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Boceprevir: serious haematological disorders

● **Monitoring blood cell counts is essential.**

In November 2013, the French Health Products Agency analysed the pharmacovigilance data collected as part of the national monitoring of *boceprevir* and *telaprevir*, used in combination with either *peginterferon alfa* or *ribavirin* to treat hepatitis C (1,2).

Data acquired during the first year of monitoring of *boceprevir* included nearly 150 reports of serious adverse effects and about 100 reports of non-serious adverse effects. The most frequent were blood cell line disorders: anaemia, neutropenia or thrombocytopenia, as well as 2 cases of agranulocytosis and 3 cases of pancytopenia (1). Infections, including 4 cases of septic shock (3 of which were fatal), and a brain haemorrhage in a patient with thrombocytopenia were also identified. The other adverse effects were: asthenia, gastrointestinal disorders (nausea, vomiting, diarrhoea), psychological disorders, dysgeusia, and skin disorders including 2 cases of DRESS (drug reaction with eosinophilia and systemic symptoms). Fourteen deaths were reported during the first year of monitoring: due to cardiac arrest, septic complications or brain haemorrhage. Adverse effects reported during the second year of monitoring were generally similar.

The first year of monitoring of *telaprevir* provided little new information (1). Serious adverse effects mainly included skin disorders, blood cell line disorders (anaemia, neutropenia and thrombocytopenia), gastrointestinal disorders including cases of pancreatitis (one patient died of necrotising pancreatitis) and hepatobiliary disorders, renal failure and hyperuricaemia.

In practice, the haematological adverse effects of the antiviral drugs used to treat hepatitis C expose patients to the risk of serious complications, especially with *boceprevir*, hence the importance of monitoring patients' blood cell counts and considering other treatment options if they drop too low. It is also important to bear in mind the serious cutaneous adverse effects of *telaprevir*.

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Selected references from Prescrire's literature search.
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Colchicine: more deaths

● **Advanced age and renal failure are risk factors.**

Colchicine is a cytotoxic drug used for symptom relief of gout attacks. It acts by attenuating the inflammatory response. Diarrhoea is a known adverse effect and the first symptom of *colchicine* overdose (1).

In 2014 the French Health Products Agency provided access to pharmacovigilance data on *colchicine* collected between January 2012 and May 2013 (2). 213 cases were analysed.

18 deaths occurred during this 17-month period, of which 14 were considered to be linked to *colchicine*. Advanced age and chronic renal failure were the main risk factors.

25 of the patients were receiving another drug known to interact with *colchicine*, mainly by inhibiting cytochrome P450 isoenzyme 3A4 or P-glycoprotein. Two patients who died were also receiving a macrolide.

Diarrhoea was reported in 88 cases, 6 of which were fatal. Severe diarrhoea occurred within 5 days after the beginning of *colchicine* treatment in about half these cases. *Colchicine* was withdrawn on the first day of severe diarrhoea in less than half the cases.

Colchicine has a narrow therapeutic index and potentially life-threatening adverse effects.

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Fluorouracil: dosing errors with infusion pumps

● **Prevention includes double-checking.**

In December 2013, the French Health Products Agency analysed 18 reports of errors related to the administration of the cytotoxic drug *fluorouracil* via an infusion pump or a portable elastomeric infusion pump. Eight of these errors resulted in a serious adverse effect. One patient died. The 10 other cases did not provoke adverse effects. An antidote was used in 8 cases (1). The types of errors reported were: incorrect programming of a pump (8 cases), incorrect preparation of an elastomeric infusion pump by the pharmacy (8 cases), wrong-patient error (1 case), and administration of 2 infusion bags of *fluorouracil* on the same day (1 case).

Fluorouracil overdose can provoke: gastrointestinal disorders including anorexia, severe mucositis, diarrhoea, nausea and vomiting, gastrointestinal bleeding; bone marrow suppression, sometimes delayed, occurring about 9 to 14 days after the overdose; neurological disorders, such as encephalopathy, neuropathy or ataxia; and cardiogenic shock (1).

Fluorouracil exposes patients to serious, sometimes fatal, dose-dependent adverse effects.

In practice, one of the measures required to prevent dosing errors when using infusion pumps is to follow a procedure that includes truly independent double checks to ensure that the correct dose is administered (2). It is also important that healthcare professionals who administer this treatment are aware of the signs of overdose, so that they can intervene rapidly if an administration error occurs.

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