



COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

CALCIUM GLUCOHEPTONATE CALCIUM GLUCONO GLUCOHEPTONATE CALCIUM GLUCONOLACTATE CALCIUM GLUTAMATE

SUMMARY REPORT

1. Calcium glucoheptonate is also referred to as calcium gluceptate or calcium glucosemonocarbonate. It is the calcium salt of the alpha-epimer of glucoheptonic acid or a mixture of the alpha and beta epimers. Calcium gluconolactate is also referred to as calcium lactate gluconate. Calcium glucoheptonate, calcium glucono glucoheptonate, calcium glutamate and calcium gluconolactate are used in both human and veterinary medicine for the treatment of hypocalcaemia and of calcium deficiency states such as parturient paresis. The indicated species are cattle, horses, sheep, goats, pigs and birds. For mammals, the normal recommended dose is 1 g calcium per 50 kg bw by slow intravenous injection. Doses from 0.03 to 0.25 g/animal are also indicated, depending from the species, for intramuscular, subcutaneous or oral administration. For egg-bound birds, the equivalent of 0.02 µg/kg calcium may be given by intramuscular injection.
2. Calcium is an essential body mineral and electrolyte and occurs naturally in plants and animals. The mean calcium concentration of cows' milk is around 1.5 g/l.

Several calcium salts including calcium acetate, calcium benzoate, calcium borogluconate, calcium carbonate, calcium chloride, calcium citrate, calcium gluconate, calcium hydroxide, calcium hypophosphite, calcium malate, calcium oxide, calcium phosphate, calcium polyphosphates, calcium propionate, calcium silicate, calcium stearate, and calcium sulphate, have already been included in Annex II of Council Regulation (EEC) 2377/90, for all food producing species.
3. In humans, calcium is absorbed predominantly from the small intestine by active transport and passive diffusion. Around 30% of the orally administered dose may be absorbed though the exact amount depends on dietary factors, serum vitamin D concentration, and the condition of the small intestine. Absorption is increased during periods of high physiological requirement such as during pregnancy and lactation. After absorption, ionized calcium enters the extracellular fluid and is then rapidly incorporated into bones and teeth. Around 99% of the body calcium is found in bone. Calcium crosses the placenta and is excreted in breast milk. Excretion of calcium occurs in the urine although 90% is reabsorbed in the renal tubules. Excretion also occurs *via* the faeces; this consists of unabsorbed calcium as well as that secreted in bile and pancreatic juice.
4. L-glutamic acid and its salts including calcium glutamate were evaluated at the 14th, 17th and 31st meetings of the Joint WHO/FAO Expert Committee on Food Additives and by the European Union Scientific Committee for Food. The Committees noted that acute and repeated-dose toxicity studies had shown no specific toxic effects, there was no evidence of carcinogenic or genotoxic potential and reproductive toxicity studies had revealed no deleterious effects on the offspring. The Scientific Committee for Food had established a group ADI not specified on the basis of the data provided and in view of the large normal dietary intake of glutamates. The Joint WHO/FAO Expert Committee on Food Additives also allocated an ADI "not specified" at their 31st meeting.

5. No classical toxicity studies were carried out with calcium glucoheptonate or calcium gluconolactate in laboratory animals. However, both salts are of low toxicity in both humans and the target species. Calcium salts have been widely used in human pregnancy by way of oral calcium supplementation and no association has been observed between calcium exposure and adverse effects on human reproduction. In humans, the absorption of calcium is increased during pregnancy and lactation.
6. In human medicine, calcium glutamate, calcium glucoheptonate and calcium gluconolactate may be given orally to correct calcium deficiency states. The normal doses are intended to provide 50 nmol of calcium daily (equivalent to 25 g/day of calcium glucoheptonate, 23 g/day calcium glutamate or 15 g/day calcium gluconolactate). In cases of hypocalcaemia, parenteral administration of 2.25 to 4.5 nmol calcium (equivalent to 1.125 to 2.25 g/day of calcium glucoheptonate 1.05 to 2.1 g/day calcium glutamate or 0.7 to 1.4 g/day of calcium gluconolactate) may be given and repeated as necessary. The reported adverse effects include gastrointestinal irritation and/or constipation after oral administration and mild to severe injection site reactions after parenteral administration. Hypercalcaemia is the main effect of overdose and is usually associated with parenteral routes of administration. Too rapid intravenous administration may cause hypotension and cardiac arrhythmias.

Conclusions and recommendations

Having considered the criteria laid down by the Committee for the inclusion of substances to Annex II of Council Regulation (EEC) No. 2377/90 and in particular that:

- calcium is an essential element,
- calcium salts are normal components of the human diet,
- calcium glutamate is of low toxicity,
- calcium glucoheptonate, calcium glucono glucoheptonate, calcium gluconolactate and calcium glutamate are used in individual animals on an infrequent basis;

the Committee concludes that there is no need to establish MRLs for calcium glucoheptonate, calcium glucono glucoheptonate, calcium gluconolactate and calcium glutamate and recommends their inclusion to Annex II of Council Regulation (EEC) 2377/90 in accordance with the following table:

Pharmacologically active substance(s)	Target species	Other provisions
Calcium glucoheptonate	All food producing species	
Calcium glucono glucoheptonate	All food producing species	
Calcium gluconolactate	All food producing species	
Calcium glutamate	All food producing species	