gyno-Tardyferon®

ROBAPHARM

Composition

*Active principles:*Ferrum (II) utFerrosi sulfas sesquihydricus, Acidumfolicum.

*Excipients:*Mucoprotease, Saccharum, Color. : E 127 (erythrosin), Excipiens pro compressoobducto.

The mucoprotease substance is extracted from jejunum of ovine origin.

Galenic form and quantity of active substance by unit

A slow-release tablet contains: Ferrum (II) 80 mg utFerrosi sulfas sesquihydricus and acidumfolicum 0.35 mg.

Indications / Possibilities of usage

Prevention and treatment of an iron-deficiency anemia and a folic acid deficiency during pregnancy, after delivery and during nursing or lactation period.

After identification of a deficiency in iron and folic acid, and their seriousness must be assessed and confirmed by adequate laboratory tests.

Posology / Label directions

Adult women

Prevention from an iron-deficiency anemia and folic acid deficiency: 1 slow-release tablet 1 x daily in the morning.

Treatment of a mild iron-deficiency anemia and folic acid deficiency: 1 slow-release tablet 1 x daily in the morning.

Treatment of a severe anemia and folic acid deficiency: 1 slow-release tablet 2 x daily, in the morning and nighttime.

Slow-release tablets must be taken on an empty stomach, before meals, swallow them with little liquids, and do not chew. During a gastrointestinal intolerance, slow-release tablets can also be taken with meals.

Treatment duration is set according to iron-deficiency degree. After hemoglobin value standardization, treatment shall be continued during a few weeks, one slow-release tablet daily, in the morning, until the serum ferritin rate shows a satisfactory reconstitution of iron reserves.

If the therapeutic success (increase of hemoglobin of approximately 0.1 g/dl of blood/day and approximately 2-3 g/dl after 3 weeks) takes time, patient's compliance and "iron deficiency" diagnosis must be reassessed and a prolonged blood loss (for example Osler disease) must be excluded.

However, total treatment duration must not exceed 6 months.

Contraindications

All anemia without confirmed iron-deficiency origin (for example megaloblastic anemia by vitamin B12 deficiency).

Iron overload (hemochromatosis, chronic hemolysis; during frequent transfusions).

Dysfunctions in the usage of iron (sideroacrestic anemia, anemia saturnism, thalassemia, porphyria cutaneatarda).

Proven intolerance (for example in case of severe inflammatory alterations of the gastrointestinal tract).

Severe kidney impairment.

Known hypersensibility to the active principle of iron sulfate and folic acid or to any other medication components.

The simultaneous intake of oral preparations and iron-based parenteral is contraindicated.

Use in children (not a title, part of the Contraindications)

Cautions and warnings

In case of inflammatory gastrointestinal diseases (such as gastritis, gastro duodenal ulcers, Crohn disease or ulcerative colitis) martial preparations by oral means must only be cautiously administered.

In case of slow gastric emptying, pylori stenosis and in presence of gastrointestinal tract patent diverticula, it is preferable to use liquid martial preparations rather than solid ones.

During fructose intolerance, glucose/galactose malabsorption or isomaltase-sucrase deficiency, gyno-Tardyferon must not be administered because of the presence of sucrose.

Interactions

Reduced effect of martial preparations and tetracycline during simultaneous administration. Tetracycline form along with iron less soluble compounds, in such a way that the iron resorption as well as that of the tetracycline are decreased.

Magnesium and calcium aluminum-based antacids, in addition to cholestramine can reduce iron resorption.

During a martial therapy, penicillin resorption auriferous components and dietary phosphates is lowered.

Other medication, of which the bioavailability can be reduced by a concomitant intake of iron-based preparations are for example chinolones, methyldopa, levodopa and cabidopa. In case treatment associated with these medications cannot be avoided, a 3-hour minimum delay between drug intakes must be observed.

Simultaneous oral administration of iron-based preparations and salicylates, phenylbutazone or oxyphenbutazone can induce mutual potentiation effects of irritation of the gastrointestinal mucus membranes.

