SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT
MAGOSIT 365 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Every tablet contains;

Active substance:
Magnesium 365 mg (605.33 mg Magnesium oxide is equivalent to 365 mg Magnesium)

Excipient(s):
Lactose monohydrate 99.17 mg

3. PHARMACEUTICAL FORM
Tablet
White, grey-spotted round tablets.

4. CLINICAL PARTICULARS
4.1. Therapeutic indications

MAGOSIT is indicated in the treatment of,

- Ameliorating the symptoms occurred in deficiency of magnesium
- Heart and vascular system: Tachycardia, cardiac arrhythmia, myocardial infarction, angina pectoris, mild severe hypertension
- Nerve and muscles: Tetani, cramps in smooth and skeletal muscle, gastrointestinal cramps, neuromuscular hyperexcitability, systema, status with cramps in infants and small children
- Gynecological and obstetric: Pre-term spasm, cervical deficiency, premature rupture of membrane, spasm in pregnancy (eclampsia/preeclampsia), tocolysis necessary to use betamimetic, dismenore
- Orthopedics: Calcification and ossifications
- Prevention of renal calculus formation: Prevention of renal calculus formation (prevention of repetition of calcium oxalate urolithiasis)
- Treatment of diabetic and migraine

4.2. Posology and method of administration
Posology/administration frequency and duration:
If the doctor does not recommend otherwise;

Recommended daily dose is 1-2 tablets for adults and adolescents (12-17 old ages).
During pregnancy and lactation term recommended daily dose is 1-2 tablets.

Method of administration:
MAGOSIT is administrated orally.

Additional information on special populations:
Renal impairment:
Patients with severe renal failure should not take magnesium since toxicity can occur as a result of accumulation.

Hepatic impairment:
There is no data is available on patients with hepatic failure.

Pediatric population:
Recommended daily dose is 1-2 tablets for adolescents over 12 years old.

Geriatric population:
No data is available on geriatric population.

4.3. Contraindications
It is contraindicated on the patients with severe renal failure or hypersensitivity to any components in the formulation.

4.4. Special warnings and precautions for use
Hypermagnesiumia and toxicity may occur as a result of decreasing of the renal clearance of absorbed magnesium (creatinine clearance <30 ml/min). Patients with renal failure should not take magnesium since toxicity may occur due to accumulation. Serum magnesium levels should be monitored in patients with creatinine clearance of <25mL/min.

Should be taken with caution patients using digital. Heart block originated from the variations in cardiac transmit.

Should be taken with caution in patients using lithium.

Diarrhea may be seen in over medium age patients due to disease or drug usage. Diarrhea may cause disorder in electrolyte balance. Serum level should be monitored for toxicity.

Oral magnesium is generally not applicable for magnesium deficiency in patient with serum magnesium concentrations of <1.5 mEq/L

Drugs comprising magnesium should be taken with food. Taking in fast conditions may cause diarrhea.

MAGOSIT contains lactose monohydrate as an excipient. Patients with rare hereditary galactose intolerance, Lapp lactose deficiency or glucose-galactose malabsorption problem should not use this drug.

4.5. Interaction with other medicinal products and other forms of interaction

MAGOSİT enhances the effect and toxicity of non-depolarized neuromuscular blockers.

MAGOSİT decreases the absorption of aminoquinolones, digoxin, nitrofurantoin, penisilamine and tetracyclines.

The concurrent usage of magnesium with oral tetracyclines may inhibit the presenting the complete effect of tetracyclines. For this reason, magnesium should be taken at least 1-3 hours before or after taking oral tetracyclines.

The concurrent usage of MAGOSİT with sodium polystyrene sulfonate decreases the effect of magnesium.
The concurrent usage of MAGOSİT with cellulose sodium phosphate may inhibit presenting the complete effect of cellulose phosphate. For this reason, magnesium should be taken at least 1 hour before of after taking cellulose sodium.

The frequency of side effects to be seen increases in concurrent usage of MAGOSIT with other preparations comprising magnesium including enemas due to occurring high magnesium blood levels.

The concurrent usage of MAGOSIT with high dose barbiturates, opioids, hypnotics can cause breathing depression risk.

The concurrent usage of MAGOSIT with nifedipine can cause hypotension.

The concurrent usage of MAGOSIT with antibiotics from fluoroquinolone group decreases the absorption of fluoroquinolones from intestine in a considerable extend.

When the drugs containing levothyroxine are taken with MAGOSIT, the two drugs should be taken at least 4 hours apart as the absorption of MAGOSIT is impaired.

Additional information on special population
No clinical interaction studies have been conducted with special populations.

Pediatric population:
No clinical interaction studies have been conducted with pediatric populations.

4.6. Pregnancy and lactation
General recommendation
Pregnancy category: B

Women with childbearing potential / Birth control (contraception)
There is no recommendation about using the drug on women have the possibility of giving birth and take contraception.

Pregnancy
There is no clinical data related to exposure during pregnancy for MAGOSIT.

Studies conducted on animals has not shown direct or indirect hazard effects related to pregnancy/embryonal/fetal improvement/birth or post-birth improvement.

Precaution should be taken while prescribing for pregnant women.

Lactation
MAGOSİT should be taken by consulting a doctor during pregnancy and breast-feeding due to its laxative effects.

Reproductivity / fertility

Reproductive studies conducted on rats, magnesium sulfate administrated by percutaneous route at high doses (1000 mg/kg bw/day, 3 times in a day) resulted as consuming less food intake, mother rat put on less weight and delayed differentiation had been occurred on offspring rats.

