

For the use only of Registered Medical Practitioners or a Hospital or a Laboratory

FEFOL SPANSULE CAPSULES

1. GENERIC NAME

Sustained-Release Capsules of Ferrous Sulphate with Folic Acid

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Spansule capsule contains:

Dried Ferrous Sulphate IP 150 mg
(In time-release form, equivalent to 46.8 mg of elemental iron)
Folic Acid IP 0.5 mg

Colour: Carmoisine

Colours: Tartrazine, Brilliant Blue FCF and Titanium Dioxide IP in empty capsule shells.

3. DOSAGE FORM AND STRENGTH

Sustained-release capsules

Each Spansule capsule contains:

Dried Ferrous Sulphate IP 150 mg
(In time-release form, equivalent to 46.8 mg of elemental iron)
Folic Acid IP 0.5 mg

Colour: Carmoisine

Colours: Tartrazine, Brilliant Blue FCF and Titanium Dioxide IP in empty capsule shells.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Prevention of iron deficiency anaemia

FEFOL SPANSULE CAPSULES is indicated for iron supplementation, especially suitable during pregnancy and lactation. It is also suitable for use as prophylaxis against iron deficiency in menstruating females of child-bearing age.

Treatment of iron deficiency anaemia

FEFOL SPANSULE CAPSULES is indicated for the treatment of adults with iron deficiency anemia in conditions such as:

- nutritional deficiency resulting from qualitative or quantitative dietary inadequacy or dietary restrictions,
- age related iron deficiencies in the elderly,
- increased requirements as in pregnant and lactating women,

- following a period of chronic blood loss as in patients with chronic menorrhagia, prolonged or recurrent hookworm infestation, bleeding peptic ulcer, bleeding piles and other conditions characterized by intractable bleeding.

4.2 Posology and Method of Administration

FEFOL SPANSULE CAPSULES should not be sucked, chewed or kept in the mouth, but swallowed whole with a glass of water and should not be taken with hot liquids.

The capsules are to be taken at sufficient intervals from meals (for instance, on an empty stomach in the morning or between two principal meals), because absorption can be reduced by ingredients of food. The duration of therapy is determined according to the laboratory follow-up study results.

If swallowing of the capsule proves difficult or is not desirable, the capsule content can also be taken without the capsule body. Therefore, the patient cautiously draws the capsule body over a spoon, in which the granules are gathered. After the granules have been taken from the spoon, the patient should drink sufficient water.

The treatment should be continued until normal values have been obtained. The treatment can be continued as long as necessary to replenish the body iron stores.

Treatment duration varies depending on the severity of the deficiency, but generally about 10 to 20 weeks treatment is required, or longer in case of persisting underlying pathology. Treatment duration in prevention of iron deficiency varies depending on the situation (pregnancy, blood donation, chronic haemodialysis, planned autologous transfusion).

Route of Administration

For oral use.

Adults

For prophylaxis

One capsule daily.

For treatment

Two capsules a day. In severe or moderately severe anaemia, the dose may be increased as advised by the physician.

Children

Contraindicated in paediatric use (see 4.3 *Contraindications*).

Elderly

There are no relevant data available.

Renal impairment

Contraindicated in severe renal dysfunction (see 4.3 Contraindications).

Hepatic impairment

Contraindicated in severe hepatic dysfunction (see 4.3 Contraindications).

4.3 Contraindications

FEFOL SPANSULE CAPSULES is contraindicated in:

- hypersensitivity to any of the product ingredients,
- oesophageal stricture, active peptic ulcer, regional enteritis and ulcerative colitis,
- all forms of anaemia not associated with iron deficiency (e.g. megaloblastic anaemia associated with vitamin B₁₂ deficiency, haemolytic anaemia, pernicious anaemia or other vitamin B₁₂ deficiency states (see 4.4 *Special Warnings and Precautions for Use*)),
- iron overload (haemosiderosis, haemochromatosis, chronic haemolysis with signs of iron accumulation, sideroblastic anaemia, repeated blood transfusion, concomitant parenteral iron),
- problems with incorporation of iron (sickle cell anaemia, anaemia associated with lead poisoning, thalassaemia, porphyria cutanea tarda) and forms of anaemia secondary to other haemoglobinopathies,
- confirmed iron intolerance (e.g. severe inflammatory changes of the gastrointestinal tract),
- severe hepatic and renal dysfunction,
- paediatric use,
- paroxysmal nocturnal haemoglobinuria,
- long term folate therapy in any patient with untreated cobalamin deficiency (see 4.4 *Special Warnings and Precautions for Use*),
- malignant disease unless megaloblastic anemia owing to folate deficiency is an important complication.

4.4 Special Warnings and Precautions for Use

Gastrointestinal inflammation

Some post-gastrectomy patients show poor absorption of iron.

