

Data Sheet

ELEVIT[®]

Tablets – film coated

Multivitamins and minerals for before, during and after pregnancy

Qualitative and Quantitative Composition

Elevit is a preparation containing multivitamins in combination with minerals and trace elements.

One film-coated tablet contains:

VITAMINS

Thiamine hydrochloride (Vitamin B1)	1.6 mg
Riboflavine (Vitamin B2)	1.8 mg
Nicotinamide (Vitamin B3)	19 mg
Pyridoxine hydrochloride (Vitamin B6)	2.6 mg
Cyanocobalamin (Vitamin B12)	4 mcg
Ascorbic acid (Vitamin C)	100 mg
Cholecalciferol (Vitamin D)	500 IU (12.5 mcg)
dl-alpha-Tocopherol (Vitamin E)	15 mg
Calcium pantothenate (Vitamin B5)	10 mg
Biotin (Vitamin B8)	200 mcg
Folic acid (Vitamin B9)	800 mcg

MINERALS AND TRACE ELEMENTS

Calcium	125 mg
Magnesium	100 mg
Phosphorus	125 mg
Iron	60 mg
Zinc	7.5 mg
Copper	1 mg
Manganese	1 mg

For excipients, see Pharmaceutical Particulars.

Pharmaceutical Form

Film coated tablets.

Clinical Particulars

Therapeutic Indications

For the prevention of dietary vitamin and mineral deficiencies due to increased needs during pregnancy and lactation. Folic acid taken at least one month prior to and during pregnancy may reduce the risk of having a child with defects of the brain and/or spinal cord (spina bifida).

For the prevention of dietary iron deficiency in pregnancy.

Posology and Method of Administration

One tablet to be taken daily with a glass of water.

In the case of morning sickness, it is recommended that the tablet be taken at noon, or if necessary in the evening.

The recommended duration of administration is at least one month before conception (or when planning a pregnancy), throughout the entire pregnancy and lactation.

Method of Administration

For oral use.

Information for Diabetics

These film-coated tablets do not contain sucrose. Therefore, they can be administered to diabetic patients.

Contraindications

- existing hypervitaminosis D
- impaired renal function
- iron accumulation and iron utilisation disorders
- copper metabolism disorders
- hypercalcaemia
- hypercalciuria
- known hypersensitivity to any component of the product.

Special Warnings and Special Precautions for Use

The recommended dosage must not be exceeded. Very high doses of some ingredients, in particular vitamin D, iron and copper, can be harmful to health.

Patients receiving other single vitamins or multivitamin preparations, any other medication or those under medical care should consult a health care professional before taking Elevit.

Elevit must be taken with particular caution together with any other products, including supplements and/or fortified foods and drinks containing Vitamin D, since large daily doses may cause hypervitaminosis D.

Elevit contains lactose and mannitol as excipients. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Folic acid, Vitamin B12 and iron may mask certain forms of anaemia.

Elevit must be used with caution in patients with impaired renal function due to potential exacerbation related to hypercalcaemic effects during therapy.

Elevit must be used with caution in patients with hyperphosphatemia due to the potential risk of metastatic calcification.

Interactions with Other Medicaments and Other Forms of Interaction

When used as recommended no specific interactions are expected. Manifold potential interactions are reported in the literature for the single ingredients, thus patients receiving any other medication or those under medical care should consult a physician before taking Elevit.

Medicine-Medicine Interactions

Oral administration of iron preparations inhibits absorption of tetracyclines from the gastrointestinal tract and vice versa, leading to decreased serum concentrations of both the antibiotic and iron. If simultaneous administration of the medicines is necessary, patients should receive the tetracycline two hours after or two hours before oral iron administration.

Concurrent administration of antacids with oral iron preparations may decrease iron absorption. An interval of three hours should be allowed between the administration of antacids and oral iron preparations.

Calcium-, magnesium-, iron-, copper- or zinc-containing products may impair the absorption of orally administered antibiotics and antivirals, resulting in lower systemic concentration. Patients taking both medications should space them at least by one to two hours.

It has been reported that Vitamin E-containing preparations should be used with caution in patients receiving anticoagulants or medicines that affect platelet aggregation.