The associated administration of chloramphenicol can delay the response to siderotherapy.

Simultaneous consumption of dietary elements, rich with phytates, phosphates (for example eggs) and tannins (particularly black tea and coffee) limit the iron resorption, whereas fish and food rich in ascorbic acids and acids found in fruits tend to increase it.

Chronic abuse of alcohol can reduce blood concentration of folic acid and by increasing iron resorption it can lead to a martial overdose.

Sulfonamides, antiepileptic and barbituric hinder folic acid absorption.

Pregnancy / Lactation period

There is no clinical data concerning the usage of pregnant women. Animal experiments showed no direct nor indirect toxicity that might have an incidence on pregnancy, the embryo development, the fetal development and/or the post-natal development.

We do not know the amount of iron and folic acid passing through breast milk from gyno-Tardyferon, and we ignore if undesirable effects occur in the breast-fed infant by a mother undergoing such a treatment.

The possibility of emergence of such effects seems however less probable. gyno-Tardyferon is taken during pregnancy and lactation period upon medical prescription (cf. Indications / Possibilities of usage)

Effects on driving and usage of machines

gyno-Tardyferon has no influence on driving capacity, nor usage of machines.

Undesirable effects

Occasional: mild gastro-intestinal disorders (fullness feeling, gastralgia, constipation, diarrhea, nausea).

A dark coloration of stools (faeces) is clinically irrelevant.

Isolated cases of cutaneous hyper-sensibility reaction (urticarial, pruritus, rash) even anaphylaxis have been reported.

Overdose

Acute overdose

Accidental intake of massive oral doses of 2 g of ferrous sulfate (II) can provoke severe intoxication that could be lethal. The iron dose threshold with toxic effects is considerably lower in children than in adults.

For infants, a global dose of approximately 0.5 g can already provoke a dangerous intoxication and a dose of 1 g can be lethal. In case of acute overdose, the first symptoms appear (about ½ hour after swallowing) following a hemorrhagic gastroenteritis: nausea, violent vomiting, strong abdominal pains, and diarrhea, and after a little time latency, tachycardia, decrease of blood pressure, dyspnea and cyanosis.

In serious cases, and sometimes after an apparent improvement of 24 to 48 hours, the passage of important iron amounts in blood provoke cramps, paralysis, toxic hepatitis, kidney failure, metabolic acidosis with Cheyne-Stockes respiration, lung edema, circulatory collapses, coma and death.

Treatment

Treatment of a *mild to average intoxication* consists in provoking vomiting and if necessary to proceed to performing gastric lavage with a 1% sodium bicarbonate solution during the first hours after intoxication.

We should bear in mind that provoked vomiting in presence of already damaged stomach lining include the risk of gastric perforation. However, eating raw eggs and milk may lead to forming complexes with iron ions and thus reduce iron resorption.

In case of severe intoxication, particularly when serum iron exceeds the total capacity of iron fixation (3.5 mg/l = 63 µ M), it is advisable to administer deferoxamin ferrochelator, as a specific antidote, by oral means and parenteral.

Dimercaprol is not recommended because of the formation of toxic complexes.

When a potentially lethal dose of a solid martial preparation swallowed cannot be evacuated through the digestive tube according to the measures indicated above, an exsanguino-transfusion and a surgery must be considered.

The treatment consists however in monitoring through common measures the circulatory collapse and other symptoms, particularly hydric equilibrium disorders and acido-basic.

Late follow ups of ‘75ne acute intoxication can appear 2 to 6 months after overdose, as an intestinal occlusion, polyre stenosis and serious scarring of the gastric mucus.

Folic acid amounts contained in the preparation draw aside any risk of folic acid overdose.

Chronic overdose

A chronic overdose can appear as a hemosiderosis and a hemochromatosis. First of all it is possible when an anemia resistant to treatment is wrongly diagnosed as an iron-deficiency anemia.

