DRUG ALERT

Eprex (recombinant human erythropoietin alfa) and pure red cell aplasia — recommendations for administration to patients with CRF

Janssen-Cilag has revised the prescribing information in the package insert for Eprex (recombinant human erythropoietin alfa) to include the following statements:

'In patients with chronic renal failure, Eprex should only be administered by the intravenous route',

and

'If PRCA is diagnosed, therapy with Eprex must be immediately discontinued and testing for erythropoietin antibodies should be considered. Patients should not be switched to another product as anti-erythopoietin antibodies cross-react with other erythropoietins. Other causes of PRCA should be excluded and appropriate therapy instituted.'

Changes to the prescribing information for Eprex have been made as a result of investigations into cases of pure red cell aplasia (PRCA), erythroblastopenia) associated with the use of erythropoietin. In patients with chronic renal failure Eprex should only be administered by the intravenous route.

International statistics

Cases of antibody-positive PRCA have been reported from post-marketing experience in patients with chronic renal failure (CRF). As of 30 September 2002, the company had received 155 reports of PRCA confirmed by bone marrow biopsy worldwide. All cases were limited to patients with chronic renal failure. Of these cases 112 tested positive for the presence of antierythropoietin antibodies, and in the remaining 43 cases, the antibody status was unknown. All patients with antierythropoietin antibodies had received Eprex via the subcutaneous route of administration, where the route of administration was known. Lack of efficacy was first noted between 4 and 24 months after the start of treatment with Eprex, in those patients who tested positive for antierythropoietin antibodies. In addition, there has been a report of PRCA in a patient who received repeated doses of Eprex subcutaneously for refractory anaemia in an unlicensed indication.

Of the total number of cases reported to date, there has been a subset of antibody-mediated PRCA cases (17/112) in patients exposed to other erythropoietin products in conjunction with Eprex. Janssen-Cilag has embarked on an extensive epidemiological study as part of the clinical programme to monitor and evaluate the occurrence of antibody-mediated PRCA associated with epoetinums in patients with chronic renal failure.

National statistics

The National Adverse Drug Event Monitoring Centre of the Medicines Control Council has 5 reports of lack of efficacy associated with the use of Eprex. All the patients had CRF and were being treated with subcutaneous Eprex. The details are set out below.

Patient	Bone marrow aspirate	Anti-erythropoietin antibodies	Outcome
1	Positive	Positive	Died due to disease progression
2	Positive	Negative	Unknown
3	Not done	Not done	Recovered from septicaemia
4	Not done	Not done	Unknown — awaiting feedback from reporter
5	Positive	Positive	Unknown

Recommendation

It is recommended that clinicians review the management of patients with chronic renal failure being treated with Eprex. Eprex administration may be continued in these patients, but only via the intravenous route. When changing from subcutaneous to intravenous administration, the same dose of Eprex should be used and the haemoglobin monitored carefully (e.g. weekly) so that appropriate changes to the dose can be made to keep the haemoglobin within the target range.

National Adverse Drug Event Monitoring Centre
Medicines Control Council

1. ADRI database, National Adverse Drug Event Monitoring Centre, Medicines Control Council.
2. Eprex package insert.