oxyhydroxide. This is thought to be most likely an adaptive response to the pharmacological effect of the medicinal product, and not clinically relevant.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Woodberry flavour
Neohesperidin-dihydrochalcone
Magnesium stearate
Colloidal anhydrous silica

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years
Shelf life after first opening of the bottle: 90 days

6.4 Special precautions for storage

Store in the original package in order to protect from moisture.

6.5 Nature and contents of container

High density polyethylene (HDPE) bottle with child-resistant polypropylene closure and foil induction seal, containing a molecular sieve desiccant and cotton. Pack sizes of 30 or 90 chewable tablets.

Child-resistant aluminium/aluminium perforated unit-dose blister, each blister containing 6 chewable tablets. Pack sizes of 30 × 1 or multipack of 90 (3 packs of 30 × 1) chewable tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Vifor Fresenius Medical Care Renal Pharma France
100–101 Terrasse Boieldieu
Tour Franklin La Défense 8
92042 Paris la Défense Cedex
France

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/943/001
EU/1/14/943/002
EU/1/14/943/003
EU/1/14/943/004

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 26 August 2014
Date of latest renewal: 25 March 2019

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

1. NAME OF THE MEDICINAL PRODUCT

Velphoro 125 mg oral powder in sachet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet contains sucroferric oxyhydroxide corresponding to 125 mg iron. The sucroferric oxyhydroxide contained in one sachet of oral powder is comprised of polynuclear iron (III)-oxyhydroxide (containing 125 mg iron), 187 mg sucrose and 175 mg starches (potato starch and pregelatinised maize starch).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral powder in sachet.

The oral powder is red-brown.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Velphoro is indicated for the control of serum phosphorus levels in adult chronic kidney disease (CKD) patients on haemodialysis (HD) or peritoneal dialysis (PD).

Velphoro is indicated for the control of serum phosphorus levels in paediatric patients 2 years of age and older with CKD stages 4-5 (defined by a glomerular filtration rate <30 mL/min/1.73 m²) or with CKD on dialysis.

Velphoro should be used within the context of a multiple therapeutic approach, which could include calcium supplement, 1,25-dihydroxy vitamin D_3 or one of its analogues, or calcimimetics to control the development of renal bone disease.

4.2 Posology and method of administration

Posology

Starting dose, dose titration and maintenance for paediatric patients 2 to <12 years of age
The recommended starting doses for paediatric patients in different age groups are described in Table 1.

Table 1 Recommended starting doses and dose titrations for paediatric patients 2 to <12 years of age

Patient age (years)	Daily starting dose	Dose increases or decreases	Maximum recommended daily dose
≥2 to <6	500 mg	125 or 250 mg	1,250 mg
≥6 to <9	750 mg	125, 250 or 375 mg	2,500 mg
≥9 to <12	1,000 mg	250 or 500 mg	3,000 mg

Serum phosphorus levels must be monitored and the dose of sucroferric oxyhydroxide up or down titrated once per two weeks by adjusting the daily dose as indicated in Table 1 until an acceptable serum phosphorus level is reached, with regular monitoring afterwards.

For patients 6 to <12 years of age Velphoro chewable tablets may be prescribed instead of or in combination with Velphoro oral powder in case the daily dose is 1,000 mg iron (2 chewable tablets) or more.

If one or more doses are missed, the normal dose of the medicinal product should be resumed with the next meal.

Additional formulation and strength available
Velphoro is also available as chewable tablets (500 mg iron) for use in adult and paediatric patients 6 years of age and older. The choice of the formulation depends on patient's age, preference, characteristics and compliance. When transitioning between formulations, the same recommended dose should be used. Velphoro oral powder was not studied in adults. For patients 2 to <6 years of age oral powder should be administered as chewable tablet formulation is not appropriate for this age group.

Paediatric population <2 years of age
The safety and efficacy of Velphoro in children below the age of 2 years has not been established. No data are available.

Renal impairment
Velphoro is indicated for the control of serum phosphorus levels in adult CKD patients on HD or PD. There is no clinical data available in patients with earlier stages of renal impairment.

Hepatic impairment
Patients with severe hepatic impairment were excluded from participating in clinical studies with sucroferric oxyhydroxide. However, no evidence of hepatic impairment or significant alteration of hepatic enzymes were observed in the clinical studies with sucroferric oxyhydroxide. See further information in section 4.4.

Method of administration

Oral use.
In order to maximise the adsorption of dietary phosphate, the total daily dose (total number of sachets) should be divided across the main meals of the day, i.e. meals with the highest phosphate content. When total number of sachets cannot be equally divided by the number of main meals, rest of the dose should be taken with one or two main meals. The optimal way to give the total daily dose of Velphoro to individual patients should be decided based on their feeding regimens.

Before administration, Velphoro oral powder should be mixed with a small amount of soft food (such as apple sauce) or with non-carbonated beverage or water and taken with meals. Each sachet of oral powder requires minimum 5 mL of liquid for suspension, e.g. 2 sachets shall be suspended in minimum 10 mL. The amount of liquid could be increased if total daily fluid intake remains in line with dietary instructions for individual patient.
Patients should take Velphoro oral powder within 30 minutes after being suspended. Velphoro oral powder should not be heated (e.g. in a microwave) or added to heated food or liquids. The mixture should be stirred vigorously as the powder will not dissolve completely and remain in suspension with a red-brown colour. If necessary, the suspension should be resuspended right before administration.

