Combined Fertility and Embryofetal Developmental Study of Cytisine in Rats
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ABSTRACT

Cytisine [(1\(\alpha\),2\(\alpha\),3\(\beta\),4\(\beta\),5\(\alpha\),6\(\alpha\)) hexahydropyrido[1,2-a][1,5]diazocin-6-\(\alpha\)-hydroxy] is a known smoking aid, relatively similar to nicotine in its pharmacological activity. Due to its potential as a smoking replacement therapy, varenicline (\(\alpha4\beta2\) nicotinic receptor subtype), Cytisine has been available for smoking replacement therapy, varenicline). Thus the NCI has conducted a comprehensive toxicological evaluation of cytisine. This study was designed to evaluate the potential for cytisine to induce developmental or reproductive toxicity in rats. Cytisine was administered to male and female rats beginning 4 weeks. The cytisine dose range was 0 (vehicle control), 0.4, 2.0, or 10.0 mg/kg/day for 13 weeks. Rats were examined for effects on mating, fertility or fecundity, embryo development (i.e., implantation, body weight, sex, ossification, organ weight, organ size, serum hormone concentrations), sperm parameters, body weight and weight gain, and clinical pathology.

RESULTS

Administration of cytisine had no adverse impact on mating, fertility or fecundity indices. All indices were 100% in the control group. No treatment related changes in percent motile sperm, epididymal or testicular weight were observed. Statistical significance decreases in mean body weight gain were seen in the Group 4 (10.0 mg/kg) females. Administration of cytisine had no adverse impact on the estrous cycle. No effects of cytisine were seen on the weight of any male reproductive organ. No treatment related changes in percent motile sperm, epididymal or testicular weight were observed. In the females, cytisine doses of up to 10 mg/kg/day beginning 4 weeks induced no evidence of developmental or reproductive toxicity in rats; cytisine toxicity was limited to reduced body weight gain.

CONCLUSIONS

The No-observed-adverse-effect level (NOAEL) of cytisine is 0 mg/kg/day. The study has demonstrated that cytisine is not embryotoxic or teratogenic in rats at doses up to 10 mg/kg/day. Cytisine is not a developmental or reproductive toxicant to rats at the doses and administration conditions evaluated in this study.

INTRODUCTION

The No-observed-adverse-effect level (NOAEL) of cytisine is 0 mg/kg/day. The study has demonstrated that cytisine is not embryotoxic or teratogenic in rats at doses of up to 10 mg/kg/day. Cytisine is not a developmental or reproductive toxicant to rats at the doses and administration conditions evaluated in this study.