

FDA strengthens warnings and changes prescribing instructions to decrease the risk of serious allergic reactions with anemia drug Feraheme (ferumoxytol)

Safety Announcement

[3-30-2015] The U.S. Food and Drug Administration (FDA) is strengthening an existing warning that serious, potentially fatal allergic reactions can occur with the anemia drug Feraheme (ferumoxytol). We have changed the prescribing instructions and approved a *Boxed Warning*, FDA's strongest type of warning, regarding these serious risks. Also added is a new *Contraindication*, a strong recommendation against use of Feraheme in patients who have had an allergic reaction to any intravenous (IV) iron replacement product. Health care professionals should follow the new recommendations in the drug label. Patients should immediately alert their health care professional or seek emergency care if they develop breathing problems, low blood pressure, lightheadedness, dizziness, swelling, a rash, or itching during or after Feraheme administration.

Feraheme is in a class of medicines called IV iron replacement products. It is used to treat iron-deficiency anemia—a condition in which there is a lower than normal number of oxygen-carrying red blood cells because of too little iron. People with anemia may feel tired or weak, and if left untreated, anemia can damage the heart, brain, and other organs. Feraheme is specifically approved for use only in adults with iron deficiency anemia in patients with chronic kidney disease. It is given as an IV infusion by health care professionals in a hospital, outpatient clinic, or medical office. Like other IV iron products, Feraheme may only be given where emergency personnel and equipment are immediately available to treat the potentially life-threatening allergic reactions that can occur with treatment.

All IV iron products carry a risk of potentially life-threatening allergic reactions. At the time of Feraheme's approval in 2009, this risk was described in the *Warnings and Precautions* section of the drug label. Since then, serious reactions, including deaths, have occurred despite the proper use of therapies to treat these reactions and emergency resuscitation measures (see Data Summary). We have evaluated this risk further and have identified ways to reduce the risk of serious allergic reactions with Feraheme.

Based on our evaluation, the prescribing instructions and other label information were updated, adding a *Boxed Warning* that describes these serious risks and recommending that health care professionals:

- Only administer IV iron products to patients who require IV iron therapy.

- Do not administer Feraheme to patients with a history of allergic reaction to Feraheme or other IV iron products.
- Only administer diluted Feraheme as an IV infusion over a minimum of 15 minutes. Feraheme should not be given as an undiluted IV injection.
- Closely monitor patients for signs and symptoms of serious allergic reactions, including monitoring blood pressure and pulse during Feraheme administration and for at least 30 minutes following each infusion.
- Carefully consider the potential risks and benefits of Feraheme administration in elderly patients with multiple or serious medical conditions, as these patients may experience more severe reactions.
- Carefully consider the potential risks and benefits of Feraheme administration in patients with a history of multiple drug allergies. Patients with multiple drug allergies may also be at higher risk.

We are continuing to monitor and evaluate the risk of serious allergic reactions with all IV iron products, and we will update the public as new information becomes available. We urge health care professionals and patients to report side effects involving Feraheme or other IV iron products to the FDA MedWatch program, using the information in the “Contact FDA” box at the bottom of the page.

Facts about Feraheme (ferumoxytol)

- Feraheme is a prescription medicine used to treat iron-deficiency anemia in adults with chronic kidney disease. Iron-deficiency anemia is a condition in which there is a lower than normal number of red blood cells because of too little iron.
- Feraheme is in a class of medicines called iron replacement products. It works by replenishing iron so that the body can make more red blood cells that carry oxygen throughout the body.
- Feraheme is given as an intravenous infusion by a health care professional in a hospital, outpatient clinic, or medical office.