The prescribed dose of Velphoro oral powder suspended in water as described above, may be administered via an enteral feeding tube >6 FR (French catheter scale). Follow the manufacturer's instructions for the feeding tube to administer the medicinal product. To ensure adequate dosing, after

administration of the oral suspension, the enteral feeding tube must be flushed with water. See section 6.6 for further details.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Haemochromatosis and any other iron accumulation disorders.

4.4 Special warnings and precautions for use

Peritonitis, gastric and hepatic disorders and gastrointestinal surgery

Patients with a recent history of peritonitis (within the last 3 months), significant gastric or hepatic disorders and patients with major gastrointestinal surgery have not been included in clinical studies with Velphoro. Velphoro treatment should only be used in these patients following careful assessment of benefit/risk.

Discoloured stool

Sucroferric oxyhydroxide can cause discoloured (black) stool. Discoloured (black) stool may visually mask gastrointestinal bleeding (see section 4.5).

Information about sucrose and starches (carbohydrates)

Velphoro contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicinal product. It may be harmful to the teeth.

Velphoro contains potato starch and pregelatinised maize starch. Patients with diabetes should take notice that one sachet of Velphoro oral powder is equivalent to approximately 0.7 g of carbohydrates (equivalent to 0.056 bread units).

4.5 Interaction with other medicinal products and other forms of interaction

Velphoro is almost not absorbed from the gastrointestinal tract. Although the potential for interactions with medicinal products seems low, for concomitant treatment with medicinal products with a narrow therapeutic window, the clinical effect and adverse events should be monitored, on initiation or dose-adjustment of either Velphoro or the concomitant medicinal product, or the physician should consider measuring blood levels. When administering any medicinal product that is already known to interact with iron (like alendronate and doxycycline) or has the potential to interact with sucroferric oxyhydroxide based only on *in vitro* studies like levothyroxine, the medicinal product should be administered at least one hour before or two hours after Velphoro.

In vitro studies with the following active substances did not show any relevant interaction: acetylsalicylic acid, cephalexin, cinacalcet, ciprofloxacin, clopidogrel, enalapril, hydrochlorothiazide, metformin, metoprolol, nifedipine, pioglitazone and quinidine.

Interaction studies have only been performed in healthy volunteers. They have been conducted in healthy human male and female subjects with losartan, furosemide, digoxin, warfarin, and omeprazole. Concomitant administration of Velphoro did not affect the bioavailability of these medicinal products as measured by the area under the curve (AUC).

Data from clinical studies have shown that sucroferric oxyhydroxide does not affect the lipid lowering effects of HMG-CoA reductase inhibitors (e.g., atorvastatin and simvastatin). In addition, post-hoc analyses from clinical studies demonstrated no impact of Velphoro on iPTH lowering effect of oral Vitamin D analogues. Vitamin D and 1,25-dihydroxy Vitamin D levels remained unchanged.

Velphoro does not affect guaiac based (Haemoccult) or immunological based (iColo Rectal and Hexagon Obti) faecal occult blood tests.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no available clinical data from the use of sucroferric oxyhydroxide on exposed human pregnancies.

Reproductive and developmental toxicity studies in animals revealed no risk with respect to pregnancy, embryonic/foetal development, parturition or postnatal development (see section 5.3). Sucroferric oxyhydroxide should only be used by pregnant women if clearly needed following careful assessment of benefit/risk.

Breast-feeding

There are no available clinical data from the use of Velphoro in breast-feeding women. Since absorption of iron from this medicinal product is minimal (see section 5.2), excretion of iron from sucroferric oxyhydroxide in breast milk is unlikely. A decision on whether to continue breast-feeding or to continue therapy with sucroferric oxyhydroxide should be made taking into account the benefit of breast-feeding to the child and the benefit of Velphoro therapy to the mother.

Fertility

There are no data on the effect of Velphoro on fertility in humans. In animal studies, there were no adverse effects on mating performance, fertility, and litter parameters following treatment with sucroferric oxyhydroxide (see section 5.3).

4.7 Effects on ability to drive and use machines

Velphoro has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

The current safety profile of Velphoro is based on a total of 778 patients on haemodialysis and 57 patients on peritoneal dialysis, who received sucroferric oxyhydroxide treatment of up to 55 weeks.

In these clinical trials, approximately 43% of the patients experienced at least one adverse reaction during Velphoro treatment, and 0.36% of the adverse reactions were reported as serious. The majority of the adverse reactions reported from trials were gastrointestinal disorders, with the most frequently reported adverse reactions being diarrhoea and discoloured faeces (very common). The vast majority of these gastrointestinal disorders occurred early during treatment and abated with time with continued dosing. No dose-dependent trends were observed in the adverse reaction profile of Velphoro.

Tabulated list of adverse reactions

Adverse reactions reported from the use of Velphoro at doses from 250 mg iron/day to 3,000 mg iron/day in these patients (n=835) are listed in Table 2.
The reporting rate is classified as very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100).

Table 2 Adverse reactions detected in clinical trials

System organ class	Very common	Common	Uncommon
Metabolism and nutrition disorders			Hypercalcaemia Hypocalcaemia
Nervous system disorders			Headache
Respiratory, thoracic and mediastinal disorders			Dyspnoea
Gastrointestinal disorders	Diarrhoea* Faeces discoloured	Nausea Constipation Vomiting Dyspepsia Abdominal pain Flatulence Tooth discolouration	Abdominal distension Gastritis Abdominal discomfort Dysphagia Gastro-oesophageal reflux disease (GORD) Tongue discolouration
Skin and subcutaneous tissue disorders			Pruritus Rash
General disorders and administration site conditions		Product taste abnormal	Fatigue

Description of selected adverse reactions

**Diarrhoea*

Diarrhoea occurred in 11.6% of patients in clinical trials. In the 55 weeks long term studies, the majority of these diarrhoea adverse reactions were transient, occurred early during treatment initiation and led to treatment discontinuation in 3.1% of the patients.

