

ANNEX I
SUMMARY OF PRODUCT CHARACTERISTICS

- ▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Velphoro 500 mg chewable tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each chewable tablet contains 500 mg iron as sucroferric oxyhydroxide also known as a mixture of polynuclear iron(III)-oxyhydroxide, sucrose, and starches.

The active ingredient sucroferric oxyhydroxide contains 750 mg sucrose and 700 mg starches.

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 should be used within the context of a multiple therapeutic approach, which could include calcium supplement, 1,25-dihydroxy vitamin D3 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

The recommended starting dose of Velphoro is 1,500 mg iron (3 tablets) per day, divided across the meals of the day. Velphoro is for oral administration only and must be taken with meals. Patients receiving Velphoro should adhere to their prescribed diets.

Titration and maintenance

Serum phosphorus levels must be monitored and the dose of Velphoro 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

The maximum recommended dose is 3,000 mg iron (6 tablets) per day.

Paediatric population

The safety and efficacy of Velphoro in children below the age of 18 years has not yet been established. No data are available.

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 Velphoro, 29.7 % were aged 65 and over, while 8.7% were aged 75 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.

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 with Velphoro in patients with earlier stages of renal impairment.

Hepatic impairment

Generally, patients with severe hepatic impairment were excluded from participating in clinical studies with Velphoro. However, no evidence of hepatic impairment or significant alteration of hepatic enzymes were observed in the clinical studies with Velphoro.

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. Tablets must be chewed and not swallowed whole; tablets may be crushed.

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 should only be used in these patients following careful assessment of benefit/risk.

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 medicine. May be harmful to the teeth.

Velphoro contains starches. 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).

Discoloured stool

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

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 Velphoro 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.

Drug-drug 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 Velphoro 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 (Haemocult) 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 sucroferic 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). Velphoro 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 Velphoro is minimal (see section 5.2), excretion of iron from Velphoro in breast milk is unlikely. A decision on whether to continue breast-feeding or to continue therapy with Velphoro 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 Velphoro (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 Velphoro treatment of up to 55 weeks.

In these clinical trials, approximately 43% of patients experienced at least one adverse reaction during Velphoro treatment, which were reported as serious adverse reactions in 0.36%. The majority of the adverse drug reactions (ADRs) reported from trials were gastrointestinal disorders, with the most frequently reported ADRs 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 ADR profile of Velphoro.

Tabulated list of adverse reactions

ADRs 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 1.

Table 1 Adverse drug reactions detected in clinical trials

System Organ Class	Very common (≥1/10)	Common (≥1/100 to <1/10)	Uncommon (≥1/1,000 to <1/100)
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 treatment-related diarrhoea adverse events were transient, occurred early during treatment initiation and led to treatment discontinuation in 3.1% of the patients.

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 should be treated by standard clinical practice.

5. PHARMACOLOGICAL PROPERTIES**5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: Drugs for treatment of hyperkalaemia and hyperphosphataemia; ATC code: V03AE05

Mechanism of action

Velphoro contains a mixture 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 Velphoro 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 Velphoro (1,000 to 3,000 mg iron/day) or low dose (250 mg iron/day) of Velphoro demonstrated superiority of the maintenance dose.

In Study-05A, 1,055 patients on hemodialysis (N=968) or peritoneal dialysis (N=87) with serum phosphorus ≥ 1.94 mmol/L following a 2-4 week phosphate binder washout period, were randomized and treated with either Velphoro, 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 hemodialysis whose serum phosphorus levels were controlled (< 1.78 mmol/L) with Velphoro in the first part of the study, were re-randomized 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 Velphoro for a further 3 weeks.

Following completion of Study-05A, 658 patients (597 on hemodialysis and 61 on peritoneal dialysis) were treated in the 28-week extension study (Study-05B) with either Velphoro (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 Velphoro (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 KDOQI (Kidney Disease Outcomes Quality Initiative) recommended range were 45.3% and 59.1% at week 12 and 51.9% and 55.2% at week 52, for Velphoro 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.

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with Velphoro in one or more subsets of the paediatric population in the treatment of hyperphosphataemia (see section 4.2 for information on paediatric use).

