

Nifuroxazide: serious immunoallergic reactions



At the beginning of 2017, the French regulatory agency (ANSM) published the results of a pharmacovigilance survey about *nifuroxazide* (1). This is a nitrofurantoin, closely related to *nitrofurantoin*. *Nifuroxazide* is used as an intestinal "anti-infective" agent in cases of diarrhoea, although its efficacy has not been demonstrated. It has been marketed in France since 1964 (1,2).

The pharmacovigilance survey covered all the data in the French pharmacovigilance database from the time of its initial marketing up to March 2016, as well as reports sent to the companies (1).

645 reports of adverse effects were analysed, of which 288 were serious. Among the 97 serious immunoallergic reactions, there were 16 cases of anaphylactic shock and 41 of angioedema. Among the 61 serious cutaneous adverse effects, there were 27 cases of severe drug-induced skin reaction for which *nifuroxazide* was the only suspect drug, including 2 cases of acute generalised exanthematous pustulosis and one case of toxic epidermal necrolysis (1).

The other serious adverse effects were haematological disorders (42 cases) including agranulocytosis, thrombocytopenia and haemolytic anaemia, liver damage (24 cases), neurological disorders (17 cases), gastrointestinal disorders (14 cases) and renal disorders (9 cases), and one case of diffuse interstitial lung disease (1).

A risk of cross-reactions with *nitrofurantoin* is not excluded (1).

In practice *Nifuroxazide* has been available in France for more than 50 years. Products based on *nifuroxazide* have no longer been reimbursed by France's national health insurance system since 2008, because its benefit was considered "insufficient" by the French National Health Authority (HAS). Some brands continue to be available without prescription (1,3). It is unacceptable to leave patients exposed to severe immunoallergic disorders and other adverse effects from a drug used to treat non-serious conditions and without proven efficacy. Patients should be advised against taking *nifuroxazide*, and the drug should be withdrawn from the market.

©Prescrire

► Translated from *Rev Prescrire* June 2017
Volume 37 N° 404 • Page 426

1-ANSM "Réunion du comité technique de pharmacovigilance. Compte rendu de la séance du 11 octobre 2016. Enquête profil général de sécurité des spécialités à base de nifuroxazide" 21 October 2016: 20 pages.

2- Prescrire Editorial Staff "Nifuroxazide in acute diarrhoea: irrational" *Prescrire Int* 1999; **8** (44): 170-172.

3- Prescrire Rédaction "Déremboursement post-réévaluation: encore des simagrées" *Rev Prescrire* 2007; **27** (281): 181.

Levothyroxine: panic attacks



In mid-2017, the Uppsala Pharmacovigilance Centre analysed 187 reports of panic attacks attributed to *levothyroxine*, recorded in the pharmacovigilance database of the World Health Organization (WHO). In several of these cases, the disorders stopped after dose reduction or temporary discontinuation of *levothyroxine* by the patient. These problems recurred in several patients after reintroduction of *levothyroxine* (1).

Levothyroxine is a thyroid hormone with a narrow therapeutic range. Signs of overdose can develop even with very slight increases in plasma concentration (2). They consist principally of palpitations, nervousness, tremors, hyperactivity, increased sweating and insomnia. These symptoms are similar to manifestations of anxiety. The onset of these symptoms seems, in some predisposed patients, to trigger a panic attack, with an intense feeling of discomfort, anxiety and fear together with symptoms such as chest pain, dizziness and palpitations (1).

In several reports, the involvement of *levothyroxine* was not recognised, resulting in a long-term impairment of the patient's quality of life. In some

cases, the patient stopped taking *levothyroxine* against medical advice, and the problems were alleviated. Sometimes the plasma concentrations of *levothyroxine* were within the target range (1).

Panic attacks are not mentioned in the Summary of Product Characteristics (SPC) of brands of *levothyroxine* marketed in France (3).

In practice Patients should be made aware of these adverse effects so that they can make the connection between experiencing these problems and taking *levothyroxine*. Careful titration of the dose is essential, and given its long half-life, a time interval of 6 to 12 weeks should be allowed after each dose adjustment.

©Prescrire

► Translated from *Rev Prescrire* June 2017
Volume 37 N° 404 • Page 426

1- Norén GN and Grundmark B "Panic attacks with levothyroxine" *WHO Pharmaceuticals Newsletter* 2017; **2**: 23-25.

2- Prescrire Rédaction "4-2. Patients hypothyroïdiens" *Rev Prescrire* 2017; **37** (401 suppl. Interactions médicamenteuses).

3- ANSM "RCP-Levothyrox" 27 septembre 2016: 5 pages.