Stool darkening

Similarly, to other oral iron products, consumption of *FEFOL SPANSULE CAPSULES* may lead to darkening of the stool, giving the appearance of tarry stool.

Teeth darkening and mouth ulcerations

Tooth discoloration may occur during therapy with ferrous-containing drugs. According to the scientific literature, this tooth discoloration can either regress spontaneously after

discontinuation of the medicinal product, or has to be removed by abrasive toothpaste or by professional dental cleaning.

Due to the risk of mouth ulcerations and tooth discolouration, capsules should not be sucked, chewed or kept in the mouth, but swallowed whole with water.

Investigations

Benzidine or similar tests for detection of faecal occult blood may yield false positives. Product must be discontinued for 3 days prior to the planned performance of this test.

Parenteral therapy

Oral and parenteral iron therapy should not be used together (see *4.5 Drug Interactions*).

Elderly

Particularly elderly people presenting with blood or iron loss of unknown origin have to be carefully examined for the cause of anaemia/ the source of haemorrhage.

Children

Iron preparation may cause poisoning especially among children. Iron overdose may be fatal (see *4.9 Overdose*).

Pernicious anaemia or vitamin B₁₂ deficiency

The folic acid content is unlikely to mask pernicious anaemia should this condition be present; pregnancy during pernicious anaemia is very rare.

Patients with vitamin B₁₂ deficiency should not be treated with folic acid unless administered with adequate amounts of hydroxocobalamin, as it can mask the condition but the subacute irreversible damage to the nervous system will continue.

The deficiency can be due to undiagnosed megaloblastic anaemia including in infancy, pernicious anaemia or macrocytic anaemia of unknown aetiology or other cause of cobalamin deficiency, including lifelong vegetarians.

Iron aspiration

Aspiration of iron sulphate tablets can cause necrosis of the bronchial mucosa which may result in coughing, haemoptysis, bronchostenosis and/or pulmonary infection (even if aspiration happened days to months before these symptoms occurred). Elderly patients and patients who have difficulties swallowing should only be treated with iron sulphate tablets after a careful evaluation of the individual patient's risk of aspiration. Alternative formulations should be considered. Patients should seek medical attention in case of suspected aspiration.

Other

Duration of treatment should generally not exceed 3 months after correction of anaemia.

Failure to respond to treatment may indicate other causes of anaemia and should be further investigated.

Patients suffering from iron overload are particularly susceptible to infection.

Treatment of iron overload should be with caution.

In cases of delayed gastric emptying, pyloric stenosis and confirmed intestinal diverticulosis, liquid rather than solid formulations of iron should be administered.

Caution should be exercised when administering folic acid to patients who may have folate dependent tumors.

FEFOL SPANSULE CAPSULES is not intended for healthy pregnant women where lower doses are recommended, but for pregnant women with folic acid deficiency or women at risk for the reoccurrence of neural tube defect.

4.5 Drug Interactions

Intravenous administration of iron salts

Administration of iron intravenously concomitantly with oral administration of iron may induce hypotension or even collapse due to the fast release of iron due to saturation of transferrin. The combination is not recommended.

Doxycycline

Orally administered iron salts inhibit the absorption and the enterohepatic circulation of doxycycline. The combination should be avoided.

Tetracyclines

The effect of iron and tetracycline products is reduced with their concurrent administration. Tetracyclines form poorly soluble combinations with iron, leading to decreased absorption of both iron and tetracycline. The interval between the administration of *FEFOL SPANSULE CAPSULES* and tetracyclines other than doxycycline (see above) should be at least 3 hours.

Cholestyramine

Cholestyramine inhibits intestinal absorption of iron.

Penicillamine, gold compounds and dietary phosphates

The absorption of penicillamine, gold compounds and dietary phosphates is decreased during treatment with iron products. Penicillamine should be administered at least 2 hours before *FEFOL SPANSULE CAPSULES*.

Salicylates, phenylbutazone and oxyphenbutazone

The concurrent oral administration of iron products and salicylates, phenylbutazone or oxyphenbutazone may enhance their irritant effect on the gastric and intestinal mucosa.

Chloramphenicol

The concomitant administration of chloramphenicol may delay the therapeutic action of iron and its compounds.

Antacids and other calcium compounds

Antacids containing oxides, hydroxides or salts of magnesium, aluminium and calcium, chelate iron salts. The interval between the administrations of these compound groups should therefore be as long as possible; the minimum time is 2 hours between the administration of the antacid and iron.

Iron complexing agents (such as oxalates, phytates, phosphates and magnesium trisilicate, trientine and zinc salts)

Compounds containing calcium and magnesium oxalates, phytates and phosphates (which are contained in vegetable food and constituents of milk, coffee and tea) or carbonates and zinc salts, also impair iron absorption by formation of insoluble complexes. The interval between the administrations of these compounds should be at least 2 hours.

