Medox® Prenatal Coated Tablets

PHARMACOLOGICAL INFORMATION

1. COMMERCIAL NAME: Medox® prenatal coated tablets
   GENERIC NAME: Vitaminic and mineral complement, prenatal

2. FORMULA:
   Each coated tablet contains:
   - Vitamin A (as beta-carotene 4,000 UI).........................8000 UI
   - Vitamin A acetate 4,000 UI).................................400.00 UI
   - Vitamin E acetate..................................................30.00 UI
   - Vitamin C (Ascorbic Acid)........................................60.00 mg
   - Vitamin B1 (Thiamine mononitrate eq. Thiamine).........1.70 mg
   - Vitamin B2 (Riboflavine)...........................................2.00 mg
   - Vitamin B6 (Pyridoxine Hydrochloride eq.)...............6.58 mg
   - Pyridoxine...........................................................8.00 mg
   - Vitamin B12 (cyanocobalamin)..................................8.00 mg
   - Nicotinamide.........................................................20.00 mg
   - Calcium pantothenate eq...........................................21.74 mg
   - Pantothenic Acid....................................................10.00 mg
   - Folic Acid..............................................................0.80 mg
   - Dibasic Calcium Phosphate eq....................................169.74 mg
   - Calcium.................................................................50.00 mg
   - Aminochelated iron eq.............................................10.96 mg
   - Iron............................................................................3.00 mg
   - Potassium iodate eq...................................................0.25 mg
   - Iodine...........................................................................0.15 mg
   - Magnesium Oxide eq..................................................16.58 mg
   - Magnesium.............................................................10.00 mg
   - Calcium-fluoride eq....................................................4.11 mg
   - Fluoride.......................................................................1.00 mg
   - Excipients q.s.

3. DESCRIPTION:
   Medox® Prenatal Coated Tablets is a formula that provides the essential vitamins and the minerals before, during and after the pregnancy.

4. THERAPEUTIC INDICATIONS:
   Vitamin A has an important role in the vision at a retina level, necessary for the growth and development of the bones, for the reproduction and the integrity of the mucous and the epithelial surfaces. Its deficiency leads to the atrophy of the aforementioned, followed by the abnormal proliferation of the basal layer, with the formation of stratified epithelia very keratinized. Vitamin D regulates the metabolism of calcium and phosphate when it comes to the intestinal absorption and their deposit in the bones and teeth. Its deficiency produces rickets in children and osteomalacia in adults.
   Vitamin E is considered as an essential nutritional element, even if its exact function is unknown. It is attributed a certain anti-oxidant action of the tocopherols, in the sense that they can protect certain metabolites, especially when it concerns the Saturated Fatty Acids. Vitamin C or ascorbic acid is essential for the collagen synthesis and the intercellular material. It is involved in the conversion of folic acid to folinic in the process of electronic transportation and it is believed to intervene in the metabolism of thyroxine. Its deficiency produces scurvy, which is rarely observed in
adults; but usually in infants. The intake of ascorbic acid is important during pregnancy and breastfeeding.

Complex B vitamins (thiamine, pyridoxine, riboflamine, cyanocobalamin) play a vital role in the transformation of carbohydrates, proteins, and fat in the tissues. The thiamine acts as a coenzyme in the metabolism of carbohydrates and in deficiency cases of this vitamin, pyruvic and lactic acids are accumulated in the tissues, which result in fatigue, anorexia, gastrointestinal disorders, tachycardia, irritability, and neurological symptoms. The pyridoxine is essential in amino acid metabolism. In patients, both adults and children, with pyridoxine deficiency, cases of seizures and hypochromic anemia, and skin and mouth injuries, have been reported. Some peripheral neuritis and neuritis associated with the INH therapy may be caused by a pyridoxine deficiency. The deficiency of riboflavine is characterized by well-defined symptoms, characterized by angular stomatitis, glossitis, red and brilliant lips, follicular seborrheic keratoses in the nasolabial, nose, and forehead folds. The cyanocobalamin is essential in the synthesis of nucleic acids and for the normal aging of red blood cells, its deficiency causes anemia, and gastrointestinal signs like glossitis, and subjective symptoms like lassitude and neurological defects producing an improvement when cyanocobalamin is administered.

