

Submitted by:

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NCCN Guidelines Panel: Supportive Care-Cancer and Chemotherapy Induced Anemia

On behalf of AMAG Pharmaceuticals, I respectfully request the NCCN (Supportive Care-Cancer and Chemotherapy Induced Anemia) panel to review the enclosed data for inclusion of Feraheme (Ferumoxytol injection) on the list of parenteral iron preparations studied in patients with cancer.

Specific Changes:

- 1) Recommend inclusion of Feraheme onto the list
- 2) Update the statement in footnote b (if it were to remain since the other IV irons do not list indications) to reflect the expansion of the approved indication to “treatment of iron deficiency anemia in adults who have intolerance to oral iron or have had unsatisfactory response to oral iron”, i.e., due to any etiology, no longer solely due to chronic kidney disease

FDA clearance: as noted in #2 above, as of February 2018 indication has been expanded

Rationale:

In response to a request from the FDA for additional data, AMAG conducted a large and rigorous double-blinded RCT vs. ferric carboxymaltose focused on serious safety events-chieflly hypersensitivity reactions, including anaphylaxis and hypotension. Based on these data strongly demonstrating the comparability of such (Adkinson et al), coupled with the data from 2 additional RCTs in such patients with IDA of any etiology vs placebo (Vadhan-Raj AJH) and vs iron sucrose (Hetzl et al AJH), the above noted expansion of the label to include adults with IDA of any etiology who were intolerant of or inadequately responsive to oral iron was granted.

Additionally, an analysis of patients with a diagnosis of cancer who participated in either the placebo-controlled or study vs iron sucrose for the treatment of IDA was conducted and published (Vadhan-Raj J of Blood Management) to examine whether the efficacy and safety observed in the subgroup with cancer differed from the overall study population. This analysis confirmed that the safety and efficacy were comparable. Patients receiving Feraheme experienced a robust 1.8g/dL increase in hemoglobin by week 5. Not unexpectedly this was less than observed in the overall population (2.7g/dL), which similarly was noted in those who received iron sucrose. There was similarly a marked improvement in patient reported outcomes such as FACIT-Fatigue. Safety was similarly comparable in the cancer subgroup.

The following articles are submitted in support of this proposed change. Copies of which are included.

- 1) Adkinson NF, Strauss W, Macdougall IC, Bernard K, Auerbach M Kaper RF, Churtow GM, Krop J. Comparative safety of intravenous ferumoxytol versus ferric carboxymaltose in iron deficiency anemia: A randomized trial. Am J Hematol. 2018;1–8 (on line open access)

- 2) Vadhan-Raj S, Strauss W, Ford D, Bernard K, Bochia R, Li Z, Allen L. Efficacy and safety of IV ferumoxytol for adults with iron deficiency anemia previously unresponsive to or unable to tolerate oral iron. *Am. J. Hematol.* 2014;89:7-12
- 3) Hetzel D, Strauss W, Bernard K, Li Z, Urboniene A, Allen L. A phase III, randomized, open-label trial of ferumoxytol compared with iron sucrose for the treatment of iron deficiency anemia in patients with a history of unsatisfactory oral iron therapy. *Am J. Hematol* 2014;89:646-650
- 4) Vadhan-Raj S, Dahl NV, Bernard K, Li Z, Strauss WE. Efficacy and safety of IV ferumoxytol for iron deficiency anemia in patients with cancer. *Journal of Blood Medicine* 2017;8 199–209

Sincerely,

William Strauss MD, FACC