Levodopa, carbidopa and methyldopa

Iron salts can also decrease absorption of other drugs including levodopa, carbidopa and methyldopa.

The simultaneous administration of ferrous sulphate and levodopa to healthy volunteers reduces the bioavailability of levodopa with 50%. The bioavailability of carbidopa is also reduced (75%). When ferrous sulphate was given at the same time as, or 1 hour or 2 hours before methyldopa, the bioavailability of methyldopa was reduced to 83%, 55% and 42% respectively. The interval between the administrations of these compounds should be as long as possible.

Bisphosphonates

Iron containing medicinal products form complexes with bisphosphonates *in vitro*. When iron salts are co-administered with bisphosphonates, the absorption of bisphosphonate may be impaired. The time-interval between the administrations of these medicinal products should be at least 2 hours. Iron supplements should not be taken within one hour before two hours ingestion of these products.

Fluoroquinolones

When iron salts are co-administered with fluoroquinolones, the absorption of the latter is significantly impaired. The absorption of norfloxacin, levofloxacin, ciprofloxacin, gatifloxacin and ofloxacin is inhibited by iron between 30 and 90%. Fluoroquinolones should be administered at least 2 hours before or at least 4 hours after ferrous-containing medicines.

Thyroid hormones

When co-administered, the absorption of thyroxine is inhibited by iron, which can affect the result of the treatment. The interval between the administrations of the compounds should be at least 2 hours.

Nonsteroidal anti-inflammatory agents

Concomitant administration of iron salts with non-steroidal anti-inflammatory agents may intensify the irritant effect on the gastrointestinal mucosa.

Sulphonamides, anticonvulsants and barbiturates

Sulphonamides, anticonvulsants and barbiturates impair the absorption of folic acid.

There is a specific interaction between phenytoin and folate such that chronic phenytoin use produces folate deficiency. Correction of the folate deficiency reduces plasma phenytoin with potential loss of seizure control. Similar but less marked relationships exist with all anti-convulsant treatments including sodium valproate, carbamazepine and the barbiturates. Sulphasalazine and triamterene also inhibit absorption.

Dimercaprol

The concomitant use of dimercaprol and iron must be avoided.

Mycophenolate mofetil

Oral iron preparations significantly reduce the absorption of mycophenolate mofetil.

Other

Administration of iron salts with food may impair the absorption of iron.

The concurrent intake of products with a high content of vegetable constituents, phosphates and tannins limits the absorption of iron, while fish, meat and food with a high content of ascorbic acid and fruit acids have the opposite effect.

Antibacterials, and co-trimoxazole, may interfere with folate metabolism.

Folate supplements enhance the efficacy of lithium therapy. Methotrexate and trimethoprim are specific anti-folates and the folate deficiency caused by their prolonged use cannot be treated by folic acid containing tablets. Folinic acid should be used. Nitrous oxide anaesthesia may cause an acute folic acid deficiency. Both ethanol and aspirin increase folic elimination.

4.6 Use in Special Populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

Children

Contraindicated in paediatric use (see 4.3 *Contraindications*).

Elderly

There are no relevant data available.

Renal impairment

Contraindicated in severe renal dysfunction (see 4.3 *Contraindications*).

Hepatic impairment

Contraindicated in severe hepatic dysfunction (see 4.3 *Contraindications*).

Pregnancy and Lactation

Fertility

There is no relevant data available.

Pregnancy

FEFOL SPANSULE CAPSULES is indicated for prevention and treatment of iron deficiency anaemia of pregnancy.

Use of any drug during the first trimester of pregnancy should be avoided if possible. Thus, administration of iron during the first trimester however requires evidence of iron deficiency. Prophylaxis of iron deficiency during the remainder of pregnancy is justified.

FEFOL SPANSULE CAPSULES is administered when prescribed by a doctor.

There are no known hazards to the use of folic acid in pregnancy, supplements of folic acid are often beneficial.

Non-drug - induced folic acid deficiency, or abnormal folate metabolism, is related to the occurrence of birth defects and some neural tube defects. Interference with folic acid metabolism or folate deficiency induced by drugs such as anticonvulsants and some antineoplastics early in pregnancy results in congenital anomalies. Lack of the vitamin or its metabolites may also be responsible for some cases of spontaneous abortion and intrauterine growth retardation.

Lactation

Folic acid is excreted in breast milk.

Accumulation of folate in milk takes precedence over maternal folate needs. Levels of folic acid are relatively low in colostrum but as lactation proceeds, concentrations of the vitamin rise. No adverse effects have been observed in breast fed infants whose mothers were receiving folic acid.

