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

Risk Assessment Report

Orbifloxacin

(Veterinary Medicinal Products)

Food Safety Commission of Japan (FSCJ)
October 2017

ABSTRACT

FSCJ conducted a risk assessment of a fluoroquinolone synthetic antimicrobials, orbifloxacin (CAS No. 113617-63-3), based on a written application for the marketing approval of new veterinary medicinal products and its attached documents. For this assessment, the data of pharmacodynamics in cattle and residues in cattle were newly presented with other documents.
Data used in the assessment include pharmacokinetics (mice, rats, pigs and cattle), residues (pigs and cattle), genotoxicity, acute toxicity (mice and rats), subacute toxicity (rats and dogs), carcinogenicity (rats), reproductive developmental toxicity (rats and rabbits), and microbiological effects.

Orbifloxacin was negative in all the *in vivo* genotoxicity studies, although it was positive in *in vitro* chromosomal aberration test, thus FSCJ considered that orbifloxacin has no genotoxicity relevant to human health. In addition, orbifloxacin was positive in both in vitro and in vivo photogenotoxicity studies, however direct effects on DNA are unlikely involved in the exertion mechanism for photogenotoxicity of orbifloxacin. Hence, FSCJ considered that orbifloxacin has no photogenotoxicity relevant to human health, thus FSCJ concluded that the ADI for orbifloxacin could be specified.

No carcinogenicity was observed in a two-year carcinogenicity study in rats.

FSCJ considered that the LOAEL observed in a 30-day subacute toxicity study in dogs, 12.5 mg/kg bw/day, was appropriate as the basis of the ADI among values obtained among various toxicity studies. FSCJ appropriately specified, therefore, the toxicological ADI for orbifloxacin to be 0.013 mg/kg bw/day based on this LOAEL applying the safety factor of 1,000, which was composed of factors due to use of LOAEL, short period of the rational study, and insufficient findings in chronic toxicity and carcinogenicity tests.

Microbiological ADI was estimated to be 0.012 mg/kg bw/day by the equation of the VICH[1].
FSCJ specified the ADI of orbifloxacin as 0.012 mg/kg bw/day as the microbiological ADI is smaller than the toxicological ADI.

[1] The International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products.