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

Risk Assessment Report

Altrenogest

(Veterinary Medicinal Products)

Food Safety Commission of Japan (FSCJ)
January 2016

ABSTRACT

FSCJ conducted a risk assessment of altrenogest (CAS No. 850-52-2), an hormonal agent, based on documents including a written application for establishing Import Tolerance, risk assessment reports of the European Medicines Agency (EMEA) , Food and Drug Administration (FDA), and the documents provided from the government of Australia.

The data used in the assessment include pharmokinetics (rats, pigs and horses), residues (pigs and horses), genotoxicity, acute toxicity (mice, rats and dogs), subacute toxicity (rats, pigs and monkeys), chronic toxicity and carcinogenicity (rats, pigs and dogs), and developmental toxicity (rats).

Although carcinogenicity study has not been conducted, the effects observed in one-year chronic toxicity study in rodents and dogs were hormone related changes. In addition, no neoplastic or preneoplastic finding was not observed. Thus, since altrenogest is considered to be non-genotoxic carcinogen, FSCJ concluded it possible to specify an acceptable daily intake (ADI) of altrenogest.

Major adverse effects of altrenogest were hormone mediated reactions including decreased absolute weight of testes, prostate and epididymis as well as histopathological changes in the hormone dependent organs (decrease in prostatic and seminal vesicle secretion as well as decrease in spermatogenesis).

Two-generation reproductive study containing developmental toxicity paramters in rats indicated no teratogenicity.

The adverse effects observed at the lowest dose were disturbance of menstrual cyclicity and serum steroid concentration in the study using monkeys observed for three menstrual cycles. These changes were considered the most reliable adverse effects of alternogest for human health. The no-observed-adverse-effect level (NOAEL) for hormonal effect of altrenogest was 0.004 mg/kg bw/day based on this study.

FSCJ specified an ADI of 0.00004 mg/kg bw/day (0.04 μg/kg bw/day) applying a safety factor of 100 to the NOAEL in three menstrual cycles in monkeys.