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 ($\leq 1\%$ of the administered dose).

The iron uptake from radiolabelled Velphoro drug 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 drug 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 drug 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 ossification) 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 suroferric oxyhydroxide. This is thought to be most likely an adaptive response to the pharmacological effect of the drug, 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 blister, each blister containing 6 chewable tablets. Pack sizes of 30 or 90 chewable tablets (multipack containing 3 individual packs of 30 chewable tablets each).

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

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**

The requirements for submission of periodic safety update reports 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 shall submit the first periodic safety update report 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 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 CHEWABLE TABLETS
OUTER CARTON – BOTTLE OF 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 500 mg iron as sucroferric oxyhydroxide.

3. LIST OF EXCIPIENTS

Contains sucrose and starches. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

30 chewable tablets
90 chewable tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Tablets must be chewed and taken with meals.
Read the package leaflet before use.
For 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

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

velphoro

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 CHEWABLE TABLETS

LABEL - BOTTLE OF 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 500 mg iron as sucroferric oxyhydroxide

3. LIST OF EXCIPIENTS

Contains sucrose and starches. Read the package leaflet before use.

4. PHARMACEUTICAL FORM AND CONTENTS

30 chewable tablets
90 chewable tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For oral use.
Tablets must be chewed and taken with meals.

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

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 500 mg iron as sucroferric oxyhydroxide.

3. LIST OF EXCIPIENTS

Contains sucrose and starches. See leaflet for further information

4. PHARMACEUTICAL FORM AND CONTENTS

30 x 1 chewable tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Tablets must be chewed and taken with meals.
Read the package leaflet before use.
For 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

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

velphoro

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 500 mg iron as sucroferric oxyhydroxide.

3. LIST OF EXCIPIENTS

Contains sucrose and starches. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

30 x 1 chewable tablets.
Component of a multipack. Can't be sold separately.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Tablets must be chewed and taken with meals.
Read the package leaflet before use.
For 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

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

velphoro

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 500 mg iron as sucroferric oxyhydroxide.

3. LIST OF EXCIPIENTS

Contains sucrose and starches. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

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

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Tablets must be chewed and taken with meals.
Read the package leaflet before use.
For 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
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13. BATCH NUMBER

Lot:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

velphoro

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

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Velphoro 500 mg chewable tablets iron as sucroferric oxyhydroxide

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

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
2. What you need to know before you take Velphoro
3. How to take Velphoro
4. Possible side effects
5. How to store Velphoro
6. Contents of the pack and other information

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. One tablet of Velphoro corresponds to 500 mg iron. Each tablet also contains 750 mg sucrose and 700 mg starches.

Velphoro is for use by adult patients who undergo haemodialysis or peritoneal dialysis (procedures to eliminate toxic substances from the blood) because of chronic kidney disease; it is used in order to help control the phosphorus level in their blood when it is too high (hyperphosphataemia).

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.

Velphoro 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 the active substance 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.

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

Children and adolescents

The safety and efficacy of Velphoro in children below the age of 18 years has not yet been established. Therefore Velphoro is not recommended for use in children.

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 or doxycycline), 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 breastfeeding

If you are pregnant or breastfeeding, 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 discuss with you whether Velphoro should be used during pregnancy or breastfeeding.

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 operate 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.

Velphoro may be harmful to the teeth.

Velphoro contains starches. If you have diabetes you should take notice that one tablet of Velphoro 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 is the equivalent of 1,500 mg iron per day (3 tablets). The maximum recommended dose is 3,000 mg iron (6 tablets) per day.

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

Method of administration

- Velphoro should only be taken 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.
- The amount of tablets taken per day should be divided across the meals of the day.

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.

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").

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), black stools.

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 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

- Each tablet contains 500 mg iron as sucroferric oxyhydroxide.
- The other ingredients are woodberry flavour, neohesperidin-dihydrochalcone, magnesium stearate, silica (colloidal, anhydrous).

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 chewable tablets each).

Not all pack sizes may be marketed.

Marketing Authorisation Holder

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For any information about this medicine, please contact the Marketing Authorisation Holder.

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