This is a 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 2013

ABSTRACT

FSCJ conducted a risk assessment of “orbifloxacin” (CAS No.113617-63-3), a family of synthetic antimicrobial agents of fluoroquinolones, based on a written application for the marketing approval of new veterinary medicinal products, its attached documents and others.

Data used in the assessment are on; pharmacokinetics (mice, rats, pigs and cattle), residues (pigs and cattle), genotoxicity, acute toxicity (mice and rats), subacute toxicity (rats and dogs), carcinogenicity (rats), reproductive and developmental toxicity (rats and rabbits), and microbiological effects.

In studies on genotoxicity of orbifloxacin, all data in vivo were negative although a part of the in vitro data was positive. Therefore, FSCJ concluded that orbifloxacin has no genotoxicity relevant to human health. In a test of photogenotoxicity, data in vitro and in vivo were all positive. However, the photogenotoxicity of orbifloxacin is not mediated directly through action of orbifloxacin to DNA. Consequently, FSCJ concluded that orbifloxacin has no photogenotoxicity relevant to human health.

It was considered that orbifloxacin was not a genotoxic carcinogen since carcinogenicity was not detected in a 2-year carcinogenicity study in rats. Hence, FSCJ concluded that an acceptable daily intake (ADI) could be specified.

From the results of toxicity studies, FSCJ considered it appropriate to use a lowest observed adverse effect level (LOAEL) of 12.5 mg/kg bw/day observed in a 30-day subacute toxicity study in dogs as the rationale for setting ADI. FSCJ also considered it appropriate to specify the toxicological ADI as 0.013 mg/kg bw/day, applying a safety factor of 1000 to this LOAEL. This safety factor of 1000 was composed of 10 for species difference, 10 for individual difference, and 10 for additional factors due to usage of LOAEL, the short period of the rational study, and insufficient findings in chronic toxicity and carcinogenicity tests.

Microbiological ADI was calculated to be 0.012 mg/kg bw/day based on the VICH (the International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products) guideline 36.

FSCJ specified the ADI of orbifloxacin as 0.012 mg/kg bw/day because the microbiological ADI is smaller than the toxicological ADI.