Ferrous salts are recommended for use in pregnancy and lactation, and no contraindications to such are known.

The amount of iron and folic acid, which is transferred from ferrous sulphate/folic acid to breast milk has not been determined and it is not known if adverse events may occur in the breastfed children of mothers who receive this form of treatment.

FEFOL SPANSULE CAPSULES is administered when prescribed by a doctor.

4.7 Effects on Ability to Drive and Use Machines

No effects on the ability to drive and use machines have been observed.

4.8 Undesirable Effects

Clinical Trial Data

Not relevant for this product.

Post Marketing Data

Adverse drug reactions (ADRs) are listed below by MedDRA system organ class and by frequency.

Frequencies are defined as:

Very common $\geq 1/10$

Common $\geq 1/100$ to $< 1/10$

Uncommon $\geq 1/1000$ to $< 1/100$

Rare $\geq 1/10000$ to $< 1/1000$

Very rare $< 1/10000$

Not known (cannot be estimated from the available data).

Gastrointestinal disorders

Common: faeces discoloured (*see 4.4 Special Warnings and Precautions for Use*)

Uncommon: abdominal bloating, abdominal pain upper, constipation (particularly in older patients which may lead to faecal impaction), diarrhoea, nausea

Rare: Flatulence

Not known: vomiting, tooth discolouration (*4.4 Special Warnings and Precautions for Use*, heartburn, abdominal pain, anorexia, gastrointestinal irritation, mouth ulceration*

*in the context of incorrect administration, when the capsules are chewed, sucked or kept in mouth. Elderly patients and patients with deglutition disorders may also be at risk of oesophageal lesions or of bronchial necrosis, in case of false route.

Immune system disorders

Not known: hypersensitivity reactions, anaphylactic reaction including anaphylaxis (*see Skin and subcutaneous tissue disorders*)

Respiratory, thoracic and mediastinal disorders

Bronchostenosis (*see 4.4 Special Warnings and Precautions for Use*)

Skin and subcutaneous tissue disorders

Very rare: dermatitis allergic

Not known: hypersensitivity reactions of the skin, e.g. exanthema, rash (sometimes severe), pruritus, dyspnea, shock and urticaria

4.9 Overdose

Symptoms of intoxication may appear after dosages as small as 20 mg of Fe^{2+} /kg body weight (BW). The appearance of serious toxic effects must be anticipated for dosages from 60 mg of Fe^{2+} /kg BW and more. Intoxications by dosages of 200 to 400 mg of Fe^{2+} /kg BW result in death when left untreated.

Overdosage of ferrous salts is particularly dangerous to young children

A dose as small as 400 mg of Fe^{2+} can lead to life-threatening states in infants.

Symptoms and signs

Iron poisoning can show several phases.

- During the first phase, about 30 minutes to 5 hours following oral administration, symptoms such as restlessness, stomachache, nausea, vomiting and diarrhoea are observed. The faeces show a tarry coloration, the vomit can contain blood. Shock, convulsions, metabolic acidosis and coma can develop.
- This is often followed by a phase of apparent recovery that may last up to 24 hours.
- Then diarrhoea, shock and acidosis reappear. Death can occur after convulsions, Cheyne-Stokes breathing, coma and pulmonary oedema.

Delayed effects of acute poisoning may appear from 2 to 6 weeks after overdose with intestinal obstruction, pyloric stenosis and extensive scarring of the gastric mucosa. The dose of folic acid contained in *FEFOL SPANSULE CAPSULES* excludes any risk of folic acid overdose.

Treatment

The ingestion of raw eggs and milk results in the formation of compounds with ferrous ions and therefore this decreases absorption.

In severe cases of poisoning, particularly if the serum iron concentration exceeds the total iron binding capacity, desferrioxamine, an iron chelating agent, should be administered orally or parenterally as a specific antidote. Severe acute poisoning in infants should always be treated with desferrioxamine at a dose of 90 mg/kg im followed by 15 mg/kg per hour I.V.

Dimercaprol is contraindicated because of the formation of toxic compounds.

Treatment also includes monitoring of the status of the circulation through standard examination and the observation of other signs, particularly fluid balance and acid-base imbalance.

Chronic overdose

Chronic overdose may present as haemosiderosis or haemochromatosis. This is especially likely if anaemia resistant to treatment is erroneously diagnosed as iron deficiency.

Further management should be as clinically indicated.

5. PHARMACOLOGICAL PROPERTIES

5.1 Mechanism of Action and Pharmacodynamic Effects

Iron provided by ferrous sulphate/folic acid aids haemoglobin regeneration. Therapy is generally continued until haemoglobin concentrations reach normal values, which may take some weeks, and then for a further 3 months or more to restore body-iron stores.