Paediatric population

In general, the safety profile of Velphoro in paediatric (2 to <18 years of age) and adult patients was comparable. The adverse reactions most frequently reported were gastrointestinal disorders including diarrhoea (very common, 16.7%), vomiting (common, 6.1%), gastritis (common, 3.0%) and discoloured faeces (common, 3.0%).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Any instances of overdose of Velphoro (e.g. hypophosphataemia) should be treated by standard clinical practice.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: All other therapeutic products; drugs for treatment of hyperkalaemia and hyperphosphataemia; ATC code: V03AE05

Mechanism of action

Velphoro contains sucroferric oxyhydroxide which is comprised of polynuclear iron(III)-oxyhydroxide (pn-FeOOH), sucrose and starches. Phosphate binding takes place by ligand exchange between hydroxyl groups and/or water and the phosphate ions throughout the physiological pH range of the gastrointestinal tract.

Serum phosphorus levels are reduced as a consequence of the reduced dietary phosphate absorption.

Clinical efficacy

One phase 3 clinical study has been performed in patients with CKD on dialysis to investigate the efficacy and safety of Velphoro in this population. This study was an open-label, randomised, active-controlled (sevelamer carbonate), parallel group study for up to 55 weeks. Adult patients with hyperphosphataemia (serum phosphorus levels ≥1.94 mmol/L) were treated with sucroferric oxyhydroxide at a starting dose of 1,000 mg iron/day followed by an 8-week dose titration period. Non-inferiority to sevelamer carbonate was determined at week 12. Subjects were continued on their study medication from week 12 to week 55. From week 12 to 24, dose titrations were allowed for both tolerability and efficacy reasons. Treatment of patient sub-populations from week 24 to week 27 with maintenance dose of sucroferric oxyhydroxide (1,000 to 3,000 mg iron/day) or low dose (250 mg iron/day) of sucroferric oxyhydroxide demonstrated superiority of the maintenance dose.

In Study-05A, 1,055 patients on haemodialysis (N=968) or peritoneal dialysis (N=87) with serum phosphorus ≥1.94 mmol/L following a 2 – 4-week phosphate binder washout period, were randomised and treated with either sucroferric oxyhydroxide, at a starting dose of 1,000 mg iron/day (N=707), or active-control (sevelamer carbonate, N=348) for 24 weeks. At the end of week 24, 93 patients on haemodialysis whose serum phosphorus levels were controlled (<1.78 mmol/L) with sucroferric oxyhydroxide in the first part of the study, were re-randomised to continue treatment with either their week 24 maintenance dose (N=44 or a non-effective low dose control 250 mg iron/day, N=49) of sucroferric oxyhydroxide for a further 3 weeks.

Following completion of Study-05A, 658 patients (597 on haemodialysis and 61 on peritoneal dialysis) were treated in the 28-week extension study (Study-05B) with either sucroferric oxyhydroxide (N=391) or sevelamer carbonate (N=267) according to their original randomization.

Mean serum phosphorus levels were 2.5 mmol/L at baseline and 1.8 mmol/L at week 12 for sucroferric oxyhydroxide (reduction by 0.7 mmol/L). Corresponding levels for sevelamer carbonate at baseline were 2.4 mmol/L and 1.7 mmol/L at week 12 (reduction by 0.7 mmol/L), respectively.

The serum phosphorus reduction was maintained over 55 weeks. Serum phosphorus levels and calcium-phosphorus product levels were reduced as a consequence of the reduced dietary phosphate absorption.

The response rates, defined as the proportion of subjects achieving serum phosphorus levels within the Kidney Disease Outcomes Quality Initiative (KDOQI) recommended range were 45.3% and 59.1% at week 12 and 51.9% and 55.2% at week 52, for sucroferric oxyhydroxide and sevelamer carbonate, respectively.

The mean daily dose of Velphoro over 55 weeks of treatment was 1,650 mg iron and the mean daily dose of sevelamer carbonate was 6,960 mg.

Post-authorisation data

A prospective, non-interventional, post-authorisation safety study (VERIFIE) has been conducted, evaluating the short- and long-term (up to 36 months) safety and effectiveness of Velphoro in adult patients on haemodialysis (N=1,198) or peritoneal dialysis (N=160), who were followed in routine clinical practice for 12 to 36 months (safety analysis set, N=1,365). During the study, 45% (N=618) of these patients were concomitantly treated with phosphate binder(s) other than Velphoro.

In the safety analysis set, the most common ADRs were diarrhoea and discoloured faeces, reported by 14% (N=194) and 9% (N=128) of patients, respectively. The incidence of diarrhoea was highest in the first week and decreased with duration of use. Diarrhoea was of mild to moderate intensity in most patients and resolved in the majority of patients within 2 weeks. Discoloured (black) faeces is expected for an oral iron-based compound, and may visually mask gastrointestinal bleeding. For 4 of the 40 documented concomitant gastrointestinal bleeding events, Velphoro-related stool discolouration was reported as causing an insignificant delay in diagnosis of gastrointestinal bleeding, without affecting patient health. In the remaining cases, no delay in diagnosis of gastrointestinal bleeding has been reported.

The results from this study showed that the effectiveness of Velphoro in a real-life setting (including concomitant use of other phosphate binders in 45% of patients), was in line with that observed in the phase 3 clinical study.

