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

Risk Assessment Report

Lomefloxacin

(Veterinary Medicinal Products)

Food Safety Commission of Japan (FSCJ)
January 2016

ABSTRACT

FSCJ conducted a risk assessment of lomefloxacin hydrochloride (CAS No. 98079-52-8), a fluoroquinolone-based antimicrobial agent, based on the documents, including the application documents on the approval of the veterinary medicinal products (ophthalmic solution for horses), according to the "Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Producta, and Cosmetics."

The data used in the assessment include pharmacokinetics (mice, rats, dogs, horses, monkeys and humans), residues (horses), genotoxicity, photogenotoxicity, acute toxicity (mice, rats and dogs), subacute toxicity (rats, dogs and monkeys), chronic toxicity (rats and monkeys), photocarcinogenicity (mice), reproductive toxicity (rats) and developmental toxicity (rats and rabbits), microbiological effects, toxicity on joints (rats and dogs) and toxicity with light irradiation.

Lomefloxacin hydrochloride was considered to have no genotoxicity relevant to human health, judging from the results of *in vitro* and *in vivo* genotoxicity studies.

The *in vitro* toxicity studies with light irradiation indicated lomefloxacin hydrochloride might have photogenotoxicity. FSCJ, however, considered that the possibility of photogenotoxicity to human caused by lomefloxacin hydrochloride via food was extremely low, as long as the lomefloxiacin products are used appropriately, based on 1) the results from pharmacokinetics and residues in horses, 2) the information on human clinical studies and post-marketing surveillance in human drugs, as well as 3) the maxim estimates of the concentration in human skin assuming the lomefloxacin products are used as ophthalmic solutions for horses.

Although no carcinogenic study was conducted, the carcinogenicity of lomefloxacin hydrochloride was considered to be low, because the results of carcinogenicity studies on other fluoroquinolone substance (enrofloxacin, danofloxacin and orbifloxacin) were negative in rodents, as well as no carcinogenicity of lomeoxacin products was indicated in human clinical use.

Cystic squamous cell carcinomas were observed in the photocarcinogenicity study in mice. The cyclopentadiene (CPD) synthesis is suggested to be involved in the mechanism. FSCJ considered that the possibility of photocacinogenicity to human was low, because the activities of nucleotide excision repairis are higher in human than in rodents, as well as the human exposure to lomefloxacin via food is extremely limited, assuming the lomefloxacin products are used for horses.

The lowest no-observed adverse effect level (NOAEL) in the toxicological studies was 2.5 mg/kg bw per day based on the toxicity study on joints in juvenile and young dogs. Toxicological an acceptable daily intake (ADI) was specified as 0.025 mg/kg bw per day applying a safety factor of 100 to the NOAEL.

The microbiological ADI was not necessary to be specified because the possibility of lomefloxacin hydrochloride via food to affect intestinal flora in human is extremely low as long as the lomefloxacin products are properly used.

FSCJ thus specified the ADI of 0.025 mg/kg bw per day for lomefloxacin hydrochloride.

The ADI should be reevaluted, when another application of veterinary medical products are submitted on the different usages or doses, as well as when new findings are obtained on the microbial effects.