Folic acid, after conversion in the body to folinic acid, takes part in reactions involved in the synthesis of nucleotides and maturation of RBCs in conjunction with vitamin B₁₂. It also plays an important role in lymphocyte-mediated immune response.

5.2 Pharmacodynamic Properties

Pharmacotherapeutic group: Iron in combination with folic acid.

ATC Code: B03AD03.

5.3 Pharmacokinetic Properties

FEFOL SPANSULE CAPSULES capsule is a haematinic developed in a 'timed release' oral preparation called the prolonged release capsule.

Each prolonged release capsule contains hundreds of tiny pellets, and each pellet has a core of sugar or starch, to which the active drug is applied. In a prolonged release capsule, there are several sets of pellets, each set coated with differing thickness of semi-permeable wax. The special coating ensures that little or no iron is released in the easily irritated stomach. As each pellet passes through the alimentary tract, fluid begins to pass gradually through the coating and is absorbed. The medicated core swells and eventually ruptures the coating, releasing the active drug. As each batch of pellets successively ruptures, the active ingredient is gradually and constantly released on its way through the GI tract. The prolonged release mechanism thus ensures that iron is made available in small quantities over a period of time in the sites of maximal absorption in the duodenum and jejunum. The high bioavailability of iron in the prolonged release capsule indicates that less iron needs to be administered to the patient for a given haematopoietic response.

5.4 Clinical Studies

Not relevant for this product.

6. NON-CLINICAL PROPERTIES

6.1 Animal Toxicology or Pharmacology

There are no relevant data available

7. DESCRIPTION

Sustained-release capsules

Each Spansule capsule contains:

Dried Ferrous Sulphate IP 150 mg
(In time-release form, equivalent to 46.8 mg of elemental iron)
Folic Acid IP 0.5 mg

Colour: Carmoisine

Colours: Tartrazine, Brilliant Blue FCF and Titanium Dioxide IP in empty capsule shells.

8. PHARMACEUTICAL PARTICULARS

List of Excipients

Non Pareil Pellets:

Sucrose, Maize Starch, Polyvinyl Pyrrolidone, Purified, Talc and Absolute Alcohol

Ferrous sulphate SR Pellets:

Non Pareil Pellets, Polyvinyl Pyrrolidone, Carmoisine Supra, White beeswax, Glyceryl monostearate, Dichloromethane, Isopropyl alcohol, Polyethylene glycol 6000 and Absolute Alcohol

Folic acid Pellets:

Non Pareil Pellets, Dibasic calcium phosphate, Maize starch, Purified Talc, Polyvinyl Pyrrolidone and Isopropyl alcohol

Hard gelatin Capsule Shell:

Gelatin, Methyl paraben, Propyl paraben, SLS, Purified water, Tartrazine, Brilliant Blue FCF and Titanium dioxide

8.1 Incompatibilities

There are no relevant data available.

8.2 Shelf Life

The expiry date is indicated on the label and packaging.

8.3 Packaging Information

Strips of capsules in a carton.

All presentations may not be marketed in India

8.4 Storage and Handling Instructions

Store in a dry place at temperature not exceeding 30° C

Keep out of reach of children.

There are no special requirements for use or handling of this product.

9. PATIENT COUNSELLING INFORMATION

Registered Medical Practitioners may counsel their patients based on the patient information provided in this section:

- This medicine has been prescribed for you personally.
- Don't pass it on to other people - it may harm them even if their symptoms seem to be the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor.

What FEFOL SPANSULE CAPSULES is and what it is used for

FEFOL SPANSULE CAPSULES contains two active ingredients: iron (a mineral that the body needs to produce red blood cells) and folic acid (a vitamin essential in the production and maintenance of new cells).

FEFOL SPANSULE CAPSULES is used for the prevention and treatment of iron-deficiency anaemia (decrease in the number of red blood cells) in pregnant and lactating women.

FEFOL SPANSULE CAPSULES is also used for the treatment of iron-deficiency anaemia in the elderly or in patients with:

- nutritional deficiency
- heavy menstrual periods
- recurrent hookworm infestations
- bleeding stomach ulcer
- bleeding piles
- bleeding from rectum.

