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

COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

LEVAMISOLE (1)

SUMMARY REPORT

1. Levamisole is an anthelmintic drug which, depending on the route of administration, has a moderate to high acute toxicity rate in rats and mice (LD_{50} values of ca 20 mg/kg intravenously and 200-500 mg/kg orally). When given at relatively low doses in subchronic studies no adverse effects were seen. Haemolytic anaemia was the major effect seen in dogs in a 1-year study where animals were given the drug daily in gelatin capsules. The NOEL was 5 mg/kg/day. There are no reported carcinogenicity studies with levamisole.

2. No effects on fertility were noted when levamisole was given to female rats 14 days prior to mating at doses of up to 160 mg/kg/day. It was not teratogenic to pregnant rats or rabbits when given over various stages of gestation and no effects were seen in 2- or 3-generation studies nor in peri- and post-natal experiments.

3. Levamisole induced chromosome gaps and breaks in human lymphocytes in vitro and in vivo after volunteers were given 2 mg/kg. No chromosomal damage occurred in mice given 2.5 mg/kg levamisole by the sub-cutaneous route.

4. Levamisole has induced various non-specific effects in humans including nauseas vomiting and skin rashes. Neutropenia and thrombocytopemia have also been reported. However, the commonest and most severe effect induced by levamisole is agranulocytosis. This can be fatal particularly if infection occurs but it is reversible. Levamisole-induced agranulocytosis is idiosyncratic and may be associated with HLA-B27 seropositive rheumatoid arthritis or other abnormalities of the immune system. It occurs at relatively low doses even when given on non-consecutive days. No NOEL can be identified and, if one exists, it is probably extremely small. Consequently all MRL of 0.01 mg/kg (0.01 ppm) is recommended for levamisole.

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