



COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

HEPTAMINOL

SUMMARY REPORT

1. Heptaminol (6-amino-2-methyl-2-heptanol) is an amine derivative which is used as cardiogenic and vasodilator in veterinary medicine. It is used as a corrector of the hypotensive effect of neuroleptics. The therapeutic doses range from 1 to 3 mg/kg bw. Heptaminol is administered under its hydrochloride salt in cattle, sheep and horses, by oral or parenteral routes.
2. Heptaminol activity is related to peripheral norepinephrine release, leading to a heart rate increase and to central vasodilatation (inotropic effects). Heptaminol also acts as a blocking agent of the pre- and postsynaptic neuromuscular transmission. This effect is associated with an increase in synaptic delay (decrease of muscular contraction amplitudes).
3. The plasma pharmacokinetics in dogs, after an oral administration of 300 mg of heptaminol, could be described by an open two-compartment model, the half-lives being 1.14 hours for the distribution phase and 3.7 hours for the elimination phase. 82 to 87% of the administered dose were recovered in urine within 10 hours, and the elimination was total within 24 hours.

In rats, following an intravenous administration of ^{14}C -heptaminol at 8 mg/kg bw or an oral administration at 12 mg/kg bw, no evidence of accumulation of the drug was seen in tissues. 68% of the radioactivity were excreted in urine at 4 hours after the intravenous administration. Heptaminol was metabolised to an hydroxylated metabolite : 6-amino-2-methyl-1,2-heptanediol which was excreted unconjugated in urine.
4. The intraperitoneal LD50 value of heptaminol was 1250 mg/kg bw in mice.
5. No information was available on the toxicological profile (repeated dose and reproductive toxicity, tolerance study, mutagenicity) of heptaminol in laboratory animal species. However, the use of this compound in humans over a long period of time did not result in undesirable effects.
6. In human, after an oral intake of 2 x 150 mg in tablet form, heptaminol was rapidly and entirely absorbed. Mean peak plasma concentrations of 1.6 mg/l were reached after 1.8 hours. The elimination half-life was approximately 2.5 hours. All the dose given was recovered unchanged in urine within 24 hours.
7. Heptaminol is used in humans against orthostatic hypotension. The usual dose is 0.75 to 1.5 mg/kg bw/day. No toxic or adverse effects of heptaminol have been reported.

Conclusion and recommendation

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

Heptaminol is recommended in a small number of individual animals and for infrequent and non-regular treatment,

Heptaminol is rapidly excreted in animals,

The Committee considers that there is no need to establish an MRL for Heptaminol and recommends its inclusion into Annex II of Council Regulation (EEC) No 2377/90 for all food producing species in accordance with the following table:

Pharmacological active substance	Animal species	Other provisions
Heptaminol	All food producing species	