Issue 3 • September 2025 • Managing ID in HF

PEER perspectives

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IV IRON IN FOCUS:

BRIDGING EVIDENCE TO PRACTICE FOR ID IN HF

INSIDE THIS ISSUE:

- Learn to differentiate iron deficiency (ID)/iron deficiency anemia (IDA), recognize symptoms in heart failure (HF) patients, and identify at-risk groups
- Understand inflammation's impact on oral iron and when IV iron is more effective
- Discover about dextran-free IV iron for flexible dosing and quick delivery in diverse clinical scenarios
- Gain insights on testing, treatment guidelines, and patient involvement in iron infusion decisions

Peer perspectives come from Ms. Vorgang and Dr. Beavers, who have been compensated by Daiichi Sankyo Inc.

Recognizing ID in Your Patients With HF

How does untreated ID in HF impact disease progression and symptom presentation in patients with HF?

CV. Most of the patients we see in our Advanced Practice Provider (APP) clinic present with New York Heart Association (NYHA) class II or III symptoms: they're fatigued and often discouraged because even climbing a flight of stairs feels impossible.[1,2] That's why we focus so much on improving their exercise capacity through comprehensive HF management. Early identification and treatment of ID is a key part of that.[3,4] Education is also essential: helping patients understand how iron repletion, when indicated, can support their overall physical capacity and, hopefully, allow them to experience life with fewer exercise restrictions.[5,6]

CB. Beyond the traditional mechanisms we associate with HF, we're now seeing how inflammation at the cellular level can interfere with iron regulation and delivery.[7,8] That's not just an abstract concept: it can have real effects on myocardial function.[9] If a patient with HF remains symptomatic or is being readmitted, I have to ask myself, "Are we missing ID?" That's why managing ID in HF is essential, as the condition itself can disrupt iron metabolism across multiple systems.[4,10,11]

What are the challenges in recognizing and diagnosing ID in HF, especially in those with comorbid complexity?

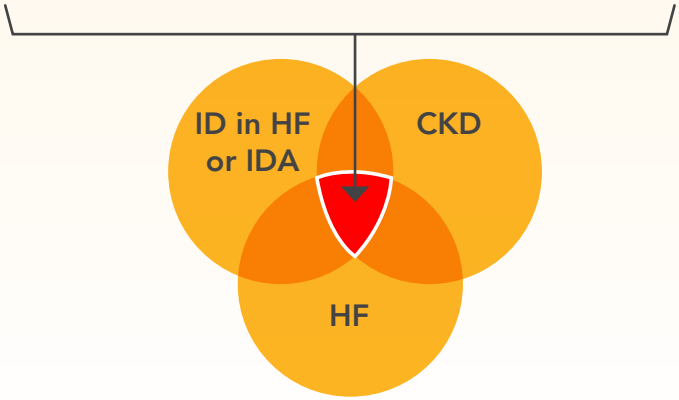
CV. We frequently see patients with HF who also have complex comorbidities like chronic kidney disease (CKD), diabetes, and obesity.[1,12,13] Managing HF in that context means working closely with other specialists to make sure those conditions are also under control. The HF–CKD connection is especially important[7,12]: we often describe it as a balancing act, where treatment decisions must account for how each condition influences the other.

CB. Managing a patient with HF is inherently complex, and comorbidities add significantly to that challenge. In our practice, we've made it a priority to build structured protocols that ensure consistency, especially when it comes to checking iron levels. Every clinician who interacts with HF patients should follow a defined pathway that outlines what needs to be assessed. We've also empowered our clinical pharmacists to screen for ID. If labs haven't been done, they can order them, and if ID is identified, they can flag it for the provider and recommend therapy. Ideally, all of this happens under a collaborative practice agreement, so that the process remains efficient.

Inflammatory conditions (such as CKD or HF) alter the body's iron sequestering methods.[7]

