Ferro sanol Duodenal

QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains: ferrous (II)-glycine-sulphate complex 567.7 mg (equivalent to 497.9mg of ferrousII)(equivalent to 100 mg Fe^{2+})

Excipients

Ascorbic acid, cellulose microcrystalline, hypromellose, hydroxypropylcellulose

methacrylic acid – ethyl acrylate copolymer, acetyltriethyl citrate, talc, sodium laurilsulphate, polysorbate 80 and purified water.

Capsule cap: gelatin, titanium dioxide (E171), red iron oxide (E172) and black iron oxide (E172)

Capsule body: gelatin, titanium dioxide (E171), red iron oxide (E172) and yellow iron oxide (E172)

PHARMACEUTICAL FORM

Capsules containing gastro-resistant pellets

Capsule cap: chocolatebrown

Capsule body: orange

CLINICAL INFORMATION

Indications

For the treatment of:

- Latent or manifest iron deficiency with and without development of anaemia.
- Iron deficiency anaemia, in particular during pregnancy and lactation and in cases of malnutrition.
- Iron deficiency anaemia in particular during pregnancy and lactation, in childhood, in persons taking low-iron diets, in acute or chronic blood loss.
- Treatment of iron deficiency with and without development of anaemia.

Dosage and Administration

Ferrous (II)- glycine - sulphate complex, 100mg, capsules, hard.

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 contents can be taken without the capsule body. 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.

After the haemoglobin values have returned to normal, the iron therapy, with monitoring of the serum ferritin value, should 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.

Route of Administration

For oral administration

Adults

Adults and children from age 6 take 1 capsule once a day. In case of pronounced iron deficiency, adults and adolescents from age 15 or from 50 kg BW (Body Weight) can be given a dosage 2 to 3 times higher at the beginning of therapy.

Children

Use in children less than 6 years is contraindicated, *see section Contraindications*

Elderly

Caution should be exercised in elderly patients, *see section Warnings and Precautions*

Renal impairment

Caution should be exercised in patients with renal diseases, *see section Warnings and Precautions*

Hepatic impairment

There are no relevant data available.

Contraindications

Contraindicated in:

- Hypersensitivity to the active substance or to any of the excipients
- Haemochromatosis
- Chronic haemolysis with signs of iron accumulation
- Sideroblastic anaemia
- Lead anaemia
- Thalassaemia and forms of anaemia secondary to other haemoglobinopathies
- Repeated blood transfusion.
- Esophageal stricture
- Children less than age 6.

Warnings and Precautions

Care should be taken in patients with existing gastrointestinal disease such as inflammatory bowel disease, intestinal stricture, diverticulae, gastritis, stomach and intestinal ulcers.

In cases of erythropoietin deficiency secondary to serious renal disease, ferrous (II) glycine-sulphate complex should be given together with erythropoietin.

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.

Iron preparations may cause poisoning especially among children, *see section Overdosage*.

Tooth discoloration may occur during ferrous (II)-glycine-sulphate complex therapy. 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.

When iron is administered orally, a dark coloration of the faeces, not resulting from occult gastrointestinal haemorrhage, may occur. Administration of ferrous (II)-glycine-sulphate complex may lead to a false positive blood stool test.

Interactions

Intravenous administration of iron salts

Administration of intravenous iron concomitantly with oral 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. *See also tetracyclines, below.*

The following combinations may require dose adjustment

Iron inhibits the absorption of many medicinal products by chelation. The interval between the administration of ferrous (II)-glycine-sulphate complex and the medicinal products mentioned below should therefore be as long as possible.

Fluoroquinolones

When iron salts are coadministered 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 (II)-glycine-sulphate complex.

Methyldopa (L-form)

When ferrous (II)-glycine-sulphate complex 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 administration of these compounds should be as long as possible.

Thyroid hormones

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

Tetracyclines

When coadministered orally, iron salts inhibit the absorption of tetracyclines. The interval between the administration of ferrous (II)-glycine-sulphate complex and tetracyclines other than doxycycline (see above) should be at least 3 hours.

Penicillamine

The absorption of penicillamine is reduced, as it may form chelates with iron. Penicillamine should be administered at least 2 hours before ferrous (II)-glycine-sulphate complex.

Bisphosphonates

Iron containing medicinal products form complexes with bisphosphonates *in vitro*. When iron salts are coadministered with bisphosphonates, the absorption of bisphosphonate may be impaired. The time-interval between the administration of these medicinal products should be at least 2 hours.

Levodopa

The simultaneous administration of iron sulphate and levodopa to healthy volunteers reduces the bioavailability of levodopa by 50%. The bioavailability of carbidopa is also reduced (75%). The interval between the administration of these compounds should be as long as possible.

Antacids

Antacids containing oxides, hydroxides or salts of magnesium, aluminium and calcium, chelate iron salts. The interval between the administration 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.

Calcium

The concomitant use of iron and calcium decreases the absorption of iron. Ferrous (II)-glycine-sulphate complex should be taken apart from calcium-containing food and beverages.

Foods and beverages

Bioavailability of ferrous (II)-glycine-sulphate complex could be reduced by iron complexing agents (such as phosphates, phytates and oxalates) contained in vegetable food and constituents of milk, coffee and tea. The interval between the administration of these 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.

Pregnancy and Lactation

Fertility

There are no relevant data available.

