European Medicines Agency
Post-authorisation Evaluation of Medicines for Human Use

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Public Statement
European Medicines Agency starts review of the safety of epoetins

The European Medicines Agency is reviewing the safety of all centrally-authorised epoetins[1]. The safety review has been initiated because new data from both unpublished and published studies suggest an increased risk of serious cardiovascular complications in patients with chronic renal failure and a possible effect on tumour progression in cancer patients. Epoetins are used for the treatment of anaemia in patients with chronic renal failure and in patients with non-myeloid malignancies receiving chemotherapy.

The European Medicines Agency, its Committee for Medicinal Products for Human Use (CHMP) and its Pharmacovigilance Working Party (PhVWP), reviewed these products in May 2004, resulting in revised dosing recommendations concerning cancer patients undergoing chemotherapy. In addition, the product information for all epoetins, in all indications, was revised to include a harmonised warning on possible stimulating effects on tumour progression, and a summary of the available evidence on survival and tumour progression.

The new information that has led to the current safety review is derived from clinical trials, including some in which epoetins were used outside their approved indications or dosing recommendations. All of the data from the studies are currently being carefully analysed by the CHMP, to determine whether further updates of the product information are necessary.

Until all of the data have been fully reviewed, the Agency informs healthcare professionals that:

- epoetins should be used strictly in accordance with their approved Summaries of Product Characteristics, regarding the indications and dosing recommendations.
- there is evidence that, in the treatment of patients with chronic renal failure, aiming at a target haemoglobin concentration above 12 g/dl is associated with an increase in serious cardiovascular morbidity and all-cause mortality. The CHMP is currently holding further discussions with expert groups to consider whether tighter dosing instructions should be issued in this regard. In the meantime, physicians should exercise caution when considering raising haemoglobin concentrations above 12 g/dl.
- there is some evidence that epoetins may be associated with increased morbidity and mortality when used in patients with solid tumours or lymphoproliferative malignancies[2] not receiving chemotherapy. Prescribers are reminded that epoetins are only authorised for the treatment of anaemia in patients with solid tumours or lymphoproliferative malignancies who are receiving chemotherapy and that they should not be used in cancer patients who are not receiving chemotherapy. Patients should be monitored closely to ensure that the lowest dose of epoetin is used to provide adequate control of the symptoms of anaemia.

[1] Centrally-authorised epoetins in the European Union/European Economic Area are Aranesp/Nespo, Dynepo and NeoRecormon. Eprex is authorised through the mutual recognition procedure; the Reference Member State of Eprex is responsible for the safety review, which is also currently ongoing, and works in close collaboration with the EMEA.

[2] Corr – “lymphoproliferative malignancies” has been added

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 74 18 84 09
E-mail: mail@emea.europa.eu http://www.emea.europa.eu

For further information, please contact:

Dr Panos Tsintis
Head of Sector
Pharmacovigilance and Post-Authorisation Safety and Efficacy of Medicines