The European Agency for the Evaluation of Medicinal Products

EMEA/MRL/039/95

COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

MAGNESIUM and ITS COMPOUNDS

SUMMARY REPORT

1. Name of the substance

Magnesium	Magnesium gluconate	Magnesium sulphate
Magnesium hydroxide	Magnesium oxide	Magnesium chloride
Magnesium stearate	Magnesium hypophosphite	Magnesium aspartate
Magnesium glutamate	Magnesium carbonate	Magnesium citrate
Magnesium orotate	Magnesium phosphate	Magnesium acetate
Magnesium aluminium silicate	Magnesium glycerophosphate	Magnesium trisilicate

2. Indication for use

- to correct magnesium deficiencies (hypomagnesemia)
- as adjunctive therapy of malignant hyperthermia in swine
- as anticonvulsant
- as saline cathartic and antacid

3. Pharmacological activity

Magnesium is the second most plentiful cation of the intracellular fluids. Magnesium is an essential cofactor for many enzymes, especially phosphotransferases, and plays a vital role in reversible association of intracellular particles and in the binding of macromolecules to subcellular organelles (e.g. ribosomes and mRNA). Magnesium plays an important role in neurochemical transmission and muscular excitability, and also in the central nervous system and in the cardiovascular system.

4. Toxicological profile

Magnesium toxicity from oral intake of magnesium is rare, since magnesium is effectively excreted by the kidneys and is also poorly absorbed (oral LD_{50}-values 32800 mg/kg). Even soluble magnesium salts are generally so slowly absorbed that oral administration causes nothing more than purging. An elevated magnesium concentration in plasma is usually due to renal insufficiency. The main symptoms are neuromuscular (paralysis) and cardiac (hypotension, bradycardia, heart block). As plasma concentrations begin to exceed 4 mEq/l the following signs and symptoms of magnesium intoxication can be observed: erythema, nausea, vomiting, bradycardia, hypotension, decreased reflexes, sedation, muscle paralysis, hypoventilation and stupor, hypotension with abnormal conduction, ventricular arrhythmias, and asystolic arrest.

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5. Pharmacokinetics

The average adult ingests about 20-40 mEq of magnesium a day in the diet, and of this approximately one third is absorbed from the gastrointestinal tract (in upper small intestine). About 50% of the magnesium in the human body is in bone, 45% exists as an intracellular cation (concentrations range from 5 to 30 mEq/kg), and 5% is in the extracellular fluid. The magnesium concentration in plasma is 1.5 to 2.2 mEq/l, with one third bound to plasma proteins. About 30% of the magnesium in the skeleton represents an exchangeable pool.

Magnesium is excreted principally by the kidney, and, under normal conditions, 3 to 5% of the filtered ion is excreted in the urine. Most of the reabsorption of magnesium occurs in the proximal tubule. Renal excretion of magnesium is increased by diuretics. Small amounts of magnesium are excreted in milk and saliva.

CONCLUSION AND RECOMMENDATION

Given that:

- magnesium and its salts have only limited use in veterinary medicine for food-producing animals, which are not intended for immediate slaughter;
- magnesium is a natural cofactor of many enzymes in humans and animals;
- 20-40 mEq (0.25-0.5 g) magnesium is ingested daily in the typical diet;
- the highest prescribed veterinary dosage is 1 kg magnesium sulphate/500 kg cow po (as a cathartic), of which only 30% will be absorbed (equivalent to 600 mg/kg meat magnesium sulphate or 120 mg/kg magnesium);
- the recommended dose in humans for prevention and treatment of hypomagnesemia is 240-600 mg magnesium daily on a chronic basis,

The Committee for Veterinary Medicinal Products concluded that use of magnesium in products for treatment of food-producing animals does not represent any risk for consumers and recommends the inclusion of these substances in Annex II of Council Regulation (EEC) No. 2377/90 as indicated in the following table:

Pharmacological active substance(s)	Animal species	Other provisions
Magnesium	All food producing species	
Magnesium gluconate	All food producing species	
Magnesium sulphate	All food producing species	
Magnesium hydroxide	All food producing species	
Magnesium stearate	All food producing species	
Magnesium glutamate	All food producing species	
Magnesium orotate	All food producing species	
Magnesium aluminium silicate	All food producing species	
Magnesium oxide	All food producing species	
Magnesium hypophosphite	All food producing species	
Magnesium carbonate	All food producing species	
Magnesium phosphate	All food producing species	
Magnesium glycerophosphate	All food producing species	
Magnesium chloride	All food producing species	
Magnesium aspartate	All food producing species	
Magnesium citrate	All food producing species	
Magnesium acetate	All food producing species	
Magnesium trisilicate	All food producing species	