Before you take FEFOL SPANSULE CAPSULES

Don't take FEFOL SPANSULE CAPSULES:

- if you are allergic (hypersensitive) to ferrous sulphate, folic acid or any other ingredients of *FEFOL SPANSULE CAPSULES* (listed under *Further Information*)
- if you have a narrowing in your oesophagus (oesophageal stricture)
- if you have an active stomach ulcer (peptic ulcer)
- if you suffer from inflammation which causes abdominal pain or diarrhea (ulcerative colitis) or any other inflammatory condition of the bowels (regional enteritis)
- if you have anaemia not related to low levels of iron for example megaloblastic anaemia - associated with vitamin B₁₂ deficiency or haemolytic anaemia, pernicious anaemia, or any other vitamin B₁₂ deficiency states
- if you have untreated cobalamin deficiency during long term therapy with folate

- if you have a disorder in which there is an iron overload such as haemosiderosis, haemochromatosis, chronic haemolysis or sideroblastic anaemia
- if you notice blood in urine (paroxysmal nocturnal haemoglobinuria)
- if you are receiving iron intravenously
- if you are receiving repeated blood transfusions
- if you have sickle cell anaemia (excessive destruction of red blood cells), anaemia associated with lead poisoning, thalassaemia and forms of anaemia secondary to other haemoglobinopathies (hereditary diseases causing problems with red blood cells)
- if you have a rare blood pigment disorder with blistering of skin when exposed to sunlight (porphyria cutanea tarda)
- if you have severe liver and kidney disease
- if you are under 18 years
- *If you are suffering from cancer*
 - If you think any of these apply to you, don't take *FEFOL SPANSULE CAPSULES* until you have checked with your doctor.

Take special care with FEFOL SPANSULE CAPSULES

Before you take FEFOL SPANSULE CAPSULES your doctor needs to know:

- If you had a gastrectomy (operation to remove all or part of the stomach)
- if you have diverticular disease (where pouches form in the bowel wall), pyloric stenosis (obstruction to move food from your stomach into the small intestine and which causes pain or vomiting)
- if you are over 65 years and have blood or iron loss of unknown origin
- if you are receiving iron intravenously (see *Before you take FEFOL SPANSULE CAPSULES*)
- if you have difficulty swallowing
- if you have co-existing deficiency of vitamin B₁₂ or folic acid including pernicious anaemia, or other vitamin B₁₂ deficiency states
- if you have haemolytic anaemia (anaemia due to destruction of red blood cells)
- if you have megaloblastic anaemia (anaemia caused by deficiency of vitamin B₁₂ or another vitamin, folic acid)
- if you have haemoglobinopathy (*disorder associated with abnormal haemoglobin*)
- if you have an iron storage or absorption disease
- if you have a folate dependent tumour

Check with your doctor if you think any of these may apply to you.

Conditions you need to look out for

FEFOL SPANSULE CAPSULES can cause serious severe allergic reactions. You must look out for certain symptoms while you are taking *FEFOL SPANSULE CAPSULES*, to reduce the risk of any problems (see *Possible Side Effects*).

While you are taking FEFOL SPANSULE CAPSULES

Your stools may be darker than usual. This is a normal effect of medicines containing iron. The presently common tests for traces of blood in the stool may be false-positive.

Don't take *FEFOL SPANSULE CAPSULES* for 3 days prior to the planned performance of these tests.

Your teeth may become discoloured during treatment with *FEFOL SPANSULE CAPSULES*. This discolouration may disappear when you stop taking *FEFOL SPANSULE CAPSULES*. If it does not, you may have to remove it with abrasive toothpaste or have professional dental cleaning.

Due to the risk of mouth ulceration and tooth discolouration, *FEFOL SPANSULE CAPSULES* should not be sucked, chewed or kept in the mouth but swallowed whole with water. If you cannot follow this instruction or have difficulty swallowing, please contact your doctor.

If you accidentally choke on a tablet, please contact your doctor as soon as possible. This is because there is a risk of ulcers and narrowing of the bronchus occurring if the tablet enters the airways. This may result in persistent coughing, coughing up blood and/or feeling out of breath, even if the choking happened days to months before these symptoms occurred. Therefore, you need to be urgently assessed to make sure that the tablet doesn't damage your airways.

Other medicines and FEFOL SPANSULE CAPSULES

Tell your doctor if you're taking any other medicines, if you've taken any recently, or if you start taking new ones.

Some medicines can affect how *FEFOL SPANSULE CAPSULES* works or make it more likely that you'll have side effects. *FEFOL SPANSULE CAPSULES* can also affect how some other medicines work (for example reduces their absorption). These include:

