



NATIONAL PBM BULLETIN

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PHARMACY BENEFITS MANAGEMENT SERVICES (PBM), MEDICAL ADVISORY PANEL (MAP), AND CENTER FOR
MEDICATION SAFETY PSCI (VA MedSAFE)

Adverse Drug Events Reported with the High Molecular Weight Formulation of Iron Dextran

I. ISSUE

There are two formulations of intravenous iron dextran available for the management of patients with iron-deficiency anemia: low molecular weight (LMW) and high molecular weight (HMW). The following Bulletin focuses on the preferential use of the LMW formulation over the HMW product due to the increased risk for major adverse drug events (ADEs) with the HMW formulation.

II. BACKGROUND

Iron dextran is listed on the VA National Formulary (VANF) without specifying the LMW or HMW formulation; therefore, either iron dextran product could be selected to treat patients with iron-deficiency anemia. A review of pertinent medical literature, as well as reviews of two reports of death potentially related to the HMW formulation of iron dextran in the VA Adverse Event Reporting System (VA ADERS), prompted further discussion of the available intravenous iron preparations.

III. DISCUSSION

Product information for the available iron dextran formulations contain a boxed warning that use has resulted in anaphylactic-type reactions with deaths reported and to use only in those patients with a clear indication and where oral iron therapy is not appropriate or effective. It is also recommended to administer iron dextran only when resuscitation techniques and treatment of anaphylactic shock is readily available. The product information also states that a test dose should be given prior to initial administration of the iron dextran products. The other available intravenous iron formulations (iron sucrose and sodium ferric gluconate) do not carry a boxed warning and a test dose may be administered at the discretion of the clinician. Retrospective evaluations have reported an increased risk of ADEs with the HMW formulation of iron dextran compared to the LMW product. An evaluation of major ADEs reported to the FDA found a significant increase in risk of total and life-threatening ADEs with the HMW iron dextran compared to LMW iron dextran; although, there was not a significant difference in the reports of death. Additional comparison between the different intravenous iron products is shown in the table below.

Comparison (Odds Ratio) of Major Adverse Drug Events (ADE) Reported to the FDA (2001-2003) with IV Iron¹

ADE	HMW Iron Dextran vs. LMW Iron Dextran	Iron Sucrose vs. LMW Iron Dextran	Sodium Ferric Gluconate vs. LMW Iron Dextran	Iron Sucrose vs. Sodium Ferric Gluconate
Total	3.2 (2.7-3.8)	0.5 (0.4-0.6)	0.5 (0.4-0.6)	1.0 (0.8-1.2)
Life-threatening	3.4 (2.0-5.9)	0.2 (0.1-0.4)	0.3 (0.1-0.7)	0.6 (0.2-1.7)
Death	1.0 (0.2-4.6)	0.2 (0.1-1.0)	0.3 (0.1-1.3)	0.5 (0.1-3.2)

Reported deaths/ estimated doses: HMW iron dextran (2/2,563,000); LMW iron dextran (5/ 6,690,000); iron sucrose (1/ 8,837,000); Sodium Ferric Gluconate (3/11,973,800)

IV. PBM AND VA MEDSAFE RECOMMENDATIONS include:

- The VANF listing for iron dextran will now specify only the LMW formulation of iron dextran; two additional formulations of intravenous iron will also be available on the VANF (iron sucrose and sodium ferric gluconate)
- Due to the potential increased risk for major ADEs compared to the other available intravenous iron preparations, providers should evaluate their patients receiving the HMW iron dextran product and switch to an alternative form of intravenous iron as listed on the VANF (i.e., LMW iron dextran, iron sucrose, or sodium ferric gluconate)
- Please report any ADEs that occur with any intravenous iron product per local protocols at your VA

V. REFERENCES

1. Chertow GM, Mason PD, Vaage-Nilsen O, Ahlmen J. Update on adverse drug events associated with parenteral iron. *Nephrol Dial Transplant* 2006;21:378-82.
2. Fletes R, Lazarus JM, Gage J, Chertow GM. Suspected iron dextran-related adverse drug events in hemodialysis patients. *Am J Kidney Dis* 2001;37:743-9.
3. McCarthy JT, Regnier CE, Loebertmann CL, Bergstralh EJ. Adverse events in chronic hemodialysis patients receiving intravenous iron dextran – a comparison of two products. *Am J Nephrol* 2000;20:455-62.