



COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

RONIDAZOLE (1)

SUMMARY REPORT

1. Ronidazole is a veterinary medicinal product traditionally used for the prevention and treatment of histomoniasis in turkeys, the treatment of trichomoniasis in pigeons, genital trichomoniasis in cattle and the prevention and treatment of haemorrhagic enteritis in pigs.
2. The safety of nitroimidazole residues in food for human consumption has been assessed on the basis of the mutagenic and carcinogenic potential of these compounds.
3. Ronidazole has shown mutagenic activity in all the bacterial tests carried out. Although such an effect might - as in the case of dimetridazole - be due to the enzyme activity of bacterial nitroreductase, this has not yet been proved. In other mutagenesis tests, ronidazole was found, in certain cases, not to have any mutagenic effects, while in other cases the results were ambiguous : slight gene mutation in fruit flies and mammal cells; equivocal but reproducible *in vivo* clastogenic effects in mice.
4. Ronidazole increases the incidence of various types of benign tumour in laboratory animals : mammary fibroadenoma in rats, lung tumors in mice. At the highest dose of 40 mg/kg/day it has induced the growth of malignant tumours - mammary adenocarcinoma - in female rats.
5. Metabolic studies carried out on pigs and turkeys show extensive metabolism of ronidazole and rapid elimination of its metabolites. The bound residues have been the subject of a detailed study which has enabled them to be identified both qualitatively and quantitatively.
6. The study of the toxicity of these bound residues has shown that in the 'Ames' test - which reveals the mutagenic power of the parent product - they did not have any mutagenic effect whatsoever. Therefore, they cannot be taken into account in the toxicological evaluation of ronidazole residues.
7. In view of the ambiguous results obtained with ronidazole in a number of mutagenesis tests, leaving aside the positive effects in the Ames test and the growth of mammary adenocarcinoma in female rats exposed to the highest experimental dose, we suggest that the same practical solution found for nitrofurans be adopted for ronidazole and that a provision MRL of 2 µg/kg be accepted for extractable residues including ronidazole and metabolites which retain the nitroimidazole structure.

The following information must be provided before 1 January 1994 :

- proposed marker metabolite and the reasons for choosing it.