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Tioconazole の毒性，生殖および一般薬理試験

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Preclinical Safety Evaluation of Tioconazole

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SUMMARY

Safety of an antifungal tioconazole was evaluated in Sprague–Dawley rats. The acute subcutaneous LD_{50} of tioconazole was estimated to be greater than 10000 mg/kg in both sexes in rats.

The rats treated subcutaneously for 1 or 6 months were well tolerated and non-toxic dose levels are considered to be 3 mg/kg and 1 mg/kg, respectively. Palpable subcutaneous induration, dose-related in size, was noted at injection sites. The induration might cause leucocytosis, increased spleen weight and reduced RBC or hemoglobin contents in rats treated subcutaneously at 10 mg/kg or more for 1 month or longer.

Females copulated after subcutaneous treatment for 14 days prior to mating with 62 day-treated males and up to day 7 of gestation induced decrease in number of implantations and live fetuses at dose levels of 30 and 100 mg/kg, but the rate of copulation and pregnancy was comparable to those of controls.

Tioconazole was given to pregnant rats during organogenesis (day 7～17) and no drug-related malformation of fetuses was found. Delayed parturition of the dams and high incidence of stillborns were noted at the two highest doses, as reported with other imidazole antifungal agents.

In the peri- and postnatal studies, female rats given tioconazole (from day 17 of gestation to day 21 of post-parturition) at 10 mg/kg showed no adverse effect in dams and offsprings, and revealed high incidence of stillborns, and lower lactation ability at 30 and 100 mg/kg.

No significant general pharmacological parameters were noted in mice or rats at subcutaneous doses of 2000～500 mg/kg of tioconazole.