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Ampiroxicam のラットおよびウサギを用いた生殖・発生毒性試験

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Reproductive and Developmental Toxicity Studies with Ampiroxicam in Rats and Rabbits

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Ampiroxicam, a nonsteroidal anti-inflammatory agent, was examined for reproductive and developmental toxicity in Sprague-Dawley rats and Japanese White rabbits.

1. Fertility study in rats

Ampiroxicam was administered orally to female rats at daily doses of 3.5, 1.4, 0.7 and 0 (control) mg/kg from 14 days before mating to day 7 of gestation. The females were mated with the males given the same doses for 70 days prior to mating. Body weight gain and food consumption were slightly reduced in females at the top dose level of 3.5 mg/kg. No significant difference in the copulation or pregnancy index was found between the control and treated groups. No embryolethal or teratogenic effect was observed at any of the dose levels used.

2. Teratogenicity study in rats

Ampiroxicam was administered orally to pregnant rats at daily doses of 7, 1.4, 0.7 and 0 mg/kg from day 7 to day 17 of gestation. Food consumption was slightly reduced in dams at 7 mg/kg. No teratogenetic effect nor any other adverse effect on fetal development was noted. Parturition disorders (prolongation and/or dystocia) were observed in 5 of 16 dams at 7 mg/kg and 3 of 15 dams at 1.4 mg/kg. Consequently, prolongation of pregnancy periods, decreases in birth index and litter size, increase in the weight of pups, and advance in external development were found in the 7 and 1.4 mg/kg groups. The viability index of pups on day 4 was slightly reduced at 7 mg/kg. There was no evidence of adverse effects on the behavior or reproductive performance of the first (F_1) generation offspring, nor were there abnormalities of the second (F_2) generation fetuses.

3. Teratogenicity study in rabbits

Ampiroxicam was administered orally to pregnant rabbits at daily doses of 75, 30, 15 and 0 mg/kg from day 6 to day 18 of gestation. Out of 18 dams at 75 mg/kg, 2 dams died and 1 dam micsarried. No difference in body weight gain or food consumption was found between the control and treated groups. No teratogenetic effect nor any other adverse effect on fetal development was noted.

4. Perinatal and postnatal studies in rats

Ampiroxicam was administered orally to female rats at daily doses of 1.4, 0.7, 0.14, 0.07 and 0 mg/kg from day 17 of gestation to day 21 after parturition. Parturition disorders (prolongation and/or dystocia) were observed at 0.14 mg/kg and above. With these doses there occurred a prolongation of the gestation period and a decrease in birth index and litter size. At 1.4 and 0.7 mg/kg, several deaths were found in the dams in which the parturition disorders were observed. Delivery index was reduced at 1.4 mg/kg. The viability index of pups on day 4 was decreased at 0.14 mg/kg and above. The weight of pups was increased at 0.7 mg/kg. The

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