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Mizolastine: prefer cetirizine or loratadine

● **More adverse effects with *mizolastine*.**

In France, *mizolastine*, a so-called non-sedative, non-antimuscarinic antihistamine, is authorised for oral administration to adults and children over 12 years of age, as symptomatic treatment for seasonal or perennial allergic rhinoconjunctivitis, and for urticaria (1,2). A copy is also available, with the same indications as the originator (1).

Oral antihistamines are only moderately effective in patients with severe symptoms of allergic rhinitis, allergic conjunctivitis or urticaria. Non-sedative, non-antimuscarinic antihistamines such as *cetirizine* and *loratadine* are the best choices. *Mizolastine* is no more effective than either of these drugs (2-5).

The adverse effect profile of *mizolastine* consists mainly of sedative effects in some patients (especially the elderly), fatigue, headache, gastrointestinal disorders, dry mouth, and increased appetite leading to weight gain (1,2,5). *Mizolastine* can also cause cardiac arrhythmias with QT prolongation, as well as bradycardia and tachycardia (2,6). The risk of QT prolongation appears to be lower with *cetirizine* and *loratadine* (7). Unlike these latter drugs, *in vitro* studies suggest that high *mizolastine* concentrations close potassium channels, an effect compatible with a risk of cardiac arrhythmias (8).

Mizolastine is metabolised by cytochrome P450 isoenzyme CYP3A4. To avoid potentiating its effects, including its cardiac adverse effects, *mizolastine* must not be combined with inhibitors of this enzyme, which include various macrolides and azole antifungals. *Mizolastine* must also be avoided in patients with risk factors for torsades de pointes (2,5).

In practice, *mizolastine* has a less favourable harm-benefit balance than other non-sedative, non-antimuscarinic antihistamines. *Cetirizine* and *loratadine* are better options for patients requiring oral therapy but should not be overused.

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Dextromethorphan: neurological disorders in children

● **Do not use in young children.**

In 2015, the Uppsala World Health Organization (WHO) pharmacovigilance centre published a review on adverse drug reactions in children attributed to *dextromethorphan*, an opioid used as an antitussive (1). In February 2015, the Uppsala pharmacovigilance database contained 110 reports of neurological disorders in children under the age of 6 years: 29 cases of ataxia, and 10 cases of coma in children aged 2 years or less, as well as reports of convulsions and dyskinesia. When the search was broadened to include all children under the age of 18 years, 51 cases of ataxia and 19 cases of coma were identified. Most of these reports did not involve accidental intake or overdose.

In France, several *dextromethorphan*-containing products are approved for cough in children from the age of 30 months or 6 years (2). This opioid should not be used lightly, and it is important to remind parents that it should not be given to young children (3).

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Desloratadine, loratadine: aggression

● **Neuropsychiatric reactions.**

In February 2015, the Netherlands Pharmacovigilance Centre, Lareb, reported 22 cases of mental disorders attributed to *desloratadine*, a "non-sedating" antihistamine without antimuscarinic activity. These disorders included abnormal behaviour such as agitation, aggression, violent thoughts, anxiety and depressed mood (1). Six reports involved children under 12 years of age. The disorders resolved after *desloratadine* cessation in 16 patients and recurred on rechallenge in 4 cases. In 21 cases, *desloratadine* was the only suspected drug.

In March 2015, the World Health Organization (WHO) Uppsala pharmacovigilance database contained 17 reports of aggressive reaction attributed to *desloratadine*. Ten involved children, including 8 aged 8 years or under. The disorders recurred in 2 children who were re-exposed at least once to *desloratadine*. *Desloratadine* is a metabolite of *loratadine* and, according to Lareb, the WHO database also contains reports of aggressive reactions attributed to *loratadine* (2,3). As of early 2016, the SPC of the *loratadine*-containing product marketed in France under the brand name Clarityne° states that "nervousness" occurred in 2.3% of exposed children, and more frequently than in children who received placebo (4).

In practice, *loratadine* and *desloratadine* are antihistamines presented as having selective effects on peripheral rather than central H1-receptors. It is best to inform patients or their carers that these drugs also have neuropsychiatric effects.

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