Simultaneous treatment with laxatives such as paraffin oil may reduce the gastrointestinal absorption of vitamin D.

Interactions with the following medicines have been observed: levodopa, biphosphonates, fluoroquinolones, penicillamine, thyroxine, digitalis and thiazide diuretics.

Medicine-Food Interactions

Since oxalic acid (found in spinach and rhubarb) and phytic acid (found in whole cereals) may inhibit calcium absorption, it is not recommended to take this product within two hours of eating foods containing high oxalic acid and phytic acid concentrations.

Pregnancy and Lactation

Elevit is indicated during pregnancy and lactation. However, the recommended dosage must not be exceeded.

Pregnancy

Chronic overdose of vitamin D might be harmful to the foetus.

For pregnant women, the Institute of Medicine (USA) has set the Tolerable Upper Intake Level (UL) of vitamin D at 50 mcg (2000 IU) per day, which is considered as safe. The New Zealand Ministry of Health Food and Nutrition Guidelines for Healthy Pregnant and Breastfeeding Women 2006) recommends a UL of 80 mcg per day. Elevit contains 12.5 mcg (500 IU) per tablet.

Lactation

Permanent overdose of vitamin D might be harmful to the neonate.

Vitamin D and calcium are excreted into breast milk. This must be taken into consideration if the infant is receiving any respective supplements.

For lactating women, the Institute of Medicine (USA) has set the Tolerable Upper Intake Level (UL) of vitamin D at 50 mcg (2000 IU) per day, which is considered as safe. The New Zealand Ministry of Health Food and Nutrition Guidelines for Healthy Pregnant and Breastfeeding Women 2006) recommends a UL of 80 mcg per day. Elevit contains 12.5 mcg (500 IU) per tablet.

Effects on Ability to Drive or Use Machines

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

Undesirable Effects

The listed adverse reactions are based on spontaneous reports - thus organisation according to CIOMS III categories is not pertinent.

In general, Elevit is well-tolerated. However, gastrointestinal symptoms (e.g. abdominal discomfort, constipation, flatulence, vomiting, diarrhoea and nausea) might occur.

In isolated cases, Elevit may cause allergic reaction. Symptoms may include hives, facial swelling, wheezing, skin reddening, rash, blisters and shock. If an allergic reaction occurs, treatment must be stopped and a health care professional consulted.

In a placebo controlled clinical trial in 2471 pregnant women who took Elevit (one tablet daily for 1 to 6 months) the percent of subjects reporting adverse events was as follows:-

- constipation (1.8%)
- diarrhoea (1.4%)
- exanthema (rash) (0.08%)

The percentages of subjects reporting these events in the placebo group were not statistically different.

A slight yellow discoloration of urine may be noticed. This effect is harmless and is due to the Vitamin B₂ contained in Elevit.

Elevit contains iron, which may lead to a black colouring of the stool. This effect is harmless and does not have any clinical relevance.

Overdose

There is no evidence that Elevit can lead to an overdose when used as recommended.

Most, if not all, reports concerning overdoses are associated with concomitant intake of high dosed single and/or multivitamin preparations. Acute or long-term overdose can cause hypervitaminosis D and hypercalcaemia, as well as iron and copper toxicity.

Uncharacteristic initial symptoms, such as abrupt onset of headache, confusion and gastrointestinal disturbances such as constipation, diarrhoea, nausea and vomiting might be indicative for an acute overdose.

If such symptoms occur, treatment must be stopped and a health care professional consulted.

Pharmacological Properties

Pharmacotherapeutic Group

Multivitamins and minerals/trace elements

Pharmacodynamic Properties

Elevit is a multivitamin/multimineral formula containing vitamins in combination with minerals and trace elements especially designed to ensure an adequate micronutrient supply for both the unborn child and the mother-to-be.

Vitamins are essential nutrients. They are indispensable for the normal development and growth of the foetus and the infant, for the metabolism and formation of carbohydrates, energy, lipids, nucleic acids and proteins, as well as for the synthesis of amino acids, collagen and neurotransmitters.

Multivitamins/multimineral preparations are indicated to prevent and correct nutritional micronutrient deficiencies. Pregnancy and lactation represent periods with increased micronutrient requirements and, as a consequence, increased risks of micronutrient deficiencies for both the mother and the child. Especially during pregnancy, micronutrient deficiencies exhibit a more serious health risk, as they may also impair the normal development of the unborn child.