Paediatric population

An open label clinical study investigated the efficacy and safety of Velphoro in paediatric patients 2 years of age and older with CKD and hyperphosphatemia (CKD stages 4-5 (defined by a glomerular filtration rate <30 mL/min/l .73 m²) or with CKD on dialysis). Eighty-five subjects were randomised to Velphoro (N=66) or active control calcium acetate arm (N=19) for a 10-week dose titration (Stage 1), followed by a 24-week safety extension (Stage 2). Most patients were ⩾12 years of age (66%). Eighty percent of patients were CKD patients on dialysis (67% on haemodialysis and 13% on peritoneal dialysis) and 20% were CKD patients not on dialysis.

The limited difference in reduction in mean serum phosphorus level from baseline to the end of Stage 1 in the Velphoro group (N=65) was not statistically significant with -0.120 (0.081) mmol/L (95% CI: -0.282, 0.043) based on the mixed model calculations with actual data showing a mean of 2.08 mmol/L at baseline and 1.91 mmol/L at the end of Stage 1 (reduction by 0.17 mmol/L). The effect was maintained during Stage 2, although some fluctuations in mean effect over time were noticed (0.099 (0.198) mmol/L (95% CI: -0.306, 0.504)).

The percentage of subjects with serum phosphorus levels within normal ranges increased from 37% at baseline to 61% at the end of Stage 1, and was 58% at the end of Stage 2, showing the sustainable phosphorus lowering effect of sucroferric oxyhydroxide. Among subjects whose serum phosphorus was above age-related normal ranges at baseline (N=40), serum phosphorus levels showed statistically significant decrease from baseline to the end of Stage 1, with the LS mean (SE) change -0.87 (0.30) mg/dL (95% CI: -1.47, -0.27; p=0.006).

The safety profile of Velphoro in paediatric patients was generally comparable to that previously observed in adult patients.

5.2 Pharmacokinetic properties

Velphoro works by binding phosphate in the gastrointestinal tract and thus the serum concentration is not relevant for its efficacy. Due to the insolubility and degradation characteristics of Velphoro, no classical pharmacokinetic studies can be carried out, e.g., determination of the distribution volume, area under the curve, mean residence time, etc.

In 2 Phase 1 studies, it was concluded that the potential for iron overload is minimal and no dose dependent effects were observed in healthy volunteers.

Absorption

The active moiety of Velphoro, pn-FeOOH, is practically insoluble and therefore not absorbed. Its degradation product, mononuclear iron species, can however be released from the surface of pn-FeOOH and be absorbed.

The absolute absorption studies in humans were not performed. Non-clinical studies in several species (rats and dogs) showed that systemic absorption was very low (≤1% of the administered dose).

The iron uptake from radiolabelled Velphoro active substance, 2,000 mg iron in 1 day was investigated in 16 CKD patients (8 pre-dialysis and 8 haemodialysis patients) and 8 healthy volunteers with low iron stores (serum ferritin <100 mcg/L). In healthy subjects, the median uptake of radiolabelled iron in the blood was estimated to be 0.43% (range 0.16 – 1.25%) on day 21, in pre-dialysis patients 0.06% (range 0.008 – 0.44%) and in haemodialysis patients 0.02% (range 0 – 0.04%). Blood levels of radiolabelled iron were very low and confined to the erythrocytes.

Distribution

The distribution studies in humans were not performed. Non-clinical studies in several species (rats and dogs) showed that pn-FeOOH is distributed from the plasma to the liver, spleen and bone marrow, and utilized by incorporation into red blood cells.

In patients, absorbed iron is expected to be also distributed to the target organs, i.e. liver, spleen and bone marrow, and utilized by incorporation into red blood cells.

Biotransformation

The active moiety of Velphoro, pn-FeOOH, is not metabolised. However, the degradation product of Velphoro, mononuclear iron species, can be released from the surface of polynuclear iron(III)-oxyhydroxide and be absorbed. Clinical studies have demonstrated that the systemic absorption of iron from Velphoro is low.

In vitro data suggest that the sucrose and starch components of the active substance can be digested to glucose and fructose, and maltose and glucose, respectively. These compounds can be absorbed in the blood.

Elimination

In animal studies with rats and dogs administered ^{59}Fe-Velphoro active substance orally, radiolabelled iron was recovered in the faeces but not the urine.

5.3 Preclinical safety data

Nonclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity and genotoxicity.

Effects seen in the rabbit embryo-foetal development toxicity study (skeletal variations and incomplete ossificaton) are related to exaggerated pharmacology, and likely not relevant for patients. Other reproduction toxicity studies showed no adverse effects.

Carcinogenicity studies were performed in mice and rats. There was no clear evidence of a carcinogenic effect in mice. Mucosal hyperplasia, with diverticulum/cyst formation was observed in the colon and caecum of mice after 2-years treatment, but this was considered a species-specific effect with no diverticula/cysts seen in long term studies in rats or dogs. In rats, there was a slightly increased

incidence of benign C-cell adenoma in the thyroid of male rats given the highest dose of sucroferric oxyhydroxide. This is thought to be most likely an adaptive response to the pharmacological effect of the medicinal product, and not clinically relevant.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maltodextrin
Microcrystalline cellulose
Xanthan gum
Colloidal anhydrous silica
Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Child-resistant twin single-dose polyethylene terephthalate/aluminium/polyethylene laminate sachet. Pack size of 90 sachets.

