



COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

2-AMINOETHYL DIHYDROGENPHOSPHATE

SUMMARY REPORT

1. 2-Aminoethyl dihydrogenphosphate (synonyms: phosphorylcolamine, phosphorylethanolamine, phosphoethanolamine) is used for the prophylaxis and treatment of pathological syndromes caused by calcium and magnesium deficiencies and it can be also used in convalescence after infections and debilitating diseases. The veterinary drugs are intended for intravenous, intramuscular and subcutaneous administration for the treatment of cattle, horses, swine, sheep and goats. The maximum recommended doses are 30 mg/kg bw/day for cattle, horses and breeding swine, 60 mg/kg bw/day for calves, foals and swine, 45 mg/kg bw/day for sheep and goats. The duration of treatment should last until the disappearance of clinical signs.
2. 2-Aminoethyl dihydrogenphosphate is a substance, which is naturally formed during the phospholipid metabolism. It is a precursor of phosphatidylethanolamine and phosphatidylcholine, the major phospholipid constituents of plasma, cellular membranes and membranes of organelles in mammalian cells. These phospholipids play an essential role in regulating the biochemical and physiochemical properties of such membranes, as well as the activity of many enzymes and enzyme systems; moreover, they are essential components of the lipoproteins involved in lipid transport and secretion.

Another important role of phosphatidylethanolamine is to be considered the donor of 2-aminoethyl dihydrogenphosphate necessary for the covalent binding of a complex glycopospholipid to cell surface glycoproteins which are found in eukaryotic organisms, including also budding yeast *Saccharomyces cerevisiae*. Besides this role in the metabolism of phospholipids, it is not clear whether 2-aminoethyl dihydrogenphosphate plays any other physiological functions.

3. The biosynthesis of phosphatidylethanolamine has been studied in isolated rat hepatocytes and confirmed the incorporation of 2-aminoethyl dihydrogenphosphate acid into phosphatidylethanolamine, pointing out that ethanolamine is the most important precursor of 2-aminoethyl dihydrogenphosphate.

The role of different enzymes (phospholipase C and phospholipase D) in the phosphatidylethanolamine synthesis in rat and mouse liver was studied, always confirming the importance of 2-aminoethyl dihydrogenphosphate as a precursor or breakdown product of phosphatidylethanolamine.

2-Aminoethyl dihydrogenphosphate can be also considered as a precursor of choline via the methylation of phosphatidylethanolamine to phosphatidylcholine. The contribution of this methylation pathway in providing choline and/or choline-containing compounds may play a part in the maintenance of their steady-state concentrations, and therefore in the regulation of phosphatidylcholine biosynthesis.

4. LD₅₀ after administration by intravenous route in mouse was 639 mg/kg bw.

5. While no studies on repeated dose toxicity, reproductive toxicity, teratogenicity, mutagenicity and carcinogenicity were provided, this information is not necessary due to the fact that 2-aminoethyl dihydrogenphosphate is a naturally occurring phospholipid compound and a precursor of endogenous molecules.

Conclusions and Recommendation

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

- 2-aminoethyl dihydrogenphosphate is a naturally occurring constituent of phospholipids of all eukaryotic cell membranes and as such may be expected at concentration of several mg/kg tissue in food of animal or plant origin,
- 2-aminoethyl dihydrogenphosphate is rapidly and completely metabolised;

the Committee considers that there is no need to establish MRLs for 2-aminoethyl dihydrogenphosphate and recommends its inclusion in Annex II to Council Regulation (EEC) No 2377/90 in accordance with the following table:

Pharmacologically active substance(s)	Animal species	Other provisions
2-Aminoethyl dihydrogenphosphate	All food producing species	