Pregnancy and Lactation

There are no known risks of using ferrous sulphate glycine complex during pregnancy and lactation

Ability to perform tasks that require judgement, motor or cognitive skills

This medicinal product has no influence on physical and mental condition as well as on the ability to drive and operate machines.

Adverse Reactions

Clinical Trial Data

Not relevant for this product.

Post Marketing Data

Adverse reactions are ranked under headings of frequency using the following convention:

Very common ≥1/10

Common ≥1/100 to <1/10

Uncommon ≥1/1000 to <1/100

Rare ≥1/10000 to <1/1000

Very rare <1/10000

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

Immune system disorders

Rare: hypersensistivity reactions *see Skin and subcutaneous tissue disorders*

Gastrointestinal disorders

Common: abdominal discomfort, constipation, diarrhoea, vomiting, nausea, heartburn, dark coloured faeces, *see section Warnings and Precautions*

Rare: tooth discoloration, *see section Warnings and Precautions*

Skin and subcutaneous tissue disorders

Rare: exanthema, rash, urticaria, *see Immune system disorders*

Overdosage

Symptoms and signs

Symptoms of intoxication may appear after dosages as small as 20 mg of Fe^{2+}/kg 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. A dose 400 mg of Fe^{2+} can lead to life-threatening states in infants.

Iron poisoning can show several phases. During the first phase, about 30 minutes to 5 hours following oral administration, symptoms such as restlessness, stomach ache, nausea, vomiting and diarrhoea are observed. The faeces show a tarry coloration, the vomit can contain blood. Shock, 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.

Treatment

The treatment consists of administration of milk and egg white to inhibit absorption. A specific antidote is desferrioxamine. To treat iron poisoning, 5 to 10 g of desferrioxamine are given orally, while 1 to 2 g are parenterally (IM) injected at the same time.

Clinical Pharmacology

Pharmacodynamics

Pharmacotherapeutic group

Antianemic

Mechanism of Action

The content of iron in the body is about 50 mg of Fe^{2+}/kg BW in men and about 38 mg of Fe^{2+}/kg BW in women. Iron deficiency may have various causes, for instance, haemorrhage, insufficient utilization of food iron, insufficient absorption or supply of iron. Substitution with the highly bioavailable ferrous (II)-glycine-sulphate complex compensates for the deficiency.

Complexed mainly with amino acids, iron is carried into the mucosal epithelial cells of the small intestine, mainly the duodenum and to a lesser extent the proximal jejunum. There the larger iron quantity from non-heme food sources, now reduced to the more soluble ferrous form (Fe^{2+}), is immediately oxidized to ferric form (Fe^{3+}), so that it enters into cell metabolism along with the already prepared heme iron. Control of iron distribution and transfer in the absorbing cell involves several receiving substances. Iron is never allowed to travel about the body unescorted. First, the iron - all now in ferric form - is bound by an initial intracellular carrier molecule, which delivers a portion to the mitochondria for the cell's metabolic needs. Then the initial cellular carrier distributes the rest of the iron, depending on the person's current iron status need, in specific proportions to its regular receptors and carriers: (1) apoferritin, the cell's special protein receptor with which the iron combines to form the immediate holding compound, epithelial ferritin; and (2) apotransferrin, the blood's special protein receptor with which the iron combines to form the circulating carrier compound, serum transferrin. The amount of ferritin already present in the intestinal mucosa cells influences the amount of ingested iron that is absorbed or rejected. When all available apoferritin has been bound to iron form ferritin, any additional iron that arrives at the binding sites is rejected and then returned to the lumen of the intestine and passed on for elimination in the faeces.

Pharmacodynamic effects

Oxygen transport

Iron is packed within the heme molecule, which is the fundamental nonprotein conjugate of haemoglobin in the red blood cells. As such, iron functions as a major transporter of the vital oxygen to the cells for respiration and metabolism. Iron is also a constituent of the similar compound myoglobin in muscle tissue.

Cellular oxidation

Although in smaller amount, iron also functions in the cells as a vital component of enzyme systems for oxidation of glucose to produce energy. For example, iron is a constituent of the cytochrome compounds, which are part of the electron transport systems producing high-energy ATP bonds.

Growth needs

During growth, demands for positive iron balance are imperative. At birth the infant has only a small supply of iron stored in the liver from fetal development. Breast-fed infants obtain some iron in breast milk. Iron is also needed for continued growth and to build up reserves for the physiologic stress of adolescence, especially the onset of menses in girls. The woman's need for iron is increased greatly during pregnancy to maintain the increased number of red blood cells in an expanded circulating blood volume and to supply the iron needed for storage in the developing fetal liver. Finally, normal blood loss during delivery reduces iron stores further.

Pharmacokinetics

Iron is taken up by a special iron transporting system into the absorptive cells of the duodenum and upper small intestine, and is transported either directly into the plasma or is stored as mucosal ferritin. Absorption appears to be regulated by a single hematopoietic transcription factor ($NF\text{-}E_2$), which links intestinal transport to erythropoiesis.

Hard capsules contain gastro-resistant granules. The capsule shell dissolves in the stomach. The granules remain intact until they are released into the duodenum. There the active ingredient iron glycine-sulphate is rapidly released.

In subjects with depleted iron stores the relative bioavailability is 95 % that of an aqueous iron sulphate solution as reference. This corresponds to a Fe^{2+} absorption in the range of 15 % for the 100 mg capsule.

Packaging:

Cartoon Box of 1,2,3 strips each of 10 capsules

Patient instruction:

Keep out of reach of children

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