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Preparation and handling

Velphoro oral powder should be mixed with a small amount of soft food (such as apple sauce) or with small amount of water or non-carbonated beverage (see section 4.2). The mixture should be stirred vigorously as the powder will not dissolve completely and remain in suspension with a red-brown colour. The suspension should be administered within 30 minutes after preparation. If necessary, the suspension should be resuspended right before administration.

Enteral feeding tube

The prescribed dose of Velphoro oral powder, suspended in water as described above, may be administered via an enteral feeding tube >6 FR (French catheter scale). The tube size considered as appropriate for the intended use and age group, is 8 to 12 FR, i.e. small to medium tubes for the feeding of children and adults.
Follow the manufacturer’s instructions for the feeding tube to administer the medicinal product. To ensure adequate dosing, after administration of the oral suspension, the enteral feeding tube must be flushed with water. The flush volumes to achieve a full dose recovery - for a tube with a length of 50

cm – are 6 mL (8 FR) to 10 mL (12 FR). As the medicinal product has a brownish color, a tube blockage or build-up of residues may be observed through transparent feeding tubes.

7. MARKETING AUTHORISATION HOLDER

Vifor Fresenius Medical Care Renal Pharma France
100–101 Terrasse Boieldieu
Tour Franklin La Défense 8
92042 Paris la Défense Cedex
France

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/943/005

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 26 August 2014
Date of latest renewal: 25 March 2019

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

Vifor France
100–101 Terrasse Boieldieu
Tour Franklin La Défense 8
92042 Paris la Défense Cedex
FRANCE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal. The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:
- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON – BOTTLE OF 30 AND 90 CHEWABLE TABLETS

1. NAME OF THE MEDICINAL PRODUCT

Velphoro 500 mg chewable tablets
iron as sucroferric oxyhydroxide

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each chewable tablet contains sucroferric oxyhydroxide corresponding to 500 mg iron.

3. LIST OF EXCIPIENTS

Contains sucrose, potato starch and pregelatinised maize starch. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Chewable tablet

30 chewable tablets
90 chewable tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Chew or crush tablets and take with meals.
Read the package leaflet before use.
Oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP
Shelf-life after first opening the bottle: 90 days
Opening date:

9. SPECIAL STORAGE CONDITIONS

Store in the original package in order to protect from moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Vifor Fresenius Medical Care Renal Pharma France
100–101 Terrasse Boieldieu
Tour Franklin La Défense 8
92042 Paris la Défense Cedex
France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/943/001 30 chewable tablets
EU/1/14/943/002 90 chewable tablets

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

velphoro 500 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

LABEL – BOTTLE OF 30 AND 90 CHEWABLE TABLETS

1. NAME OF THE MEDICINAL PRODUCT

Velphoro 500 mg chewable tablets
iron as sucroferric oxyhydroxide

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each chewable tablet contains sucroferric oxyhydroxide corresponding to 500 mg iron.

3. LIST OF EXCIPIENTS

Contains sucrose, potato starch and pregelatinised maize starch. Read the package leaflet before use.

4. PHARMACEUTICAL FORM AND CONTENTS

Chewable tablet

30 chewable tablets
90 chewable tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Chew or crush tablets and take with meals.
Read the package leaflet before use.
Oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP
Shelf-life after first opening the bottle: 90 days
Opening date:

9. SPECIAL STORAGE CONDITIONS

Store in the original package in order to protect from moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Vifor Fresenius Medical Care Renal Pharma France
100–101 Terrasse Boieldieu
Tour Franklin La Défense 8
92042 Paris la Défense Cedex
France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/943/001 30 chewable tablets
EU/1/14/943/002 90 chewable tablets

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON –30 CHEWABLE TABLETS (5 BLISTERS OF 6 CHEWABLE TABLETS)

1. NAME OF THE MEDICINAL PRODUCT

Velphoro 500 mg chewable tablets
iron as sucroferric oxyhydroxide

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each chewable tablet contains sucroferric oxyhydroxide corresponding to 500 mg iron.

3. LIST OF EXCIPIENTS

Contains sucrose, potato starch and pregelatinised maize starch. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Chewable tablet

30 × 1 chewable tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Chew or crush tablets and take with meals.
Read the package leaflet before use.
Oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in the original package in order to protect from moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Vifor Fresenius Medical Care Renal Pharma France
100–101 Terrasse Boieldieu
Tour Franklin La Défense 8
92042 Paris la Défense Cedex
France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/943/003

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

velphoro 500 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON – 30 CHEWABLE TABLETS (5 BLISTERS OF 6 CHEWABLE TABLETS), PART OF MULTIPACK (WITHOUT BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Velphoro 500 mg chewable tablets
iron as sucroferric oxyhydroxide

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each chewable tablet contains sucroferric oxyhydroxide corresponding to 500 mg iron.

3. LIST OF EXCIPIENTS

Contains sucrose, potato starch and pregelatinised maize starch. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Chewable tablet
30 × 1 chewable tablets.
Component of a multipack. Can't be sold separately.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Chew or crush tablets and take with meals.
Read the package leaflet before use.
Oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in the original package in order to protect from moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Vifor Fresenius Medical Care Renal Pharma France
100–101 Terrasse Boieldieu
Tour Franklin La Défense 8
92042 Paris la Défense Cedex
France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/943/003

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

velphoro 500 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (MULTIPACK) – 90 (3 PACKS OF 30) CHEWABLE TABLETS

1. NAME OF THE MEDICINAL PRODUCT

Velphoro 500 mg chewable tablets
iron as sucroferric oxyhydroxide

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each chewable tablet contains sucroferric oxyhydroxide corresponding to 500 mg iron.

