Naming, labelling and packaging of medicines put patients at risk

Findings from Prescribe
Assessing therapeutic advance

Providing healthcare professionals with the information they need about drugs and therapeutic strategies

- efficacy
- adverse reactions
- convenience
  - safety
  - usability
  of packaging, labelling (leaflet and associated devices included)
Systematic analysis by Prescrire’s Packaging Working Group

- Every item of the packaging is examined in detail using a standardised form.
- When the drug is part of an umbrella range, we compare its appearance with the other products in the range.
- We check the labelling for the legibility and position of key information (INN, dose strength, storage, etc.).
- We test whether tablets are easily divisible.
- We prepare formulations that require reconstitution.
- We test the quality of blister pack films and bottle caps, especially for dangerous drugs.
- We try out dosing devices, referring to the patient leaflet.
- We check whether oral delivery syringes could be attached to an injection needle.
- We analyse the usability and safety of the information provided, especially in the patient leaflet, including symbols, pictograms and dosing schedules.
The Prescrire Packaging Awards

Prescrire analyses the packaging of about 150 drugs every year, and has examined over 5000 products in the past 30 years.

The Packaging Awards focus on the quality of packaging for drugs evaluated during the previous year in the New Products section of our French edition

- Packaging Awards
- Yellow cards
- Red cards
Packaging, labelling and naming issues beyond "New products" and changes

- Medication errors reported to Prescrire Programme Éviter l’Évitable (Preventing the Preventable)
- In-depth analysis of types of errors or packaging problems
- Prescrire’ responses to public consultations (European Commission, European and national medicines agencies, others)
Oral methotrexate

Weekly oral methotrexate therapy: raise awareness of fatal dosing errors

France’s decision to remove all sentences referring to fractionation of the weekly dose from the summaries of product characteristics (SPCs) for products based on oral methotrexate does not go far enough: the packaging must also be improved. Methotrexate dosing errors can be fatal.

Methotrexate, a cytotoxic agent, is used as an anticancer drug and also as an immunosuppressant, at low weekly doses, for severe forms of rheumatoid arthritis and psoriasis (1,2). Methotrexate overdose can cause severe and even life-threatening disorders, including mouth ulceration as well as haematological, hepatic, renal, gastrointestinal, cutaneous and pulmonary disorders (1).

In early 2013, three brands of oral methotrexate were available in France: Methotrexate Bellion® tablets (2.5 mg) and Novatrex® tablets (2.5 mg) (3).

The use of bulk bottles without a safety cap creates a risk that children may accidentally ingest massive amounts of methotrexate, with fatal consequences (2).

The weekly dosing schedule of oral methotrexate is unusual (2), and a common cause of oral methotrexate overdose is daily ingestion of entire weekly doses. Deaths are regularly reported (see inset, right) (4).

SPCs: a single weekly dose. In 2011, in an attempt to prevent overdose due to dosing errors, the marketing authorisation committee of the French health products agency (ANSM, formerly Afsaps) recommended that the SPCs of products based on oral methotrexate should no longer mention the possibility of splitting the weekly dose for patients who do not tolerate the single weekly dose (5).

In early 2013 the SPCs and patient leaflets of Methotrexate Bellion® and Novatrex®, but not those of Inmeth®, were modified accordingly (4)(5,6).

The phrase (our translation) “take the prescribed dose only once a week” now appears on the boxes and bottles of all three brands but is not always easy to read, especially on the bottles of Methotrexate Bellion®.

ADVERSE EFFECTS

In practice, splitting the weekly dose of oral methotrexate may be useful for some patients who do not tolerate the single weekly dose (5). However, simply removing sentences mentioning this possibility from the SPCs does not eliminate the risk of error: it would be better to provide specific information on how to split the weekly dose, along with packaging appropriate for once-weekly dosing. In addition, patients, family members and caregivers must be properly alerted to this danger.

Healthcare professionals must take care when writing prescriptions and when adding written information to the packaging; they must also take time to inform patients, family members and caregivers of the risk (7). These warnings must be repeated until the severity of methotrexate dosing errors is fully grasped.

PREVENTING THE PREVENTABLE

Fatal methotrexate overdose

A 90-year-old man was admitted to hospital, via a busy emergency unit, for a fracture. He was dependent and had difficulty expressing himself (1).

Consulted a few days later for a suspected infection of the surgical wound, a doctor, on examining his ongoing treatments and laboratory results (showing neutropenia), realised that the patient had received a methotrexate overdose due to daily administration of the weekly dose.

A junior doctor, on reading a prescription for Novatrex® 2.5 mg 6 tablet (once/week), entered Novatrex® 2.5 mg 2 tab morning; midnight; evening into the ward’s prescribing software. The dosing error was not detected on the patient’s transfer to a surgical ward, or when his drug regimen was analysed.

The methotrexate thus administered had not been dispensed by the hospital pharmacy but had been brought along by the patient himself. The nursing staff had administered methotrexate from the patient’s box, but had failed to notice the warning printed on the box and the patient leaflet (our translation): “Do not take this drug every day.” Thus, instead of 15 mg once a week, the patient had received a total of about 50 mg of methotrexate over 5 days.

Despite methotrexate withdrawal and folic acid and folic acid administration, the patient died 5 days after the error was first detected (1).
Inaccurate dosing devices


Gare aux graduations. Les mises en garde des dispositifs dosiers sont variées, et sont à l’origine par patient. Elles font prendre de vue la quantité réelle administrée (9).

Les mentions figurant sur les dispositifs dosiers (gradation, dénomination, concentration) sont parfois difficiles lisible (1,2,7,10).

Confusions entre dispositifs. Les

Prescrire Case study
10/10/2013
Prescrire calls for patient safety

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Abstract

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