This is provisional English translation of an excerpt from the original full report.

Risk Assessment Report

Albendazole
(Veterinary Medicinal Products)

Food Safety Commission of Japan (FSCJ)
September 2015

ABSTRACT

The Food Safety Commission of Japan (FSCJ) conducted a risk assessment of albendazole (CAS No. 54965–21–8), a parasiticide, based on the documents including assessment reports from the Joint FAO/WHO Expert Committee on Food Additives (JECFA), the European Medicines Agency (EMEA), and the Australian Pesticides and Veterinary Medicines Authority (APVMA).

The data used in the assessment include pharmacokinetics (mice, rats, cattle, sheep, pigs and humans), residues (cattle and sheep), genotoxicity, acute toxicity (mice, rats, etc.), subacute toxicity (mice, rats and dogs), chronic toxicity/carcinogenicity (mice and rats), reproductive and developmental toxicity (mice, rats, rabbits and sheep). The data on albendazole sulphoxide, a metabolite of albendazole, were also used.

Genotoxicity was suggested in several albendazole studies. Since albendazole is reported to bind to tubulin and inhibit its polymerization to microtubules, FSCJ considered that the genotoxicity is rather caused by aneuploidies induced through the protein interactions, but not by DNA damage. Albendazole is considered to be of no concern for genotoxicity relevant to human health as long as used appropriately as a veterinary medicinal product, though this compound may have a genotoxic potential. The combined chronic toxicity/carcinogenicity study and carcinogenicity study in mice and rats showed no carcinogenicity. Therefore, a threshold level as acceptable daily intake (ADI) is possible to be established for the toxicity.

Major adverse effects of albendazole include hepatocellular vacuolization, seminiferous tubular degeneration and decrease in white blood cell count (WBC).

In developmental toxicity studies in rats and rabbits, clear teratogenicity was observed at the doses equal to or higher than 10 mg/kg bw/day. The abnormality including craniofacial defects, anophthalmia or microphthalmia, micromelia and dwarfism was observed.

FSCJ compared the no-observed-adverse-effect levels (NOAELs) from various toxicity studies, and adopted the NOAEL of 5 mg/kg bw/day obtained in a 6-month subacute toxicity study in dogs, and also in developmental toxicity studies in rats and in rabbits for ADI estimation.

On the setting the safety factor, FSCJ considered the following points; i) the aneuploidies were induced in a genotoxicity studies, ii) clear teratogenicity was observed at the dose two times higher than the NOAEL in a developmental toxicity study, iii) a rather limited formation of an active metabolite, albendazole sulphoxide, was, however, observed in humans than in rats and rabbits. FSCJ concluded it appropriate to apply an additional safety factor of 5.

FSCJ specified the ADI of 0.01 mg/kg bw/day, applying a safety factor of 500 to the NOAEL of 5 mg/kg bw/day.

It has been evident that albendazole is metabolized to albendazole sulphoxide *in vivo*, and veterinary medicinal products containing albendazole sulphoxide as a main ingredient are used overseas. Therefore, FSCJ specified the group ADI of 0.01 mg/kg bw/day for the combined level of albendazole and albendazole sulphoxide (as albendazole eq.) considering the effect of albendazole sulphoxide.