Author's response to reviews

Title: Determination of Iron Sucrose (Venofer) or Iron Dextran (DexFerrum) removal by hemodialysis: An In-Vitro Study

Authors:

Dr Harold J Manley (manleyh@umkc.edu)
Dr Darren W Grabe (grabed@ACP.edu)

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PDF covering letter
Reply to 2nd Reviewer: D Schneditz

Title: Determination of Iron Sucrose (Venofer) or Iron Dextran (DexFerrum) removal by hemodialysis: An In-Vitro Study

Version: 2

Date: 26 November 2003

To: Emma Parkin, Editorial Administrator, BMC Journals

Ms. Parkin,

Thank you for your comments. Dr. Grabe and I have revised our manuscript to address your concerns. Below please find your specific comments and our reply (bulleted).

Please contact me if you have any other concerns.

Kind regards,

Harold J. Manley, Pharm.D., BCPS
Assistant Professor

1) Page 4, line 7 from bottom: The reason for the high molecular weight of Venofer® remains unclear. Neither iron hydroxide nor sucrose have a high molecular weight. Thus, some additional information on the composition of this substance explaining its low dialysability would be helpful:

Venofer is a complex of polynuclear iron (III)-hydroxide in sucrose for intravenous use. Iron sucrose is also known as iron saccharate and described as polynuclear iron (III) hydroxide sucrose complex. Iron sucrose has a molecular weight of approximately 34,000 – 60,000 Daltons and a proposed structural formula: [Na₂Fe₅O₈(OH)₃(H₂O)]ₙ*m(C₁₂H₂₂O₁₁).

In the attempt to find more information on Venofer the following information was found at this website:
http://www.rxlist.com/cgi/generic2/venofer_cp.htm

“Venofer® is not dialyzable through CA210 (Baxter) High Efficiency or Fresenius F80A High Flux dialysis membranes. In in vitro studies, the amount of iron sucrose in the dialysate fluid was below the levels of detection of the assay (less than 2 parts per million).”

Is this information based on the results of the study presented in this manuscript? Have the results of the study already been published?

- Page 4 paragraph 4 was added to address this issue. We have included recommended text as well as text from our comments to reviewer 1.
- Information provided at the website listed above is reflective of our report. American Regent, the sponsor of this report, submitted our results to the Food and Drug Administration. Additionally, an abstract of the data was published and presented at the most recent American Society of Nephrology meeting in San Diego, CA, USA. (Manley HJ, Grabe DW. Determination of Iron Sucrose (Venofer) or Iron Dextran (DexFerrum) removal by hemodialysis: An In-Vitro Study. J Amer Soc Nephrol 2003; 14: 498A (abstract SA-P0907)

- This data is NOT under consideration for publication at any other journal.

2) On page 8, line 7 from the bottom, please, replace the “100mg/mL/6000mL” by “100mg/6000mL”.

- Changed as suggested.

3) A point missed in the first review could be clarified (page 10, Tables 1 through 3). Clearance relating to removal of substance from the system is usually given as a positive value. The authors present removal as negative values and accumulation in the system as positive values. This may lead to confusion especially in the dialysis community and should be clarified (Tables 1, 2, and 3).

On page 10, Eq. 1, for clarification, add a note that removal from the tank is modeled as a negative rate constant Khd, whereas accumulation leads to a positive Khd, and that clearances will have corresponding signs.

- As suggested, statements on how to interpret the data presented (for both Clearance AND elimination rate) are added to the text (page 10 after Eq. #1 and page 11 after Eq. 3) and tables 1-3.