Properties / Effects

Code ATC: B03AD03

Action mechanism / Pharmacodynamics

gyno-Tardyferon is a slow-release martial preparation. Thanks to mucoproteosis adjunction in the galenic composition of core gyno-Tardyferon, iron ion release Fe2+ is slowed down and an initial concentration rich in iron is avoided.

This helps in reducing the percentage of undesirable secondary effects and facilitates compliance.

Furthermore, slow release of iron also leads to the presence of iron ions Fe2+ in intestine distal segments. These segments are able to absorb iron through an adaptation process, whereas is case of martial saturation, intestinal absorption remains somehow limited to upper segments in intestine.

Alike all other iron-based preparations, gyno-Tardyferon has no effects on erythropoiesis, nor on an iron-deficiency anemia.

Pharmacokinetic

Absorption / Distribution

Iron

Administered orally, soluble iron as it is found in gyno-Tardyferon is mainly absorbed in the duodenum and proximal jejunum.

Iron absorption depends on patient’s iron reserves and on preparation administration mode (on an empty stomach, 2 hours before meals, during meals).

When gyno-Tardyferon is taken as recommended in the posology (little before, during or after meals) iron absorption measured on the basis of iron serum levels is higher than with a release of non-slow iron, i.e. without mucoproteosis. After the daily administration of 2 slow-release gyno-Tardyferon tablets (160 mg of Fe2+) taken a little bit before meals by anemic

subjects having empty iron reserves (serum ferritin < 10 µ g/l), serum concentrations increase continuously to reach after 4 hours their maximum values.

To assess the bioavailability, it is somehow necessary to know the use of the iron oral intake, namely the iron fraction fixed on hemoglobin by gyno-Tradyferon. Measured thanks to gyno-Tardyferon containing radioactive iron (54Fe), this fraction reaches in therapeutic conditions 25%, which almost represents a maximum theoretical value that can be obtained.

Iron absorption is tightly linked to the sederopenia degree. For low hemoglobin values and a small iron-reserve filling, it is the highest and it decreases as these parameters come back to normal.

It can't exceed the maximum capacity of transport of protein of transport, even if we administer high dosages of iron; this capacity can be limited by the administration of some nutriments and medication (cf. Interactions).

In the blood, iron ions are linked to transferrin and transported to their site of usage. In the liver, the spleen and the bone marrow, iron is stored under ferritin form.

Folic acid

Folic acid is rapidly resorbed, and with no problems, from the tablet's envelop, especially in the small intestine, namely the duodenum and the jejunum. After administration of one slow-release tablet of gyno-Tardyferon, a plasmatic peak of folic acid of 43.7 ± 25.6 ng/ml is reached after 99 minutes and it is doubled with 2 slow-release tablets.

Metabolism / Elimination

Only a little part of iron-release by hemoglobin degradation (20 to 30 mg per day) is excreted (1-2 mg per day, mainly by faeces). The biggest amount is reused by the organism, mainly for hemoglobin synthesis.

Iron and folic acid cross the placenta barrier and enter in small amounts in the mother's milk.

Preclinical data

There is no relevant specific data for the usage of the preparation.

Particular notes

Information

Alike any other oral martial therapy, gyno-Tardyferon intake can lead to a dark coloration of stools (faeces) and simulate a melena.

Conservation

Medication cannot be used after expiry date clearly appearing on medication packaging or labelling, next to “EXP”.

Storage notes

Store at room temperature (15-25 °C).

Knowing that the smallest gyno-Tradyferon packaging of 30 slow-release tablets contains a total iron dosage that can provoke a life-threatening intoxication in a child due to accidental ingestion, this medication must absolutely be stored out of reach of children.

Authorization number

38959 (Swissmedic)

Holder of authorization

Robapharm SA. 4123 Allschwil.

Information updates:

March 2007

Presentation

	Quantity	RebateCat
GYNO TARDYFERON tablet storage	30 pieces	C
	100 pieces	C

Issued on 16/07/2008