3. LIST OF EXCIPIENTS

Contains sucrose, potato starch and pregelatinised maize starch. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Chewable tablet
Multipack: 90 (3 packs of 30) chewable tablets.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Chew or crush tablets and take with meals.
Read the package leaflet before use.
Oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in the original package in order to protect from moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Vifor Fresenius Medical Care Renal Pharma France
100–101 Terrasse Boieldieu
Tour Franklin La Défense 8
92042 Paris la Défense Cedex
France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/943/004

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

velphoro 500 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER OF 6 CHEWABLE TABLETS

1. NAME OF THE MEDICINAL PRODUCT

Velphoro 500 mg chewable tablets
iron as sucroferric oxyhydroxide

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Vifor Fresenius Medical Care Renal Pharma France

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON – 90 SACHETS

1. NAME OF THE MEDICINAL PRODUCT

Velphoro 125 mg oral powder in sachet
iron as sucroferric oxyhydroxide

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each sachet contains sucroferric oxyhydroxide corresponding to 125 mg iron.

3. LIST OF EXCIPIENTS

Contains sucrose, potato starch and pregelatinised maize starch. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Oral powder
90 sachets.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Mix with a small amount of soft food or with small amount of water or non-carbonated beverage.
Stir vigorously as the powder will not dissolve completely.
Read the package leaflet before use.
Oral use.
After reconstitution:
Administer within 30 minutes.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Vifor Fresenius Medical Care Renal Pharma France
100–101 Terrasse Boieldieu
Tour Franklin La Défense 8
92042 Paris la Défense Cedex
France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/943/005

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

velphoro 125 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL - SACHET

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Velphoro 125 mg oral powder in sachet
iron as sucroferric oxyhydroxide
Oral use.

2. METHOD OF ADMINISTRATION

Mix with a small amount of soft food or with small amount of water or non-carbonated beverage.
Stir vigorously as the powder will not dissolve completely.
Read the package leaflet before use.
After reconstitution:
Administer within 30 minutes.

3. EXPIRY DATE

EXP

4. BATCH NUMBER<, DONATION AND PRODUCT CODES>

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

Keep out of the sight and reach of children.

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Velphoro 500 mg chewable tablets
iron as sucroferric oxyhydroxide

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
– Keep this leaflet. You may need to read it again.
– If you have any further questions, ask your doctor or pharmacist
– This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
– If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Velphoro is and what it is used for

Velphoro is a medicine that contains the active substance sucroferric oxyhydroxide, which is made up from iron, sugar (sucrose) and starches.

This medicine is used to control high blood phosphate levels (hyperphosphataemia) in:
- adult patients who undergo haemodialysis or peritoneal dialysis (procedures to eliminate toxic substances from the blood) because of chronic kidney disease;
- children from 2 years of age and adolescents with chronic kidney disease stages 4 and 5 (severe decrease in the ability of the kidneys to work properly) or on dialysis.

Too much phosphorus in the blood can lead to calcium being deposited in tissues (calcification). This can result in stiffening of the blood vessels, making it harder for the blood to be pumped around the body. It may also lead to calcium deposits in soft tissues and bone causing effects such as red eyes, itchy skin and bone pain.

This medicine works by binding phosphorus from food in your digestive tract (stomach and intestines). This reduces the amount of phosphorus that can be absorbed into the bloodstream and thus lowers phosphorus levels in your blood.

2. What you need to know before you take Velphoro

Do not take Velphoro

– if you are allergic to sucroferric oxyhydroxide or any of the other ingredients of this medicine (listed in section 6);
– if you have a history of abnormal iron build-up in your organs (haemochromatosis);
– if you have any other disorder associated with too much iron.

If you are not sure, talk to your doctor before taking this medicine.

Warnings and precautions
Talk to your doctor or pharmacist before taking Velphoro:
– if you have had peritonitis, an inflammation of the peritoneum (the thin tissue that lines the inner wall of the abdomen) within the last 3 months;
– if you have significant stomach and/or liver problems;
– if you have had major surgery on your stomach and/or intestines.

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

This medicine can cause black stools. Any potential bleeding from your digestive tract (stomach and gut) may be hidden by these black stools. **If you have black stools and also have symptoms like increasing tiredness and breathlessness contact your doctor immediately** (see section 4).

Children and adolescents
The safety and efficacy in children below the age of 2 years has not yet been established. Therefore, this medicine is not recommended for use in children under 2 years.

Other medicines and Velphoro
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

If you are taking any other medicine that is known to be affected by iron (for example medicines containing the active substance alendronate (used to treat certain bone disorders) or doxycycline (an antibiotic)) or has the potential to be affected by iron (for example medicines containing the active substance levothyroxine (used to treat thyroid function disorder)), make sure that you take this medicine at least one hour before taking Velphoro or at least two hours after taking Velphoro. Ask your doctor if you are not sure.

Pregnancy and breast-feeding
There is no information on the effects of this medicine if taken during pregnancy or breast-feeding. If you are pregnant or breast-feeding, or you think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Your doctor will advise you whether Velphoro should be used during pregnancy, based on benefit and risk assessment for use during pregnancy.

If you are breast-feeding, your doctor will discuss with you whether to continue breast-feeding or to continue therapy with Velphoro, taking into account the benefit of Velphoro therapy to you and the benefit of breast-feeding to your child.

It is unlikely that this medicine would pass into the mother’s milk.

Driving and using machines
This medicine has no significant effect on your ability to drive or to use tools or machines.

Velphoro contains sucrose and starches (carbohydrates)
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.
This medicine may be harmful to the teeth.

