European Medicines Agency
Veterinary Medicines and Inspections

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COMMITTEE FOR MEDICINAL PRODUCTS FOR VETERINARY USE

TOSYLCHLORAMIDE SODIUM
(Extension to horses)

SUMMARY REPORT (3)

1. Tosylchloramide sodium (N-chloro-p-toluenesulfonamide, sodium salt, chloramine T) is an organic chlorine compound with biocidal effect, with an available chlorine content of 28 – 30%. It is used in fish farming for prevention and control of bacterial gill disease as follows: 10 mg/l in water of flow-through basin for 1 hour for preventive purposes, which may be repeated every 15 to 30 days; 10 mg/l in water of flow-through basin for 1 hour for therapeutic purposes, which may be repeated up to 3 times within 1 week. Tosylchloramide sodium is also used for teat and udder disinfection to prevent udder disease in lactating cows. To obtain effective concentrations at least 50 to 100 mg active chlorine per litre solution are required. This is achieved if a 0.3% tosylchloramide solution is used. The teats of lactating cows are dipped in the solution after each milking throughout the lactation period and in nonlactating cows once daily. According to prescription 0.5 ml of the solution ready for application (3 mg per ml) should be used for each teat, i.e. 6 mg per animal.

   Tosylchloramide sodium was previously assessed by the CVMP and is currently included in Annex II of Council Regulation (EEC) No 2377/90 in accordance with the following table:

Pharmacologically active substance(s)	Animal species	Other provisions
Tosylchloramide sodium	Fin fish	For water borne use only
	Bovine	For topical use only

   An application has now been submitted for the extension for tosylchloramide sodium to horses. The proposed indication for horses is skin desinfection, especially treatment of phlegmone (cellulitis). The recommended use is as a 0.5% tosylchloramide sodium solution to be applied on the skin and on the bandage (spraying or flushing), twice daily for 3 to 4 consecutive days.

2. A pharmacokinetic study in horses has been conducted to determine concentrations of p-toluenesulfonamide, the primary reaction product and marker metabolite for tosylchloramide sodium, in serum after topical application of the intended 0.5 % solution. Six horses with wounds (injuries with and without loss of substance) were treated twice a day at intervals of 8 hours over 72 h (6 treatments/per animal in total) by washing (3 animals) or spraying (3 animals). The amount of solution applied to the wounds depended on the size of the wound and the type of application (200 ml to 1000 ml for the washing application and 100 to 250 ml for spraying application). Blood samples were collected immediately prior to each treatment, at 2, 4, 6, and 8 h after the first treatment and at 2, 4, 6, 12, and 24 h after the last treatment. Samples were analysed for p-toluenesulfonamide by HPLC-Diode Array Detector. The method involved a hydrolysation to convert tosylchloramide to p-toluenesulfonamide. The limit of quantification was 10 µg/l and the limit of detection 3.2 µg/l. Residues were below the limit of quantification of 10 µg/l in all samples analysed. P-toluenesulfonamide was only detectable in 2 samples from the 5th treatment. Concentrations were in the low µg/l range (4.4 µg/l and 6.0 µg/l, below limit of quantification). Tosylchloramide was not detected in any of the samples.

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The utilised method of analysis was sufficiently validated with respect to accuracy and precision, limit of quantification/detection and specificity against matrix components.

In conclusion, the study showed that concentrations in serum were generally undetectable or very low which is indicative of poor dermal absorption and/or rapid metabolism and excretion of the active substance. The highest observed p-toluenesulfonamide concentrations in serum were in the same range than those reported for milk samples following udder treatment of cows (see EMEA/MRL/782/01-Final).

Conclusions and recommendations

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

- absorption of tosylchloramide sodium following dermal treatment is poor,
- the amount of residues likely to be ingested by the consumer is very low and of no toxicological or microbiological concern (see also the assessments for the MRL applications for tosylchloramide sodium for fin fish (EMEA/MRL/570/99-FINAL) and bovine species (EMEA/MRL/782/01-FINAL);

the Committee for Medicinal Products for Veterinary Use concludes that there is no need to establish an MRL for tosylchloramide sodium 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
Tosylchloramide sodium	*Equidae*	For topical use only