

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 fre-

quency 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.

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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°, 3° 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- Baitie 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.

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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]