- iron administered intravenously (concomitantly with oral iron treatment - may lead to low blood pressure or even collapse) (see 'Take special care with *FEFOL SPANSULE CAPSULES*'-under *Before you take FEFOL SPANSULE CAPSULES*)
- antibiotics (used to treat bacterial infections) such as tetracyclines (doxycycline), fluoroquinolones (ciprofloxacin, levofloxacin, norfloxacin, gatifloxacin and ofloxacin), sulphonamides (sulfamethoxazole), trimethoprim, co-trimoxazole and chloramphenicol
- bisphosphonates (used to treat bone problems) such as alendronate, clodronate, risedronate
- mineral supplements (for example zinc salts) and compounds containing calcium and magnesium oxalates, phytates and phosphates ('Food and drink with *FEFOL SPANSULE CAPSULES*' under *Before you take FEFOL SPANSULE CAPSULES*)
- antacids (used to treat indigestion) containing oxides, hydroxides and salts of calcium, magnesium and aluminium
- non-steroidal anti-inflammatory drugs (pain relievers) such as salicylates (for example acetylsalicylic acid), phenylbutazone and oxyphenbutazone
- L-methyldopa (used to treat high blood pressure)
- levodopa and carbidopa (used to treat Parkinson's disease)
- penicillamine, gold compounds (used to treat rheumatic diseases)
- cholestyramine (used to treat high blood cholesterol)
- antiepileptics (used to treat seizures) such as phenytoin or other drugs for epilepsy such as sodium valproate, carbamazepine or barbiturates such as phenobarbital
- medicines used to treat thyroid deficiency such as levothyroxine
- dimercaprol used for the treatment of acute poisoning by certain heavy metals
- trientine (for Wilson's disease)
- zinc or ascorbic acid (vitamin C) supplements
- lithium for mental health problems.

- methotrexate (for rheumatoid arthritis or cancer).
- sulphasalazine (for bowel problems or rheumatoid arthritis)
- triamterene, a diuretic (or 'water tablet')
- alcohol
- mycophenolate mofetil (medicine which lowers the body's resistance to disease)
- you need to breathe a gas and air mixture to put you to sleep for an operation or to relieve pain while you are awake

Tell your doctor if you are taking any of these. Your doctor may decide to adjust your dose.

Food and drink with FEFOL SPANSULE CAPSULES

FEFOL SPANSULE CAPSULES prolonged-release capsules should be taken at least two hours before or after eating or drinking the following products: tea, coffee, milk, eggs, wholemeal bread, cereals or other fiber-containing food (vegetables). These products can reduce the absorption of iron. Fish, meat and products containing vitamin C or fruit acids can increase the absorption of iron. Follow the advice of your dietician or doctor when taking *FEFOL SPANSULE CAPSULES* capsules with any of the food or drink listed.

Pregnancy and breast-feeding

FEFOL SPANSULE CAPSULES can be taken to prevent iron deficiency while you're pregnant or breastfeeding.

During the first 12 weeks of pregnancy only take this medicine if your doctor has specifically recommended it. During the second and third trimester of the pregnancy and while breast-feeding *FEFOL SPANSULE CAPSULES* can be taken to prevent iron deficiency, however, ask your doctor for advice before using this medicine to make sure you need to take it.

The ingredients in *FEFOL SPANSULE CAPSULES* can pass into breast milk. Check with your doctor before you take *FEFOL SPANSULE CAPSULES*.

Driving and using machines

FEFOL SPANSULE CAPSULES is unlikely to affect your ability to drive or use machines.

How to take FEFOL SPANSULE CAPSULES

The treatment should continue until you reach normal blood iron levels, this requires usually 10 to 20 weeks, or longer in case of persisting underlying condition.

Treatment duration in prevention of iron deficiency varies depending on the situation (for example pregnancy, chronic haemodialysis).

How much to take

Always take *FEFOL SPANSULE CAPSULES* exactly as your doctor has told you to. Check with your doctor if you're not sure.

Adults

Prevention of iron-deficiency anaemia:

The usual dose of *FEFOL SPANSULE CAPSULES* is one capsule a day.

Treatment of iron-deficiency anaemia:

The usual dose of *FEFOL SPANSULE CAPSULES* is two capsules a day. Your doctor may decide to increase your dose, depending on the iron deficiency.

Don't take any more *FEFOL SPANSULE CAPSULES* than your doctor has recommended.

How to take FEFOL SPANSULE CAPSULES

Swallow your *FEFOL SPANSULE CAPSULES* capsule whole, with a glass of water. Don't take it with hot liquids. Don't chew or crush the capsules.

Alternatively, the capsule may be opened, and the granules taken from a spoon, with a glass of water (but they must not be chewed, sucked or kept in mouth).

Iron preparations are best absorbed on an empty stomach (in the morning or between two principal meals).

If you forget to take FEFOL SPANSULE CAPSULES

Don't take a double dose to make up for a missed dose. Just take it as soon as you remember.

If you are not sure what to do, ask your doctor.

If you take too much FEFOL SPANSULE CAPSULES

Overdose in children may be fatal.

If you take too many capsules of *FEFOL SPANSULE CAPSULES* you may be more likely to have symptoms such as restlessness, stomach pain, feeling sick (nausea), vomiting, diarrhoea, dark stools, fits (seizures), metabolic changes such as too much acid in the blood (acidosis), a dangerous decrease of blood pressure which, if untreated, may lead to collapse, loss of consciousness and death, Cheyne-Stokes breathing (abnormal pattern of breathing, characterized by alternating periods of shallow and deep breathing) and build-up of fluid in the lungs causing breathlessness (pulmonary oedema).

