The European Agency for the Evaluation of Medicinal Products
Veterinary Medicines Evaluation Unit

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COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

2-AMINOETHANOL

SUMMARY REPORT

1. 2-Aminoethanol is used as an excipient and pH-stabilising agent in human and veterinary medicinal products. The veterinary drugs are intended for intravenous, intramuscular, subcutaneous, oral and dermal administration for the treatment of horses, cattle, swine, sheep, goats or poultry. Concentrations of 2-aminoethanol range from 0.02% up to 11% in drugs for intramuscular injection. The dose range may be assumed to lie between 0.03 to 11 mg 2-aminoethanol/kg bw for single injections in food producing mammals and up to 40 mg/kg bw in poultry.

2. 2-Aminoethanol is a normal component of human food. It is part of the membrane constituting class of glycerophospholipids and a degradation product of the amino acid serine. The metabolic pool for 2-aminoethanol in rat liver was calculated to be 1.1 µmol/liver, corresponding to about 6 mg/kg. From this it can be concluded that 2-aminoethanol is present in food in concentration in the order of mg/kg.

3. After intraperitoneal administration of 1,2-^{14}C-aminoethanol to rats 54% of the dose were found in liver, spleen, kidneys, heart, brain, and diaphragm. 11.5% was expired as $^{14}CO_2$ within 8 hours. Most of the radioactivity in tissues was found in the lipid fraction.

   Liver was shown to be the major site for metabolism of dermally applied 2-aminoethanol, with over 24% of the applied radioactivity. Kidneys, lungs, brain, and heart contained 2.53, 0.55, 0.27, and 0.15% of the radioactivity, respectively.

4. The metabolism and incorporation of 2-aminoethanol into phospholipids in animal tissues is via formation of phosphorylethanolamine (2-aminoethanol dihydrogenphosphate) and cytidine diphosphate ethanolamine (cytidine 5'-(trihydrogen diphosphate), mono(2-aminoethyl) ester) as intermediates to the cephalin phosphatidylethanolamine. Surplus amounts of 2-aminoethanol may be converted via acetaldehyde to carbon dioxide. Phosphatidylethanolamine is one of the precursors of other phospholipids containing for instance choline. Within 5 minutes after intraportal injection of (2-^{3}H)-aminoethanol a high percentage of the dose was reported to be at first incorporated into phosphorylethanolamine followed by incorporation into phosphatidylethanolamine. The metabolic pool for aminoethanol-containing compounds in rat liver was calculated as 1.1 µmol 2-aminoethanol/liver, 3.8 µmol phosphorylethanolamine/liver, 0.239 µmol cytidine diphosphate ethanolamine, and 80.6 µmol phosphatidylethanolamine/liver.

   The available pharmacokinetic and metabolism data lead to the conclusion that 2-aminoethanol is rapidly metabolised and incorporated into lipids and other biomolecules.

5. Oral LD_{50} values reported for 2-aminoethanol are 1200 to 2500 mg/kg bw and 1100 to 2700 mg/kg bw in male and female rats, and 700 to 1500, 600 and 1000 to 2900 mg/kg bw in mice, guinea pigs and rabbits, respectively. The dermal LD_{50} in rabbits was reported to be 1000 to 2500 mg/kg bw.

6. 2-Aminoethanol is an alkaline substance and an apparent primary skin and eye irritant. Skin sensitisation, however, has not been demonstrated for this compound.

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7. In a 4-week toxicity study rats were fed 160 to 2670 mg/kg bw/day. Only short summaries were available: at 1280 mg/kg bw/day mortality and changes in kidney and liver histology and at 640 mg/kg bw/day altered liver and kidney weights were reported, while at 160 mg/kg bw/day no effects were reported. But due to limited documentation including no details, a NOEL cannot be derived from this study.

8. An adequately performed recent study in 25 Wistar rats per dose level, which were treated by gavage with 2-aminoethanol in an aqueous solution at dose levels of 0, 40, 120, or 450 mg/kg bw at gestation days 6 through 15, revealed no significant teratogenic, embryotoxic or foetotoxic effects of 2-aminoethanol. Fifteen animals were allowed to whelp and rear their pups until day 21 of lactation. No treatment related effects were noted in the dams of the low and mid-dose group, but significant reductions in food consumption, mean body weight and body weight gain at various time of treatment were observed in dams at the highest dose level, but not in their pups. No signs of developmental toxicity or increased malformation were noted at any dose level, including the 450 mg/kg bw group.

   Three inadequately reported and partly inadequately performed oral teratogenicity studies with 2-aminoethanol in rats and mice produced contradictory results, possibly due to different study design, and the use of charges of different purity. An evaluation is not possible due to the poor quality of the reports of these studies.

   In a study on the developmental toxicity of dermally applied 2-aminoethanol in rats and rabbits no teratogenic effects were noted after doses of up to 225 mg/kg bw in rats and 75 mg/kg bw in rabbits. Maternal toxicity induced by irritating effects (severe skin lesions with the corresponding general sequelae) was observed at 225 mg/kg bw in rats and at 25 to 75 mg/kg bw in rabbits.

9. Several Ames tests with and without metabolic activation as well as a gene conversion assay in *Saccharomyces cerevisiae* and a clastogenicity tests measuring chromosomal aberrations in the rat liver cell line RL_4 revealed negative results, with the exception of one publication were weak mutagenic action in various test systems was reported.

10. Although no data on the carcinogenicity, on immunotoxic properties, on possible microbiological properties, and on possible pharmacological or toxicological effects of 2-aminoethanol in humans were provided, this information is not thought to be necessary due to the fact that 2-aminoethanol, as a naturally occurring phospholipid base, is a constituent of the normal human diet.

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-aminoethanol is a naturally occurring phospholipid base in all living eukaryotic organisms and may be expected at concentrations of an order of magnitude of several mg/kg tissue in food of animal or plant origin,
- 2-aminoethanol is rapidly and completely metabolised,

the Committee concludes that there is no need to establish MRLs for 2-aminoethanol 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-Aminoethanol	All food producing species	