Folic Acid is a member of the vitamin B group, it is necessary for several processes of the metabolism. The deficiency produces megaloblastic anemia, administering folic acid produces a remission of the blood picture, with the reticulocyte response, an increase of erythrocytes, hemoglobin and the megaloblastic hyperplasia of the bone marrow. The deficiency of Nicotinamide intervenes in the enzymatic processes related to cell oxidation and its presence is necessary for the functional integrity of the skin, digestive mucous, and the central nervous system mainly. Its deficiency (factor PP) produces a denominated illness called pellagra with inflammatory injuries and ulcers in the skin, mouth and intestine mucous. The calcium pantothenate is present in the living tissues and is commonly considered a member of the complex B vitamins. It is a member of the coenzyme, which intervenes in the acetylation processes in the tricarboxylic acid cycle of Krebs.

Calcium is mainly used in the treatment for hypocalcemia or deficiency of calcium, to counteract or decrease demineralization such as osteoporosis. Iron is an essential element for life and it intervenes in the breathing processes, mainly in the transportation of oxygen in the hemoglobin and the mioglobin and in cell oxydation in tissue enzymes. Iron deficiency produces microctic hypochromic anemia. In these cases the administration of iron produces good results. First, there is an increase in the percentage of reticulosis; then there is an increase of hemoglobin and in the number of erythrocytes, and in the relative volume of red blood cells centrifuged (hematocrit). The cell value and the hematocrit values that were low were also brought back to normal. A symptomatic improvement is produced and soon the paleness, loss of appetite, shortage of breath, palpitations, glossitis, and dysphagia, when present, disappeared.

Iodine is used to prevent hypothyroidism and must be ingested daily. Magnesium is an electrolyte essential for the organism, it is a cofactor in numerous enzymatic systems, it is involved in the transfer of phosphates, muscular contractility, and nervous transmission. It is also believed that it is essential for the structural stabilization of the nucleic acids. Its activity is frequently competitive which the one of the calcium. Fluoride is used to prevent teeth cavities.

5. **PHARMACOKINETICS AND PHARMACODYNAMICS IN HUMANS:**

Vitamin A is absorbed in the small intestine. It is stored in the liver in the form of palmitate. It is transformed and degrades almost entirely in the organism and a little is excreted in the emunctories; it goes to the bile but it is reabsorbed in the intestine. It goes well through breast milk.

Vitamin D is absorbed by the lymph, then going to the blood and stored in the liver mainly and also in the fat tissue, kidneys and spleen. It is transformed in 25-hydroxycholecalciferol metabolite. Vitamin D and its metabolites are mainly eliminated through bile in the intestine and very little through urine. It goes through breast milk.
Vitamin E is absorbed from the gastrointestinal tract, once absorbed, it goes to the blood through the lymph and then it is stored in the liver, fat tissue, muscles, and adrenal gland. Vitamin E is mainly metabolized in the liver, and their metabolites are excreted in the urine, and very little vitamin E is eliminated in urine and a little more in milk.

Ascorbic acid is absorbed quickly and completely in the intestinal tract. It goes through the blood and it is stored in the organs; but its concentration is higher in those of great metabolic activity like the adrenal hypophysis, thymus (young), liver, brain, sex glands, and thyroid. It is metabolized and partially destroyed in the tissues (50-70%) and the rest is excreted through urine. The ascorbic acid goes through breast milk.

The thiamine is absorbed by the gastrointestinal tract but 20-25% is lost through stool. Part of the absorbed thiamine is stored in the liver, brain, kidneys, and heart, essentially in the form of thiamine pyrophosphate. It is partially destroyed in the organism and 20-40% is excreted through urine and some through sweat and milk. This excretion depends on the dosage and lack in the organism; if there is not enough thiamine, the organism retains the vitamin.