4.7. Effects on ability to drive and use machines
MAGOSIT has no hazard effect on ability to drive and using machines.

4.8. Advers effects
In common severe adverse effects have not been seen. Diarrhea is the most frequently seen (more than 10%) adverse effect on using oral magnesium.

Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1.000 to <1/100); rare (≥1/10.000 to <1/1.000); very rare (<1/10.000); not known (cannot be predicted according to the available data).

Immune system disorders
Not known: Allergic reaction, redness, itching

Psychiatric disorders
Common: Mental depression, confusion

Nervous system disorders
Common: Coma

Vascular disorders
Common: Hypotension, EKG variations

Respiratory, thoracic and mediastinal disorders
Common: Breathing depression

Gastrointestinal disorders
Common: Nausea, vomiting
Very common: Diarrhea

Musculoskeletal, connective tissue and skeletal disorders
Not known: Cramp

General disorders and administration site conditions
Not known: Tiredness feelings, thinness

4.9. Overdose and Treatment
Serum magnesium reference range:
Children: 1.5-1.9 mg/dL (1.2-1.6 mEq/L)
Adults: 1.5-2.5 mg/dL (1.2-2.0 mEq/L)

In overdose situation, symptoms like blurred or double vision, coma, dizziness or syncope, severe acedia, decreased or increased urinary excretion, slowness of heartbeats, difficulty in breathing are occurred. Overdose has been seen rarely on adult individuals have normal renal functions. Hypermagnesemia has been occurred especially at acute and chronic renal disorders and treated effectively by dialysis method.

5. PHARMACOLOGICAL PROPERTIES

5.l. Pharmacological properties

Pharmacotherapeutic group: Vitamin, Mineral and Other Nutritional Products
ATC code: A12CC10

General properties

Magnesium is the second most abundant intracellular substance in the body, and as a cofactor of more than 300 enzymatic reactions related to energy metabolism and protein and nucleic acid synthesis; It also acts as a coenzyme in amino acids, fats, carbohydrates and steroid metabolisms.

Magnesium directs electrophysiological, electromechanical and hemodynamic events in the body. It has an important role in physiology of heart muscle transmit.

Magnesium is a natural antagonist of calcium. It stabilizes biological membranes and reduces fluidity by forming complexes with phospholipids and ATP.

Magnesium is a vital element for the organism. Inadequate intake of magnesium may cause fatigue, tremor, convulsions, cardiac arrhythmias, hypokalemia and hypocalcemia.

Inadequate intake or excessive consumption of magnesium via nutrition leads to impairment in enzymatic systems and metabolism.

Studies indicated that chronic latent magnesium deficiency may play a role in atherosclerosis, myocardial infarction, hypertension, cancer, kidney stones, premenstrual syndrome and psychiatric disorders.

5.2. Pharmacokinetic properties

Absorption:

The absorption of orally administrated magnesium is initiated from small intestine after 1 hour and completed within 8-12 hours. After 12 hours, the unabsorbed part reaches the large intestine. Absorption can take place here very little.

Distribution:

A 70 kg weight human body has about an average of 1 mole magnesium. Almost half of the magnesium in the body is present in the soft tissue and the other half in the bone tissue. The fraction less than 1% of total body magnesium is present in blood. One third of the magnesium in serum is found as bounded to proteins; 25% of total serum magnesium is bounded to albumin, and 8% to globulin. Approximately 92% of the ultra-filterable 2/3 portion is present as free ion (61% of total serum magnesium) and 8% is phosphate, citrate complexes and other compounds (5.5% of total serum magnesium).

Biotransformation:
Magnesium exists in three different states in biological systems; bounded to protein, in status formed complexes with anions and as free. Within these forms free form of magnesium is the one that has biological activity. Magnesium acts as a cofactor in the activation of enzymatic reactions related to magnesium energy metabolism and protein and nucleic acid synthesis.

Elimination:
Unlike other cations, more than 50% of magnesium is re-absorbed from the rising part of Henle's handle. Magnesium participates to bloodstream following absorption and the free ionic state is filtered through ultrafiltration in the kidneys. Approximately 30% of the absorbed magnesium ions are excreted by the urine. Unabsorbed magnesium is excreted via the feces. Half life is about 4.5 hours.

Linearity/Nonlinear status:
It presents linear pharmacokinetics.

5.3. Preclinical safety data
Traditional safety pharmacology does not present a particular hazard to people based on repeated dose toxicity, genotoxicity, carcinogenic potential and reproductive toxicity studies.

6. PHARMACEUTICAL PARTICULARS

6.l. List of excipients
Poloxamer P188
Lactose monohydrate
Polyethylene glycol 8000
Low substituted hydroxypropyl cellulose
Copovidone
Magnesium stearate

6.2. Incompatibilities
Not applicable

6.3. Shelf life
24 months.

6.4. Special precautions for storage
Store at room temperature under 25°C and dry place. Keep out of reach of children and in package.

6.5. Nature and contents of container
MAGOSIT is packed in transparent PVC/PE/PVDC/ Al folio blister. Every cartoon box comprises 30 tablets.

6.6. Special precautions for disposal and other handling
No special requirements.

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORIZATION NUMBER:

2015/145

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION:

Date of first authorization: 16.02.2015
Renewal date of authorization: 23.01.2020

10. DATE OF REVISION OF THE TEXT:

20.07.2017