Supplementation with folic acid or folic acid-containing multivitamins is recommended to decrease the risk of congenital malformations including neural tube defects. Neural tube defects develop in the first weeks after conception, a period during which pregnancy may not have been diagnosed yet - thus, supplementation with folic acid is essential at the stage when pregnancy is being planned.

A large randomised placebo-controlled trial conducted by Czeizel et al evaluated the efficacy and safety of Elevit (including Vitamin A 4000 IU) in the periconceptional period (one month before conception until the third month of gestation) and found no neural tube defects in the Elevit group (n = 3953) compared to 6 cases of neural tube defects in the placebo group (n = 3952). This difference was statistically significant (p = 0.016) and was confirmed in a subsequent pharmaco-epidemiological two-cohort study in which 1 neural tube defect occurred in the group taking Elevit compared to 9 cases in a routine care group without vitamin supplementation (n = 3056 evaluated matched pairs).

Moreover, in both studies the total rate of major congenital malformations (e.g. urinary tract anomalies, cardiovascular defects, limb deficiencies and hypertrophic pyloric stenosis) was found to be reduced in the groups taking Elevit compared to the placebo or routine care group without supplementation respectively.

A specific analysis of the first 1000 pregnant women (500 in each group) has shown that the incidence of nausea, vomiting and vertigo was markedly lower (by around 50%) in women treated with Elevit compared to the placebo group.

Folate levels in blood erythrocytes is an accepted indicator for mother's risk of having a neural tube defect (NTD) affected baby. The folate threshold associated with the lowest risk of NTD affected pregnancies has been established at 906 nmol/L. A preparation similar to Elevit has been tested in the frame of a controlled human trial (Bramswig et al. in press 2008). The goal of this study was to evaluate the effects of supplementation with this preparation on improving erythrocyte folate concentrations in women of child-bearing age to levels exceeding 906 nmol/L and to establish the time frame required.

The results indicate that after an average of 4.2 weeks of daily supplementation with this preparation the mean erythrocyte folate levels increased above 906 nmol/L. In the light of the

early phase of the embryonic neuronal tube development (within 3 – 4 weeks of conception) a periconceptional and effective supplementation with folic acid is critical for maximum protection. In this respect, the 800 mcg of folic acid contained in the preparation tested (and also in Elevit) is shown to reach effective blood concentration within 4 weeks of supplementation.

Pharmacokinetic Properties

Human health and well-being is naturally dependent on the continuous uptake and management of vitamins and minerals, and their absorption, distribution, metabolism and elimination are maintained by specific physiological mechanisms.

The active ingredients in Elevit – vitamins, minerals and trace elements – are essential micronutrients which are widely distributed in the human body. The discrimination between the physiological nutrient concentration in the plasma and its changes after additional intake of corresponding pharmaceutical preparations is, on the one hand, difficult to assess and conveys, on the other hand, little or no information on the biological activity of the individual nutrient in the target tissue. The plasma and tissue levels of micronutrients are homeostatically regulated and affected by various factors such as diurnal fluctuations, nutritional status, growth, and pregnancy and lactation. No pharmacokinetic data are available on the active ingredients in this preparation, but the pharmacokinetic properties of the individual components have been extensively documented.

Preclinical Safety Data

There is no specific study with Elevit, but the preclinical safety of the individual components has been extensively documented.

Pharmaceutical Particulars

Presentation

Elevit is supplied as yellow-greyish, oval film-coated tablets, with a break-line on one face,

List of Excipients

Each tablet contains macrogol, glycerol distearate, gelatin, cellulose, sodium starch glycollate, povidone, lactose, mannitol, magnesium stearate, ethylcellulose, hypromellose, talc, titanium dioxide, iron oxide yellow.

Incompatibilities

None are known.

Storage Conditions

Protect from light and moisture. Store below 25°C.

Nature and Contents of Container

Elevit is supplied in blister packs of 30 and 100 tablets

Special Precautions for Disposal and Other Handling

No special requirements.

Medicine Classification

Pharmacy Only Medicine

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Date of Preparation

5 January 2009

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