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

Risk Assessment Report

Vedaprofen

(Veterinary medicinal products)
Food Safety Commission of Japan (FSCJ)
November 2013

ABSTRACT

FSCJ conducted a risk assessment of “vedaprofen” (CAS No. 71109-09-6), an anti-inflammatory drug, based on assessment reports from the European Medicines Agency (EMEA) and other documents.

The data used in the assessment were on: pharmacokinetics (humans, dogs, and horses), residues (horses), genotoxicity, acute toxicity (mice and rats), subacute toxicity (dogs), reproductive and developmental toxicity (rats, rabbits, and dogs), human clinical tests and others.

Results of genotoxicity studies indicated that vedaprofen has no genotoxicity relevant to human health. Although no result of carcinogenicity studies was available, vedaprofen has been classified neither as carcinogens nor as potential carcinogens, and no carcinogenic risks of vedaprofen have been reported by EMEA to date. Therefore, FSCJ concluded that the acceptable daily intake (ADI) of vedaprofen could be specified by adopting additional safety factors.

The effects observed at the lowest dose in various toxicological studies were those observed in a 90-day subacute toxicity study in dogs, such as occult blood in faeces and blackish faeces (bloody faeces) in both sexes, changes of blood chemistry parameters such as decreased values for total protein and albumin as well as erosions in the pyloric mucosa of the stomach in females. The no observed adverse effect level (NOAEL) in this study was 0.125 mg/kg body weight/day. The adverse effects observed in this study (i.e. general symptoms such as occult blood in faeces and bloody faeces, changes in erythrocytic and leukocytic parameters, erosions and ulcers in the mucosa of alimentary tracts, etc.) were similar to those reported as side effects of nonsteroidal anti-inflammatory drugs, and were all reversible.

Although the number of animals per group in the 90-day subacute toxicity study in dogs was small, pharmacokinetics studies suggested that the half-life of vedaprofen through oral dose was shorter in humans than in dogs. Taking into account various factors comprehensively including the fact that no chronic toxicity and carcinogenicity studies were conducted, FSCJ concluded that the additional safety factor of 10 was appropriate.

Hence, FSCJ specified the ADI of vedaprofen to be 0.00013 mg/kg body weight/day, dividing the NOAEL of 0.125 mg/kg body weight/day in the 90-day subacute toxicity study in dogs by the safety factor of 1,000 (10 for species differences, 10 for individual differences, and 10 for the additional factor).