



COMMITTEE FOR MEDICINAL PRODUCTS FOR VETERINARY USE

DINOPROSTONE

SUMMARY REPORT

1. Dinoprostone (CAS 363-24-6) is a synthetic analogue of prostaglandin E₂ (PGE₂), an autocrine/paracrine hormone. Dinoprostone is structurally similar to dinoprost, a synthetic analogue of prostaglandin F₂ alpha (PGF₂α). The two substances differ in that where dinoprostone contains a cyclopentanone group, dinoprost contains a cyclopentanol group. Both are used as oxytocic agents.
2. Dinoprost tromethamine was previously evaluated by the Committee for Veterinary Medicinal Products (CVMP). In single dose and repeat dose studies dinoprost tromethamine was seen to have low toxicity. Following oral administration, the most sensitive organ was assessed to be the uterus of the near term pregnant woman. Based on this finding the ADI was considered to be 0.83 µg/kg bw (corresponding to 50 µg in a 60 kg person). Pharmacokinetic data demonstrated that dinoprost is rapidly removed from the animal body. Subsequently, as a result of a request for clarification, the CVMP considered the case of dinoprost, the active moiety of dinoprost tromethamine and concluded that, from a consumer safety point of view, the free acid and the tromethamine salt were not significantly different. Both substances are included in Annex II of Council Regulation (EEC) No 2377/90, in accordance with the following table:

Pharmacologically active substance	Animal species	Other provisions
Dinoprost tromethamine	All mammalian species	
Dinoprost	All mammalian species	

3. The CVMP has now been requested to consider whether dinoprostone would be covered by the existing assessments for dinoprost tromethamine and dinoprost or whether a separate MRL application would be required.
4. *In vivo*, dinoprostone is rapidly metabolised to dinoprost. In human medicine dinoprostone is used for the induction of labour. Published literature indicates that following intravenous administration dinoprostone is rapidly distributed and metabolised, with only 3% of unchanged drug remaining in the blood after 15 minutes.
5. The CVMP considers that given the structural similarity of dinoprostone and dinoprost, and the fact that dinoprostone is rapidly metabolised to dinoprost, the safety assessments performed for dinoprost tromethamine and dinoprost also apply to dinoprostone.

Conclusions and recommendation

Having considered that:

- dinoprostone is an analogue of an endogenously occurring prostaglandin,
- dinoprostone is structurally similar to dinoprost,
- dinoprostone is rapidly metabolised to dinoprost,
- dinoprostone is metabolised very rapidly;
- the assessments performed for dinoprost tromethamine and dinoprost also apply to dinoprostone;

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

Pharmacologically active substance	Animal species	Other provisions
Dinoprostone	All mammalian species	