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Review of the article *"Preclinical toxicity profile of oral bilastine"*

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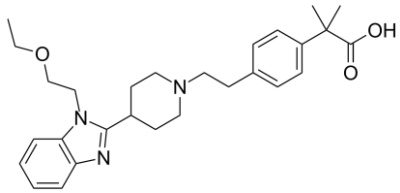
Bilastine is a long-acting, non-sedating histamine antagonist with selective antagonist affinity for peripheral H_1 receptors and no affinity for muscarinic receptors.

Chemical structure of bilastine



For the future marketing of bilastine it is necessary to evaluate its **toxicity profile**.

The results they obtained when evaluating the toxicity profile are summarized below: Toxicokinetic analyses conducted in tandem to evaluate systemic exposure, gender differences, and dose proportionality in the different animal species indicated that animals were systemically exposed to bilastine during treatment. Repeated-dose toxicity studies in beagle dogs (52 weeks) and in rats and mice (13 weeks) showed that bilastine at doses up to 2,000 mg/kg/day was not associated with any mortality, ocular effects, or nodules/masses. no bilastine-associated neoplastic lesions were observed in rats and mice after 104 weeks of treatment with bilastine at doses up to 2,000 mg/kg/day. In general, bilastine-related clinical signs, body-weight changes, food consumption, clinical chemistry, haematology, and macro- and microscopic findings were of low order and reversible, with effects present only at the highest doses administered. Bilastine (up to 1,000 mg/kg/day) was well tolerated in pregnant/lactating rats and in their offspring and subsequent generations. With respect to effects on embryofoetal development in rabbits, bilastine at 400 mg/kg/day (the highest dose evaluated) was assessed to be the no observed adverse effects level. Overall, bilastine demonstrated a favorable toxicity profile in all animal models investigated and at higher doses than the corresponding recommended daily human dosage[1].

Toxicological studies of bilastine have demonstrated a favorable toxicity profile in all investigated animal models, including long-term repeated dose exposure and in models that have evaluated embryotoxicity and pre and postnatal development and maternal function, at doses higher than the corresponding RDA in humans. The clinical signs observed were low order and remitted once the treatment was completed.

[1] María Luisa Lucero BSc, Joseba K. Arteche BSc, E. W. Sommer Dr & AgustínCasadesus BSc (2012) Preclinical toxicity profile of oral bilastine, Drug and Chemical Toxicology,35:sup1, 25-33, DOI: 10.3109/01480545.2012.682652