This medicine contains starches. If you have diabetes you should take notice that one tablet of this medicine is equivalent to approximately 1.4 g of carbohydrates (equivalent to 0.116 bread units).

3. How to take Velphoro

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

The usual recommended starting dose:
- in children 6 to less than 9 years is 750 mg iron per day *,
- in children and adolescents 9 to 12 years is 1,000 mg iron (2 tablets) a day,
- for adults and adolescents above 12 years of age is 1,500 mg iron per day (3 tablets).

Your doctor may adjust the dose during the treatment course depending on the phosphorus level in your blood.

The maximum recommended dose:
- in children 6 to less than 9 years is 2,500 mg iron (5 tablets) per day,
- in children and adolescents 9 to 18 years and adults is 3,000 mg iron (6 tablets) per day.

* Velphoro is also available as oral powder in sachet (equivalent to 125 mg iron) for use in children 2 to less than 12 years.

Method of administration

– Take this medicine only by mouth.
– Take the tablet during a meal and chew it (if necessary, the tablet may be crushed to make this easier for you). DO NOT swallow it whole.
– Divide the amount of tablets taken per day across the meals of the day.
– When taking Velphoro you should adhere to your recommended diet and treatments prescribed by your doctor such as calcium supplements, vitamin D_3 or calcimimetics (used to treat problems with parathyroid glands).

Only for the blister packs:
– Separate the blister pack at perforations.
– Peel back the paper foil at the corner.
– Push the tablet through the aluminium foil.

If you take more Velphoro than you should
If you have accidentally taken too many tablets, do not take any more and talk to your doctor or pharmacist immediately.

If you forget to take Velphoro
If you have missed a dose, just take the next dose at the usual time with a meal. Do not take a double dose to make up for a forgotten dose.

If you stop taking Velphoro
Do not stop taking the medicine before talking to your doctor or pharmacist as the phosphorus level in your blood may increase (see section 1).

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Black stools may occur very commonly in patients taking Velphoro. If you also have symptoms like increasing tiredness and breathlessness contact your doctor immediately (see section 2 “Warnings and precautions”).

The following side effects have also been reported in patients taking this medicine:

Very common (may affect more than 1 in 10 people): diarrhoea (generally occurring early on in the treatment, and improving over time).

Common (may affect up to 1 in 10 people): feeling sick (nausea), constipation, vomiting, indigestion, pain in stomach and gut, gas, tooth discolouration, change in taste.

Uncommon (may affect up to 1 in 100 people): bloating (abdominal distension), inflammation of the stomach, abdominal discomfort, difficulty swallowing, acid coming back up from the stomach (gastro-oesophageal reflux disease), tongue discolouration, low or high calcium levels in the blood seen in tests, tiredness, itch, rash, headache, shortness of breath.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Velphoro

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton, bottle or blister after "EXP". The expiry date refers to the last day of that month.

After first opening of the bottle the chewable tablets can be used for 90 days.

Store in the original package in order to protect from moisture.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Velphoro contains
- The active substance is sucroferric oxyhydroxide which is comprised of polynuclear iron(III)-oxyhydroxide, sucrose, and starches. Each chewable tablet contains sucroferric oxyhydroxide corresponding to 500 mg iron. Each tablet also contains 750 mg sucrose and 700 mg starches. See section 2 for further information on sucrose and starches.
- The other ingredients are woodberry flavour, neohesperidin-dihydrochalcone, magnesium stearate, colloidal anhydrous silica.

What Velphoro looks like and contents of the pack
The chewable tablets are brown, circular, and embossed with PA500 on one side. The tablets have a 20 mm diameter and a thickness of 6.5 mm.

The tablets are packed in high density polyethylene bottles with a child resistant polypropylene closure and a foil induction seal, or in child resistant aluminium blister.

Velphoro is available in packs containing 30 or 90 chewable tablets. Multipacks are available for the blister packs with 90 chewable tablets (containing 3 individual packs of 30 × 1 chewable tablets each).

Not all pack sizes may be marketed.

Marketing Authorisation Holder
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Manufacturer
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This leaflet was last revised in

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

Package leaflet: Information for the patient

Velphoro 125 mg oral powder in sachet
iron as sucroferric oxyhydroxide

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– This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
– If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Velphoro is and what it is used for

Velphoro is a medicine that contains the active substance sucroferric oxyhydroxide, which is made up from iron, sugar (sucrose) and starches.

This medicine is used to control high blood phosphate levels (hyperphosphataemia) in:
– adult patients who undergo haemodialysis or peritoneal dialysis (procedures to eliminate toxic substances from the blood) because of chronic kidney disease;
– children from 2 years of age and adolescents with chronic kidney disease stages 4 and 5 (severe decrease in the ability of the kidneys to work properly) or on dialysis.

Too much phosphorus in the blood can lead to calcium being deposited in tissues (calcification). This can result in stiffening of the blood vessels, making it harder for the blood to be pumped around the body. It may also lead to calcium deposits in soft tissues and bone causing effects such as red eyes, itchy skin and bone pain.

This medicine works by binding phosphorus from food in your digestive tract (stomach and intestines). This reduces the amount of phosphorus that can be absorbed into the bloodstream and thus lowers phosphorus levels in your blood.

2. What you need to know before you take Velphoro

Do not take Velphoro
– if you are allergic to sucroferric oxyhydroxide or any of the other ingredients of this medicine (listed in section 6);
– if you have a history of abnormal iron build-up in your organs (haemochromatosis);
– if you have any other disorder associated with too much iron.

If you are not sure, talk to your doctor before taking this medicine.

