Risk Assessment Report on
Bovine and Swine Injections Containing Marbofloxacin as the Active Ingredient
(Marbocyl 2% and Marbocyl 10%)

(Veterinary Medicines)

Food Safety Commission of Japan (FSCJ)

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Marbocyl 2% and Marbocyl 10%

Active ingredient, efficacy/effects, and dosage/administration of Marbocyl formulation are as below.

(1) Main active ingredient

Marbofloxacin.

(2) Efficacy and effects

Marbocyl 2% and Marbocyl 10% are effective in bovine bacterial pneumonia (effective for *Pateurella multocida*, *Mannheimia haemolytica*, and *Mycoplasma bovis*), and swine pleural pneumonia animals (effective for *Pateurella multocida* and *Actinobacillos pleuropneumoniae*).

(3) Dosage and administration

For bovine animals, Marbocyl 2% is intravenously or intramuscularly administered in the form of marbofloxacin once/day at a dose of 2 mg/kg bw (0.1 mL/kg bw in formulation), whereas in swine animals, it is intramuscularly administered at 2 m/kg bw (0.1 mL/kg bw in formulation) for 3 to 5 days, respectively. Marbocyl 10% is administered in the form of marbofloxacin once/day at 2 mg/kg bw (0.02 mL/kg bw in formulation) for bovine animals, and in swine animals, it is intramuscularly administered at 2 m/kg bw (0.02 mL/kg bw in formulation) for 3 to 5 days, respectively. For both concentrations, the withdrawal period is 3 days for bovine animals, 48 hours for milk, and 3 days for swine animals.

(4) Other substances

D-mannitol (tonicity agent), glucono-δ-lactone (solubilizing agent), m-cresol (preserving agent), alpha thioglycerin (antioxidative agent), and edentate sodium (stabilizing agent) are used. Among these, D-mannitol and glucono-δ-lactone are designated additives and the ADIs for these substances have not been identified in JECFA's assessment. Use of edentate sodium as an additive for veterinary medicines has been discussed. The assessment concludes that as long as used properly, the risk of the edentate sodium formulation affect human health through food can be negligible. The effects of m-cresol and alpha thioglycerin on human health are considered negligible because they are used only in minute amounts in formulations and sufficient withdrawal periods are regulated.

Findings regarding safety

As mentioned above, veterinary medicines containing marbofloxacin as the main ingredient are used to treat bacterial skin infections in dogs and cats in Japan. In EU member countries, they are

additionally used to treat bovine and swine animals. While the EMEA stipulates the ADI to be 4.5μg/kg bw/day, the JECFA and other international organizations have not conducted assessment. In Japan, where residual standards are established [1], no ADI has been settled. Veterinary medicines containing marbofloxacin are not used in medical products for humans.

Risk assessment

While veterinary medicines containing marbofloxacin as the main ingredient are used as an injection for bovine and swine animals, no detailed toxicological assessment for these formulations has been conducted in Japan. There is no record of the use of these formulations as veterinary medicines for animals raised for human consumption. In light of these facts, the ADI for marbofloxacin was established as described in the Appendix.

As the conclusion of the risk assessment for marbofloxacin, it is recommended that the following ADI be established.

Marbofloxacin: 0.0032 mg/kg bw/day

It should be noted that the evaluation of this substance is currently under review to incorporate the effects mediated by drug-resistant bacteria.

[1] A new set of standards regulated by Notice No. 499 of the Ministry of Health, Labour and Welfare (2005).