Translated from ***Rev Prescrire*** **May 2013; 33 (355): 340**

ferumoxytol

NEW DRUG

An intravenous iron, riskier than iron sucrose

● **Pharmacovigilance data and the results of a clinical trial show that serious adverse events are more frequent with *ferumoxytol* than with *iron sucrose*.**

NOT ACCEPTABLE

In patients with chronic renal failure, *iron sucrose* is the standard treatment for iron-deficiency anaemia when the intravenous route is preferable to the oral route (1-3). IV *iron polymaltose* has no clinical advantages, and IV *iron dextran* carries too high a risk of severe hypersensitivity reactions.

Ferumoxytol (Rienso° Takeda), another intravenous iron product, has been authorised for use in this setting. It is a colloidal complex of iron and sugar dextran, also known as polyglucose sorbitol carboxymethylether (3). Does it have any advantages over IV *iron sucrose*?

A trial versus IV iron sucrose. According to reports issued by the European and US drug regulatory agencies, clinical evaluation of IV *ferumoxytol* is based on three randomised, unblinded trials versus oral iron in 837 patients with chronic renal failure, not all of whom were on haemodialysis (3,4).

A randomised, unblinded trial comparing IV *ferumoxytol* with IV *iron sucrose* in 605 patients in whom oral iron had failed showed no difference between the groups in terms of the increase in haemoglobin during the 5 weeks of treatment (5).

More serious adverse effects. In the three trials versus oral iron, the adverse effect profile of IV *ferumoxytol* was similar to that of other IV iron products, and included cutaneous disorders, gastro-intestinal disorders, fever, muscle and joint pain, and hypersensitivity reactions (**a**)(3,4).

In the unblinded trial versus IV *iron sucrose*, adverse effects were similarly frequent with the 2 products, but severe adverse effects occurred in 4.2% of patients treated with *ferumoxytol* versus 2.5% of those receiving *iron sucrose* (5).

A US pharmacovigilance review of different IV iron products examined adverse effects reported between October 2009 and June 2010 (6). The frequency of fatal, severe or serious adverse reactions per million units sold was significantly higher with *ferumoxytol* than with *iron sucrose* and with another *iron dextran* product.

Pregnancy. Animal studies of *ferumoxytol* have shown reproductive toxicity; this drug should therefore be avoided during pregnancy (7).

Convenience. *Iron sucrose* is infused slowly, after dilution, while *ferumoxytol* is injected rapidly, without dilution. In dialysis patients, *ferumoxytol* is injected directly into the dialysis line, as is *iron sucrose*.

In practice: do not use. In patients requiring intravenous iron administration, there is no firm evidence that *ferumoxytol* is more effective than *iron sucrose*, while it appears to have more serious adverse effects. It is better to avoid using *ferumoxytol* and to choose *iron sucrose* instead.

a- Ferumoxytol has paramagnetic properties that may affect the diagnostic performance of magnetic resonance imaging (ref 7).

Selected references from Prescrire's literature search.

Despite our request for information, Takeda provided us with no documentation on its product.

1- Prescrire Rédaction "SMR "insuffisant" du fer dextran: à quand son retrait du marché?" *Rev Prescrire* 2012; **32** (349): 819.
2- Prescrire Rédaction "fer polymaltose intraveineux-Ferinject°. 3e fer intraveineux: prudence" *Rev Prescrire* 2011; **31** (328): 97 + (329): Inside front cover.
3- EMA - CHMP "Assessment report-Rienso. EMEA/H/C/2215" 19 April 2012: 79 pages.
4- US FDA - CDER "Application number 22-180. Medical review(s)-ferumoxytol" 17 December 2008: 121 pages.
5- Hetzel D et al. "Potential new treatment option for iron deficiency anemia patients with a history of unsatisfactory oral iron therapy-results of a phase III, randomized, open-label, active-controlled trial of ferumoxytol" *Blood* 2012; **120** (21): abstract 2099.
6- Bailie GR "Comparison of rates of reported adverse events associated with i.v. iron products in the United States" *Am J Health Syst Pharm* 2012; **69** (4): 310-320.
7- European Commission "SPC-Rienso" 29 October 2012: 14 pages.

ferumoxytol

RIENSO°

Solution for IV injection

- **510 mg** of iron *(ferumoxytol)* per 17-ml vial (30 mg/ml)

antianaemic

■ **Indication:** *"(..) iron deficiency anaemia in adult patients with chronic kidney disease (…)".*
[EU marketing authorisation, centralised procedure]