Warnings and precautions
Talk to your doctor or pharmacist before taking Velphoro:
– if you have had peritonitis, an inflammation of the peritoneum (the thin tissue that lines the inner wall of the abdomen) within the last 3 months;
– if you have significant stomach and/or liver problems;
– if you have had major surgery on your stomach and/or intestines.

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

This medicine can cause black stools. Any potential bleeding from your digestive tract (stomach and gut) may be hidden by these black stools. **If you have black stools and also have symptoms like increasing tiredness and breathlessness contact your doctor immediately** (see section 4).

Children and adolescents
The safety and efficacy in children below the age of 2 years has not yet been established. Therefore this medicine is not recommended for use in children under 2 years.

Other medicines and Velphoro
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

If you are taking any other medicine that is known to be affected by iron (for example medicines containing the active substance alendronate (used to treat certain bone disorders) or doxycycline (an antibiotic)) or has the potential to be affected by iron (for example medicines containing the active substance levothyroxine (used to treat thyroid function disorder)), make sure that you take this medicine at least one hour before taking Velphoro or at least two hours after taking Velphoro. Ask your doctor if you are not sure.

Pregnancy and breast-feeding
There is no information on the effects of this medicine if taken during pregnancy or breast-feeding. If you are pregnant or breast-feeding, or you think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Your doctor will advise you whether Velphoro should be used during pregnancy, based on benefit and risk assessment for use during pregnancy.

If you are breast-feeding, your doctor will discuss with you whether to continue breast-feeding or to continue therapy with Velphoro, taking into account the benefit of Velphoro therapy to you and the benefit of breast-feeding to your child.

It is unlikely that this medicine would pass into the mother’s milk.

Driving and using machines
This medicine has no significant effect on your ability to drive or to use tools or machines.

Velphoro contains sucrose and starches (carbohydrates)
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

This medicine may be harmful to the teeth.

This medicine contains starches. If you have diabetes you should take notice that one sachet of Velphoro powder is equivalent to approximately 0.7 g of carbohydrates (equivalent to 0.056 bread units).

3. How to take Velphoro

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

For children 2 years and above, the doctor will decide the right dose based on the age of the child. The starting dose of Velphoro oral powder is taken three times daily with food as shown below:

Child age	Recommended daily starting dose
2 to less than 6 years	500 mg iron (4 sachets)
6 to less than 9 years	750 mg iron (6 sachets)
9 to less than 12 years	1,000 mg iron (2 tablets or 8 sachets)

Your doctor may adjust the dose during the treatment course depending on the phosphorus level in your blood.

Velphoro is also available as chewable tablets for use in children and adolescents 6 to 18 years and in adults.

The maximum recommended dose:
– in children 2 to less than 6 years is 1,250 mg iron (10 sachets) per day,
– in children 6 to less than 9 years is 2,500 mg iron (5 tablets) per day,
– in children and adolescents 9 to 18 years is 3,000 mg iron (6 tablets) per day.

Method of administration
– Take this medicine only during meal.
– Mix Velphoro oral powder with:
  - small amount of soft food, such as apple sauce, or
  - small amount of non-carbonated beverage or water

  The powder will not dissolve completely and will remain in suspension with a red-brown colour.
– Drink powder suspension within 30 minutes after being prepared.
– Mix the powder again, if necessary, right before drinking.
– Do not heat Velphoro oral powder (such as in a microwave) and do not add it to heated food or liquids.
– When taking Velphoro you should adhere to your recommended diet and treatments prescribed by your doctor such as calcium supplements, vitamin D_3 or calcimimetics (used to treat problems with parathyroid glands).

If you take more Velphoro than you should
If you have accidentally taken too many sachets of oral powder, do not take any more and talk to your doctor or pharmacist immediately.

If you forget to take Velphoro
If you have missed a dose, just take the next dose at the usual time with a meal. Do not take a double dose to make up for a forgotten dose.

If you stop taking Velphoro
Do not stop taking the medicine before talking to your doctor or pharmacist as the phosphorus level in your blood may increase (see section 1).

4. Possible side effects

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Black stools may occur very commonly in patients taking Velphoro. If you also have symptoms like increasing tiredness and breathlessness contact your doctor immediately (see section 2 “Warnings and precautions”).

The following side effects have also been reported in patients taking this medicine:

Very common (may affect more than 1 in 10 people):
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Uncommon (may affect up to 1 in 100 people):
bloating (abdominal distension), inflammation of the stomach, abdominal discomfort, difficulty swallowing, acid coming back up from the stomach (gastro-oesophageal reflux disease), tongue discolouration, low or high calcium levels in the blood seen in tests, tiredness, itch, rash, headache, shortness of breath.

Reporting of side effects

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5. How to store Velphoro

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton or sachet after “EXP”. The expiry date refers to the last day of that month.

Take the reconstituted suspension within 30 minutes of reconstitution.
This medicine does not require any special storage conditions.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Velphoro contains
- The active substance is sucroferric oxyhydroxide which is comprised of polynuclear iron(III)-oxyhydroxide, sucrose, and starches. Each sachet contains sucroferric oxyhydroxide corresponding to 125 mg iron. Each sachet also contains 187 mg sucrose and 175 mg starches. See section 2 for further information on sucrose and starches.
- The other ingredients are maltodextrin, microcrystalline cellulose, xanthan gum, magnesium stearate, colloidal anhydrous silica.

What Velphoro looks like and contents of the pack
Velphoro oral powder is red-brown, packed in child resistant twin single-dose sachets.

Velphoro oral powder is available in packs containing 90 sachets.

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