The pyridoxine is well absorbed orally. Once in the blood circulation, it is distributed to every organ, especially the liver, heart and kidneys. Part of it is metabolized in these organs. It is transformed in 4-pyridoxic acid that is excreted through urine.

The riboflavine is absorbed well in the intestine, when it is administered orally, once absorbed it goes to the blood and it is distributed in all the organs, especially liver, kidneys, heart, and all the cells transform in mono. It is partially metabolized in the organism and the rest is excreted in the urine and in breast milk. The cyanocobalamin is linked in great proportion to the transcobalamins of the plasma. It is absorbed from the gastrointestinal tract, but its absorption is not regular when it is administered in great dosages and the absorption is limited in patients that lack the intrinsic factor, with syndrome of malabsorption, with disease or abnormalities in the intestine, or after a gastrectomy. It is stored in the liver, excreted in the bile and suffers a re-absorption enterohepatic. Part of the dosage is excreted in urine, the majority in the first 8 hours.

Folic acid is perfectly absorbed when administered orally. Its absorption is altered in diarrheas and especially in the malabsorption syndromes, where high dosages are necessary. Once absorbed, folic acid goes to the blood and its level in the serum rises, becoming normal in the case of megaloblastic anemia. Folic acid goes to breast milk, becoming active in the breast-fed baby. The main excretion is done by the kidneys in form of folic acid and its active metabolite, this excretion corresponds to 5 to 90% of the dosage administered (average 50%) with a higher dosage, higher excretion and depending on the lack of folic acid, this excretion is done in practically 24 hours.

The nicotinamide is quickly absorbed by the gastrointestinal tract. Once absorbed, it goes to the blood and it is distributed in all the organs, especially the liver, kidneys and muscles, but there is little cellular storage at the level of all the cells. The nicotinamide is transformed in the liver, being the principal metabolites N -methyl nicotinamide, and 6-pyridon-N-methyl nicotinamide, and nicotinic acid. The excretion is partially done in urine in the form of nicotinamide, but the majority as metabolites. Small quantities go through the milk. The calcium pantothenate is absorbed quickly from the digestive tract. Apparently it is not broken down in the body since the ingestion and the excretion are approximately the same. Around 70% of the absorbed is excreted through urine. The organic or inorganic calcium salts are absorbed in the same manner, since they solubilize in the acid in the gut. The absorption is mainly done in the upper part of the small intestine. Once absorbed, it goes to the blood plasma and it is distributed in
99% in the bone system and the rest of the extracellular liquid in the organism, especially in the muscles and the skin; on the other hand, the concentration of calcium in the intracellular liquid is very weak. In the stool, 80% of the ingested calcium that represents the non-absorbed in the intestine and the excreted. 20% of the ingested calcium is excreted by urine.

Iron is absorbed through the cells of the mucous, in the duodenum and the jejunum (especially in the second), while the ileum and the colon absorb a little. Iron in the form of organic salts or inorganic are generally absorb very little. This absorption is made through the mucous cells. Once absorbed, the iron goes to the blood increasing its concentration in the blood plasma. It then goes to the bone marrow to make hemoglobin and to other organs where it is stored, especially in the liver and spleen. The organism has very little capacity to excrete iron since the majority is stored. The majority of the iron is absorbed and accumulated as reserve or used to make hemoglobin. It is excreted in important quantities in the stool, but small quantities are excreted in bile and the peeling of the intestinal epithelium; it is barely eliminated in urine, 0.5mg daily of iron, and around 1 mg through menstruation in adult women.

