DIVERGENT POSITION EXPRESSED BY CHMP MEMBERS

The safety database submitted in the marketing authorization application for Rienso (ferumoxytol) consists of a total of 1,726 subjects enrolled into 11 completed studies. Of those, 1,562 subjects received Rienso in case of chronic kidney disease (CKD). The primary safety information in support of ferumoxytol in CKD population comes from 3 pivotal studies with similar study design, which included 665 subjects treated with ferumoxytol.

Post marketing data derived from a survey on 3 US studies including > 8,500 patients with > 33,000 exposures to ferumoxytol has been submitted to further support the safety data. These data showed the overall rate of serious adverse events (SAEs) to be 0.2% in the post marketing survey compared with an overall rate of SAEs of 7.1% and related SAE rate of 0.2% in the pivotal studies.

Moreover, a recently published analysis reported AEs with different i.v. iron products in the US (Bailie GR. *American Journal of Health-System Pharmacy*; 2012 69(4):310-320). Iron sucrose and sodium ferric gluconate were associated with much lower rates of AEs per million units sold than iron dextran or ferumoxytol, for all reported AE classifications (ie, deaths, serious AEs, other major AEs, and other AEs). The huge difference (by roughly factors 10-100) in risk for hypersensitivity may be at least in part explained by a reporting period close to first availability of ferumoxytol on the US market. Nevertheless, this adds uncertainty to any conclusion from the limited available safety database.

There is no unmet medical need that would justify making ferumoxytol available to patients in the claimed indication despite this uncertainty around its risks. The benefit:risk ratio is thus considered negative for the time being.

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