Additional Information for Patients and Caregivers

- Serious allergic reactions, some of which resulted in death, have occurred in patients receiving Feraheme (ferumoxytol).
- Inform your health care professional if you have any drug allergies or a prior history of reactions to intravenous iron products before receiving Feraheme for the first time and before each dose of Feraheme.
- Immediately notify your health care professional or seek emergency care if you develop any of the following signs and symptoms during and after Feraheme administration:
 - Breathing problems
 - Low blood pressure
 - Dizziness or lightheadedness, which are symptoms of low blood pressure
 - Swelling

- Rash or itching
- Talk to your health care professional if you have any questions or concerns about Feraheme.
- Report side effects from Feraheme to the FDA MedWatch program, using the information in the "Contact FDA" box at the bottom of this page.

Additional Information for Health Care Professionals

- Fatal and serious hypersensitivity reactions including anaphylaxis have occurred in patients receiving Feraheme (ferumoxytol). Initial symptoms may include hypotension, syncope, unresponsiveness, and cardiac/cardiorespiratory arrest with or without signs of rash.
- All intravenous (IV) iron products carry a risk of anaphylaxis; therefore, these products should be administered only in patients who require IV iron therapy. Feraheme is only approved for use in adults with iron-deficiency anemia in the setting of chronic kidney disease.
- Feraheme is contraindicated in patients with a history of hypersensitivity to Feraheme or any other IV iron product.
- Only administer Feraheme and other IV iron products when personnel and therapies are immediately available for the treatment of anaphylaxis and other hypersensitivity reactions.
- Patients with a history of multiple drug allergies may have a greater risk of anaphylaxis with parenteral iron products. Carefully consider the potential risks and benefits before administering Feraheme to these patients.
- Feraheme should only be administered as an IV infusion in 50-200 mL of 0.9% sodium chloride or 5% dextrose over a minimum period of 15 minutes following dilution. Do not administer Feraheme by undiluted IV injection.
- Closely monitor patients for signs and symptoms of hypersensitivity reactions, including monitoring blood pressure and pulse during administration and for at least 30 minutes following each infusion of Feraheme.
- Elderly patients 65 years of age and older with multiple or serious comorbidities who experience hypersensitivity reactions or hypotension or both following administration of Feraheme may have more severe outcomes.
- Advise patients to immediately report any signs and symptoms of hypersensitivity that may develop during and following Feraheme administration, such as respiratory distress, hypotension, dizziness or lightheadedness, edema, rash, or itching. Advise patients to seek immediate medical attention if these signs and symptoms occur.
- Allow at least 30 minutes between administration of Feraheme and administration of other medications that could potentially cause serious hypersensitivity reactions or hypotension or both, such as chemotherapeutic agents or monoclonal antibodies.
- Report adverse events involving Feraheme to the FDA MedWatch program, using the information in the "Contact FDA" box at the bottom of this page.

Data Summary

In the initial clinical trials of Feraheme (ferumoxytol), conducted predominantly in patients with chronic kidney disease, serious hypersensitivity reactions were reported in 0.2 percent (3/1,726) of patients receiving Feraheme. Other adverse reactions potentially associated with hypersensitivity (e.g., pruritus, rash, urticaria or wheezing) were reported in 3.7 percent (63/1,726) of these patients. In other trials that did not include patients with chronic kidney disease, moderate to severe hypersensitivity reactions, including anaphylaxis, were reported in 2.6 percent (26/1,014) of patients treated with Feraheme.

Since the approval of Feraheme on June 30, 2009, cases of serious hypersensitivity reactions, including death, have occurred. A search of the FDA Adverse Event Reporting System database identified 79 cases of anaphylactic reactions associated with Feraheme administration, reported from the time of approval to June 30, 2014. Of the 79 cases, 18 were fatal, despite immediate medical intervention and emergency resuscitation attempts. The 79 patients ranged in age from 19 to 96 years. Nearly half of all cases reported that the anaphylactic reactions occurred with the first dose of Feraheme. Approximately 75 percent (60/79) of the cases reported that the reaction began during the infusion or within 5 minutes after administration completion. Frequently reported symptoms included cardiac arrest, hypotension, dyspnea, nausea, vomiting, and flushing. Of the 79 cases, 43 percent (34/79) of the patients had a medical history of drug allergy, and 24 percent had a history of multiple drug allergies.