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

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June 1997

COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

TETRACAINE

SUMMARY REPORT

1. Tetracaine (synonym: amethocaine), 4-(butylamino) benzoic acid 2-(dimethylamino)ethyl ester hydrochloride is a potent local anaesthetic of the ester type soluble in water. It is used in cattle, sheep, swine and horses for surface, conduction and infiltration anaesthesia. The common therapeutic dose range was not included. Tetracaine can also be used topically in the eye at concentrations of 1% solution in large animals.

2. Tetracaine acts on the central nervous system, cardiovascular system, neuromuscular junctions and ganglion synapse. Tetracaine is a local anaesthetic, its mechanism of action is to prevent the generation and conduction of the nerve impulse. Local anaesthetics block conduction by decreasing or preventing the large transient increase in the permeability of excitable membranes to Na^+ that is produced by a slight depolarisation. This action of local anaesthetics is due to their direct interaction with voltage-sensitive Na^+ channels.

   Tetracaine is mainly hydroxylated in the metabolite para-aminobenzoic acid (PABA) that inhibits the action of sulphonamides.

3. Tetracaine is rapidly absorbed following mucosal and parenteral administration. It is also well absorbed after tracheal instilation. Tetracaine is widely distributed in the body, crosses the placenta and is metabolised in the liver and in the plasma by non-specific cholinesterases (its metabolism is 4-5 fold slower than procaine). Tetracaine and its metabolite PABA are excreted into urine. In man, plasma protein binding of tetracaine is about 75.6%.

4. The acute oral toxicity of tetracaine was moderate. However after intravenous administration it was highly toxic. The acute intravenous LD_{50} values ranged from 6.6-7.3 mg/kg bw in mice to 4.5 mg/kg bw in rat. The acute oral LD_{50} value was 160 mg/kg bw in mice.

5. While no studies on repeated dose toxicity, reproductive toxicity including embryotoxicity/ foetotoxicity and tolerance in target species were presented, submission of such studies was not considered necessary as tetracaine has a long history of safe use in human and veterinary medicine and is rapidly eliminated.

6. The mutagenicity of tetracaine was tested in an *in vitro* study. The Ames test (*Salmonella typhimurium* strains TA100 and TA98), with and without activation (rat liver microsomes induced by Araclor 1254 and phenobarbital) did not reveal any mutagenic activity. The maximum non-toxic quantity tested/plate was 10 mg.

7. In view of the rapid elimination of the substance and the negative findings in the available mutagenicity study, carcinogenicity studies were not considered necessary.

8. In humans, tetracaine after intravenous administration of 2.5 mg/kg produces symptoms of central nervous system toxicity. However, the common signs or accidents also include respiratory and cardiovascular troubles and foetal disorders. Absorption of tetracaine from mucous membranes is rapid and adverse reactions can occur abruptly without the appearance of prodromal signs or convulsions. Allergic reactions were described with tetracaine after intradermal administration. PABA appears to be responsible for these clinical manifestations. Duration of tetracaine anaesthesia is approximately 175 minutes in man.

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9. While no residue depletion studies were available these studies were considered necessary as pharmacokinetic data indicate rapid elimination of tetracaine.

Conclusions and Recommendation

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

- the substance is used in individual animals on an infrequent basis,
- treated animals are unlikely to be send for slaughter after treatment,
- the substance is rapidly eliminated;

the Committee concludes that there is no need to establish an MRL for tetracaine when used as a local anaesthetic and recommends its inclusion in Annex II of Council Regulation (EEC) No 2377/90 in accordance with the following table:

Pharmacologically active substance(s)	Animal species	Other provisions
Tetracaine	All food-producing species	For use as local anaesthetic only