Orally, the iodine is transformed to iodide and is stored in the thyroid gland as thyroglobulin. The iodides that are not retained are excreted in the urine, and small portions in the saliva, stool, and sweat. It goes through the placenta and is excreted in breast milk. The magnesium salts are absorbed slowly in the small intestine when it is administered orally. Once it is absorbed it goes to the blood, where 70% is diffusible and in ionic state, while the rest binds to the proteins. Magnesium is a dominant cellular cation, and it is mainly distributed in bones and muscles, and also in the liver and kidneys. It is mainly excreted through the kidneys and a considerable quantity of non-absorbed magnesium is lost in the stool. The fluorides are mainly absorbed in the gastrointestinal tract, lungs, and skin. It is mainly deposited in the skeleton and teeth. The kidneys are the main excretion route; however it is also excreted in small quantities through the sweat glands, breasts during breastfeeding, and the gastrointestinal tract.

6. CONTRAINDICATIONS:
No contraindications are presented if the indicated dosage is taken. In case there is hypersensitivity to any of the ingredients of the formula. It is contraindicated in patients with pernicious anemia and in rare cases of hypersensitivity to folic acid.

7. PRECAUTIONS AND RESTRICTIONS IN USAGE DURING PREGNANCY AND BREASTFEEDING:
The massive ingestion of this product may result in a dangerous intoxication, so it must be kept out of the reach of children. The recommended dosage must not be exceeded since it may cause hypervitaminosis, especially of vitamin D and A. Do not exceed the recommended dosage.

8. SIDE EFFECTS AND ADVERSE REACTIONS:
It presents good tolerance and excellent security. It may produce gastrointestinal discomfort due to the iron. If this occurs, it must be taken after meals. Cases of allergic sensitization after administering folic acid have been reported.

9. DRUG AND OTHER INTERACTIONS:
It must not be administered with thyroxine and methyldopa since iron decreases their absorption. High quantities of folic acid may counteract the effect of the anti-seizures of the Phenobarbital and primidone and increase the frequency of the seizures in susceptible children. The antiparkinsonian effects of the levadopa may be inhibited by the pyridoxine. The contraceptives increase the concentration of vitamin A in the plasma.
10. OVERDOSE OR ACCIDENTAL INGESTION, MANIFESTATIONS AND HANDLING:
The intoxication by overdose of vitamin A or hypervitaminosis is not frequent since high dosages are necessary; sometimes it has been seen in adults when they ingest 180 mg which is 600,000 UI a day, taken for months or years. The symptoms of intoxication by vitamin A are the following: skin pigmentation, hyperkeratosis, alopecia, itching, anorexia, weakness, and osteoarticular pains.
The treatment consists in interrupting the administration of the vitamin, which quickly leads to a regression of the disorders, except the hyperostosis that lasts a few months.
The intoxication by overdose of vitamin D or hypervitaminosis D is caused by dosages higher than 3.75 mg which is 150,000 UI a day, administered continuously during months. The main symptoms are digestive, nervous, of the kidney, bones, and metabolism.
Digestive disorders: anorexia, vomits, diarrhea, being the first ones to appear.
Nervous and general disorders: lassitude, muscular weakness, dizziness, headaches, pale skin.
Kidney disorders: albuminuria, nicturia, nitrogenous retention (kidney insufficiency by nephrocalcinosis).
Bone alterations: osteoporosis, in spite of calcification of the metaphysis, descaling of the diaphysis.
The metabolic alterations: hypercalcaemia and hypercalciuria.
The treatment consists in suppressing the administration of the medication, ceasing the symptoms. In case of elevated hypercalcemia, corticosteroids are useful, 40 to 100 of prednisone a day or its equivalents.
The vitamin is relatively safe and only extremely high dosages during a long period of time are capable of producing some nervous disorders like: muscular weakness, headaches, and blurry vision, which cease when suspending the treatment.
No overdose by a topical route has been reported.

11. DOSAGE AND ADMINISTRATION ROUTE:
Administration route: Oral.
Dosage: a daily coated tablet before, during and after pregnancy, or the dosage that the doctor recommends.

12. PRESENTATION:
Medical sample: blister with 4 coated tablets
Pharmacy: box with 30 and 100 coated tablets
Hospital: box with 1000 coated tablets

References:
- USP DI. Información de Medicamentos. Pages 1005-1009.