- Don't delay. Contact your doctor or your nearest hospital emergency department immediately. If possible, show them the *FEFOL SPANSULE CAPSULES* pack.

Possible side effects

Like all medicines, *FEFOL SPANSULE CAPSULES* can have side effects, but not everybody gets them.

Conditions you need to look out for Severe allergic reactions. These are very rare in people taking *FEFOL SPANSULE CAPSULES*. Signs include:

- raised and itchy rash (hives)

- swelling, sometimes of the face or mouth (angioedema), causing difficulty in breathing
- Get medical help immediately if you get any of these symptoms. Stop taking *FEFOL SPANSULE CAPSULES*.

Common side effects

These may affect **up to 1 in 10** people:

- darkening of the stools (see ‘While you are taking *FEFOL SPANSULE CAPSULES*’ under ‘Before you take *FEFOL SPANSULE CAPSULES*’)

Uncommon side effects

These may affect up to 1 in 100 people:

- bloating
- stomach pain (upper)
- constipation
- diarrhea
- feeling sick (nausea)

Rare side effects

These may affect up to 1 in 1,000 people:

- excessive gas in the stomach or bowel (Flatulence)

Very rare side effects

These may affect up to 1 in 10,000 people:

- skin rash due to allergy

Other side effects

Other side effects have occurred in a very small number of people, but their exact frequency is unknown:

- vomiting
- tooth discolouration (see ‘While you are taking *FEFOL SPANSULE CAPSULES*’ under ‘Before you take *FEFOL SPANSULE CAPSULES*’)
- heartburn
- stomach pain
- loss of appetite
- gastrointestinal irritation
- allergic (hypersensitivity) reactions of the skin for example rash, extensive skin rash (exanthema), itchy, bumpy rash (hives)
- severe allergic reaction (anaphylactic reaction)
- mouth ulceration (in case of incorrect use, when *FEFOL SPANSULE CAPSULES* is chewed, sucked or left in the mouth)

Elderly patients and patients with difficulty swallowing may also be at risk of ulceration of the throat, oesophagus (the tube that connects your mouth with your stomach) or bronchus (the major air passages of the lungs) if the capsule enters the airways.

All patients, but especially elderly patients and patients with difficulty swallowing may also be at risk of ulceration of the throat, oesophagus (the tube that connects your mouth with your stomach). If the tablet enters the airways, there may be a risk of ulceration of the bronchus (the major air passages of the lungs), resulting in bronchial narrowing.

Tell your doctor if any of the side effects listed becomes severe or troublesome, or if you notice any side effects not listed in this leaflet.

How to store *FEFOL SPANSULE CAPSULES*

This product contains iron. Keep out of the sight and reach of children.

Don't take *FEFOL SPANSULE CAPSULES* after the expiry date shown on the pack.

Store in a dry place at temperature not exceeding 30° C

There are no special requirements for use or handling of this product.

Don't dispose of medicines in wastewater or household waste.

Further information

What *FEFOL SPANSULE CAPSULES* contains

The active substance is ferrous sulphate.

Each prolonged-release capsule contains 150 mg of ferrous sulphate – equivalent to 47 mg of elemental iron and 0.5 mg of folic acid.

Iron waxed pellets (containing ferrous sulphate pellets, bees wax white, methylene chloride, isopropyl alcohol, glyceryl monostearate, polyvinyl pyrrolidone, PEG 6000), Folic acid pellets, Non Parel Seeds (NPS), Carmoisine.

Empty hard gelatin capsule shells containing Gelatin, Methyl paraben, Propyl paraben, Sodium Lauryl Sulphate (SLS), Purified water, Tartrazine, Brilliant Blue FCF and Titanium Dioxide.

What FEFOL SPANSULE CAPSULES looks like and contents of the pack

Strips of capsules in a carton.

All presentations may not be marketed in India

10. DETAILS OF MANUFACTURER

The Manufacturing Site details are mentioned on the label and packaging

For further information, please contact:
GlaxoSmithKline Pharmaceuticals Limited.

Registered Office:
Dr. Annie Besant Road, Worli,

Mumbai 400 030, India.

11. DETAILS OF PERMISSION OR LICENSE NUMBER WITH DATE

Manufacturing License number is indicated on the label and packaging

12. DATE OF REVISION

22-Apr-2021

Trade marks are owned by or licensed to the GSK group of companies.

Version: FEF/PI/IN/2021/01

Adapted from Non Central Data Sheet (NCDS) Version number: 05 for Ferrous sulphate/Folic acid dated 17th September 2019.