COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

ALBENDAZOLE

SUMMARY REPORT (1)

1. Albendazole is a benzimidazole anthelminic which is used in cattle and sheep.

   It is also used in human medicine to treat gastrointestinal parasitic infections, the dose normally employed is 400 mg per person.

2. Albendazole is of low acute oral toxicity. Oral dosing results in low plasma levels of albendazole because of rapid first-pass metabolism in the liver. The compound is metabolised to the sulphoxide and the sulphone; the carbamate molety is then cleaver to produce 2-aminosulphone.

   In mice, repeat oral dosing produced anaemia, leukoponia, testicular degeneration and hepatocellular vacuolation; the no-observed-effect level was 25 mg/kg bw per day. Neutropenia, hypercholesterolaemia, testicular degeneration and fatty vacuolation of hepatocytes were observed in rats; the no-observed-effect level was 7 mg/kg bw per day. Albendazole was not carcinogenic in rats or mice.

   Albendazole was not mutagenic in a range of *in vitro* assay. Its 2-aminosulphone metabolite was not mutagenic in an *in vitro* assay.

   Albendazole was not teratogenic in mice at dose levels of up to 30 mg/kg bw per day. In rabbits, foetal growth retardation was observed at 10 mg/kg bw per day; the no-observed-effect level was 5 mg/kg bw per day. Albendazole was teratogenic in sheep and in rats at high dose levels; the no-observed-effect levels were 10 mg/kg bw per day and 5 mg/kg bw per day respectively.

3. Albendazole had no significant antimicrobial activity.

4. An ADI of 0-0.005 mg/kg bw per day has been estimated by applying a safety factor of 1000 to the no-observed-effect level of teratogenicity of 5 mg/kg bw per day. The large safety factor was considered necessary because of the teratogenic effect.

5. More than 95% of the residues at four days withdrawal time or longer are bound residues, of which less than 15% of bioavailable. Albendazole is metabolised in the target species to various metabolites including the 2-aminosulphone and the corresponding sulphoxide. For practical reasons the residue analysis involves chemical oxidation of the residues to the 2-aminosulphone. The following provisional MRLs are therefore expressed as the 2-aminosulphone :

milk	0.1 mg/litre
muscle	0.1 mg/kg
fat	0.1 mg/kg
kidney	0.5 mg/kg
liver	0.1 mg/kg

   Total intake of extractable residues is 310 µg/day which is compatible with the ADI in paragraph 4.

6. Sensitive analytical techniques are available including a method based on HPLC which has a limit of sensitivity of 0.05 mg/kg.

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7. Additional information is required before 31 December 1994 on the following :

- a "marker" residue substance for milk;

further information on the quantitative relationship between the concentrations of the 2-aminobenzidazole sulphone metabolite and total residues, in muscle, kidney and fat of cattle and sheep.