# CLINICAL EFFICACY AND SAFETY OF THE ANTIHISTAMINIC DRUG EBASTIN

**Berezniakov A., Bondariev Ye.**
*National University of Pharmacy, Kharkiv, Ukraine*
*Department of Clinical Pharmacology*
*an-ber@ukr.net*

**Introduction.** Antihistamines (AHP) are widely used in the treatment of allergic diseases such as allergic rhinitis, atopic dermatitis, urticaria, etc. The widespread use of AHP is due to their ability to reduce the intensity of allergic inflammation. The most common underlying mechanism of these diseases is an immediate allergic reaction (IgE mediated or type I). An allergic reaction, triggered by either immune or non-immune mechanisms, has both an early phase (developing within minutes) and a late phase (occurring 8-12 hours later). The late phase of the allergic response is clinically less pronounced than the early phase, but it is precisely this that leads to the chronicity of the allergic process.

**Objective.** Understanding the pharmacokinetics and pharmacodynamics, as well as having confidence in the predictability of clinical effects and the safety of H1-histamine receptor blockers, is crucial when choosing the appropriate medication for a specific clinical situation [1].

**Materials and methods.** First-generation antihistamines (with pronounced sedative and anticholinergic effects), used for the treatment of allergic diseases, are considered classical, whereas second generation antihistamines, which lack these side effects, are regarded as modern.

The pharmacological effects and therapeutic indications of first- and second-generation antihistamines are similar. However, unlike first-generation drugs, second-generation antihistamines contain hydrophilic fragments that reduce their lipophilicity, resulting in poor penetration through the blood-brain barrier, which minimizes central nervous system side effects. However, unlike the first generation, the second-generation drugs contain hydrophilic fragments that help reduce lipophilicity and, as a consequence, poor penetration through the blood-brain barrier, which minimizes central nervous system side effects [2]. The features of second-generation antihistamines include high affinity for H1 receptors, the absence of blockade of other receptor types, lack of tachyphylaxis, no dryness of mucous membranes or impaired mucus clearance, good absorption from the gastrointestinal tract, and no dependency on food intake. They also have a rapid onset of action, as well as sufficient duration of the main effect (up to 24 hours, and more than 48 hours for ebastine), which allows patients to take the medication in a highly compliant regimen – once per day. The chemical structure of ebastine significantly distinguishes it from many systemic antihistamines. What sets ebastine apart is that it does not form stereoisomers and enters the body as a pure substance rather than a mixture of racemates. This advantage ensures the highest affinity for H1 histamine receptors, duration of the clinical effect and a better safety profile by minimizing unwanted pharmacological effects and the absence of toxicity [3].

**Results.** Ebastine has high bioavailability and after oral administration is rapidly absorbed in the intestines (up to 95%) and extensively metabolized during the first pass through the liver into the pharmacologically active substance – karebastine [4]. Research data on the pharmacokinetics of ebastine demonstrate that its administration does not require dose adjustment depending on gender and age [5]. In both preclinical and clinical studies, ebastine has established itself as a drug with a favorable safety profile. First of all, the guarantee of safety is the absence of toxic effects associated with the medicinal substance, both general and specific (such as carcinogenicity, mutagenicity, and teratogenicity) [6]. Additional evidence of the safety of ebastine includes the absence of mutagenic potential and reproductive toxicity (teratogenicity, feto- and embryotoxicity, decreased fertility) even at doses exceeding 100 mg/kg in preclinical studies. The absence of carcinogenic activity of ebastine has been confirmed in studies using a dosage of 36 mg/kg/day, which is 200 times higher than the therapeutic dose for humans. The safety of long-term use of ebastine was observed in 6 studies involving 1,286 patients with chronic urticaria, of whom 567 received the medicine for a year at doses of 10 or 20 mg. It was noted that the recommended doses were well tolerated by the patients. Out of the reported 1,924 adverse events, 140 were serious, but only 15 could be presumably linked to the use of ebastine [7]. The safety of ebastine (and its pharmacologically active substance, karebastine) regarding its potential impact on cardiac electrophysiology has been thoroughly studied and evaluated in numerous in vitro and in vivo studies, including placebo-controlled, comparative trials and different age groups. It has been established that any changes in the QT/QTc interval associated with ebastine administration are not clinically significant [8].

**Conclusion**. Numerous studies characterize ebastine as one of the most promising second generation antihistamines with a favorable safety profile, making it a recommended option for managing various allergic reactions.

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