Translated from ***Rev Prescrire*** **October 2008; 28 (300): 747**

Mydriatic eye drops: severe adverse effects in children

● **Systemic reactions.**

In May 2008 the French Health Products Safety Agency (Afssaps) released the results of a national pharmacovigilance survey focusing on the systemic adverse effects of atropinic mydriatic eye drops based on *atropine*, *cyclopentolate* or *tropicamide* in children and the elderly. The report listed 150 cases, observed up to 13 March 2007, in 133 children and 17 patients aged over 75. There were a total of 277 systemic adverse effects (1). Nine cases were life-threatening, 7 of which involved infants under one year of age.

Neuropsychiatric disorders were most frequent (118 cases) and mainly affected children under the age of 4. They included delirium, hallucinations, confusion, agitation and seizures.

Fever accounted for 8% of adverse effects in children under the age of 8. Their temperature was usually below 39°C, and fever was associated with flushed cheeks, which is a sign of atropinic effects. Intestinal occlusion was the most frequent adverse effect observed in infants. Urinary disorders were exclusively reported in patients over age 75.

It is well known that eye drops can have systemic, dose-dependent adverse effects (2). The dose must be carefully tailored to the patient's age, and the patient (or parents) must be informed of warning signs.

Selected references from Prescrire's literature search.

1- Agence française de sécurité sanitaire des produits de santé "Commission nationale de pharmacovigilance. Compte rendu de la réunion du mardi 25 March 2008" 20 May 2008. afssaps.sante.fr accessed 3 August 2008: 21 pages.

2- Prescrire Rédaction "Fiche n°4. Le syndrome atropinique en bref" *Rev Prescrire* 2007; **27** (290 Interactions supplement).

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Corticosteroids: neuropsychiatric effects in children and adolescents

● **Neuropsychiatric adverse effects, even when inhaled.**

Whether they are inhaled, injected or taken orally, corticosteroids have known neuropsychiatric adverse effects, including euphoria, insomnia, excitation, confusion, manic episodes, depression and seizures (1).

The Toulouse Regional Pharmacovigilance Centre and the French Association of Pharmacovigilance Centres identified 95 spontaneous reports in the French Pharmacovigilance Database. These reports described 136 neuropsychiatric adverse effects observed in children and adolescents between January 1994 and March 2007 (2). Fifteen cases were considered serious.

The patients' mean age was 10.4 years; 57 patients (60%) were under 6 years old; and 46 patients (48.4%) were boys.

In 29 cases the events occurred after an overdose (16 cases) or an excessive dose (13 cases), due to errors in prescription or administration. In the other 13 cases the steroid had been intentionally given at a high dose to treat a major health problem (severe asthma, leukaemia, or nephrotic syndrome).

The most frequently reported adverse effects were agitation or excitation (59 times, 43.4%) and sleep disturbances (25 times, 18.4%) (2).

The steroid was administered orally in 72 cases (69.9%), intravenously in 13 cases (12.6%) and by inhalation in 10 cases (11.7%).

In 75% of cases the reaction occurred during the first week of treatment. Most patients recovered after steroid withdrawal.

These cases serve as a reminder to use the minimum effective dose of corticosteroids, even when inhaled.

Selected references from Prescrire's literature search.

1- Prescrire Rédaction "18-1-5 Patients sous corticoïde" *Rev Prescrire* 2007; **27** (290 Interactions supplement).

2- Montastruc-Fournier J et al. "Psychiatric adverse drug reactions to glucocorticoids in children and adolescents: an analysis of the French pharmacovigilance database" 29th pharmacovigilance meeting, Clermont-Ferrand: 9-11 April 2008. *Fundamental Clin Pharmacol* 2008; **22** (suppl 1): 75 (abstract 364).

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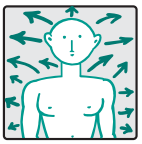

Translated from ***Rev Prescrire*** **December 2008; 28 (302): 907**

Sitagliptin: serious allergies

● **Risks greater than benefits.**

In October 2008, at the express request of *Prescrire*, the European Medicines Agency (EMEA) released a review of the allergic adverse effects of *sitagliptin*, a blood glucose-lowering agent indicated in type 2 diabetes (1,2).

The EMEA had been notified of hypersensitivity reactions that included anaphylaxis, angioedema and skin reactions, occurring during the first 3 months of *sitagliptin* therapy. Some cases occurred after the first dose.

There were 8 reports of skin reactions, 6 of which were serious. They included 3 cases of Stevens-Johnson syndrome, "exfoliative rashes" and one case of erythema multiforme.

Exposing patients to these risks is not justified, given the very limited efficacy of *sitagliptin*. It is better to use established oral antidiabetics such as *metformin* and *glibenclamide* (2).

Selected references from Prescrire's literature search.

1- European Medicines Agency "CHMP variation assessment report - Januvia°" 24 January 2008 + letter to Prescrire 6 October 2008: 3 pages.

2- Prescrire Editorial Staff "Sitagliptin" *Prescrire Int* 2008; **17** (93): 12-15.