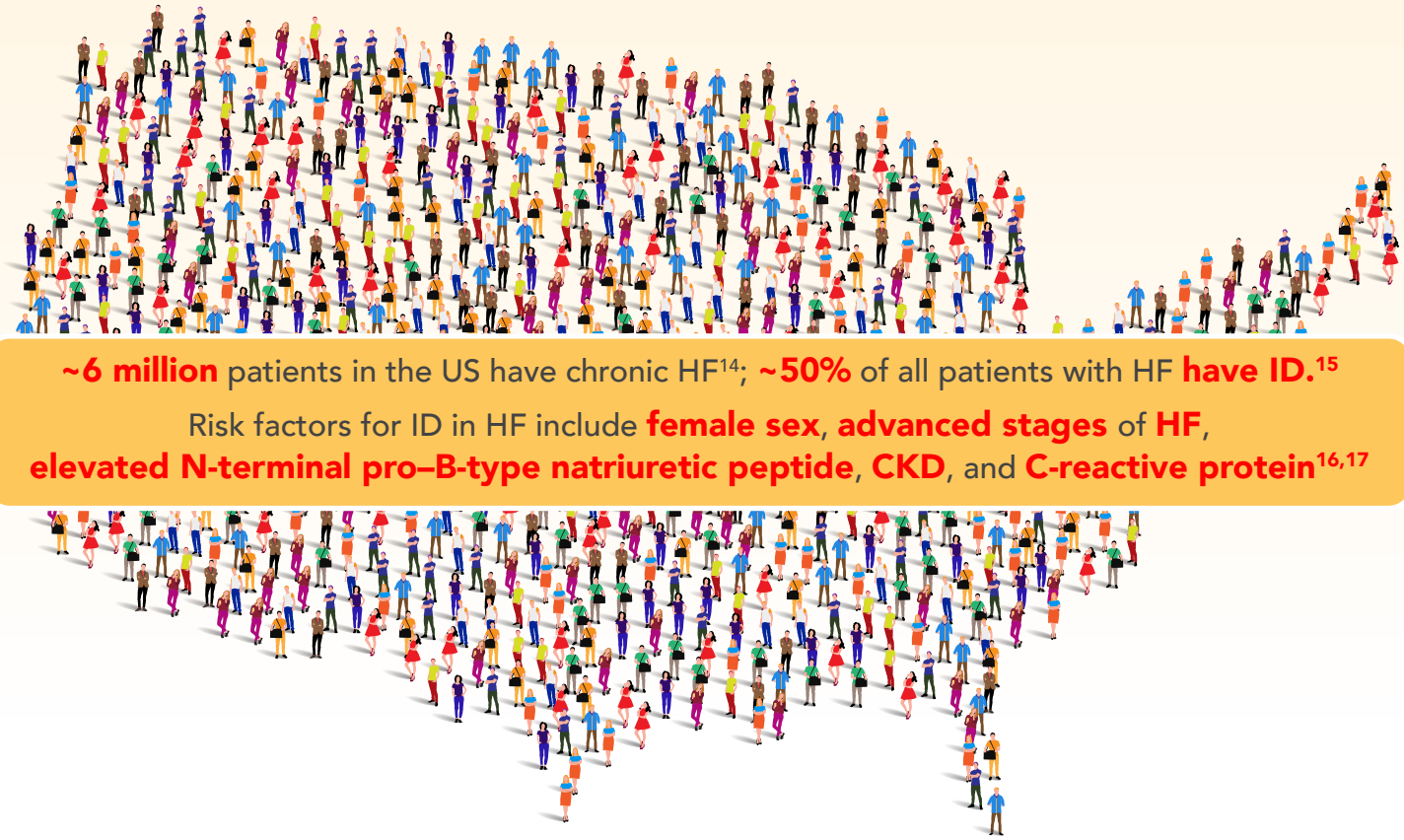
These conditions also modulate the relationship between iron stores and serologic markers, rendering conventional thresholds insensitive for detecting ID in HF and complicating clinical decision-making.[7]

The coexistence of CKD and HF with ID results in decreased exercise capacity.[12]



If a patient with HF remains symptomatic or is being readmitted, I have to ask myself, "Are we missing ID?"
– Dr. Craig Beavers, clinical pharmacist

Recognizing ID in Your Patients With HF (cont'd)



~6 million patients in the US have chronic HF[14]; **~50%** of all patients with HF **have ID.**[15]

Risk factors for ID in HF include **female sex**, **advanced stages** of **HF**, **elevated N-terminal pro–B-type natriuretic peptide**, **CKD**, and **C-reactive protein**[16,17]

What is the prevalence of ID in the patients with HF seen at your practice?

CV. I'd estimate that over half of our patients with HF have ID.[16,17] It's much more common than people realize. Patients often ask, "Am I like others with this condition?" And the answer is almost always, "Yes." ID is a consistent finding in our clinic population[15], which helps normalize the experience and opens the door to meaningful conversations about treatment.

CB. In our clinic, ID isn't an exception. It's quite common. We see it frequently in patients with HF, which makes recognizing its prevalence all the more important. When patients with HF consistently show diminished iron stores upon admission, it reinforces that addressing ID should be a routine, standard part of HF management for care teams in our institution.

> ***ID is a consistent finding in our clinic population, which helps normalize the experience and opens the door to meaningful conversations about treatment.***
> – Cassie Vorgang, nurse practitioner

Optimizing Diagnosis on ID in HF

How do you determine when to test iron levels in patients, particularly in those with nonspecific or overlooked symptoms?

CV. We updated the assessment and plan section of our APP notes to include prompts for iron follow-up, because we noticed it was often overlooked. Now, we aim to reassess iron levels every 3 to 6 months, particularly in patients reporting reduced exercise tolerance.[5,18] If ID is identified, we act on it. Not just to check a guideline box, but because treating it can make a real difference in how patients feel and function day-to-day.

CB. HF is a progressive condition, so it's essential to establish baseline iron labs early; ideally, at the first encounter if they haven't already been drawn.[3,19] Just because a patient isn't iron deficient today doesn't mean they won't be in the future. I always stress the importance of reassessing iron status every 3 to 6 months.[18] It might be the missing piece behind persistent symptoms, even in patients who appear optimized on other therapies.

We aim to reassess iron levels every 3 to 6 months, particularly in patients reporting fatigue or reduced exercise tolerance. If ID is identified, we act on it.
– Cassie Vorgang, nurse practitioner

How do clinical guidelines for ID in HF influence your approach to routine iron testing for early identification and improving functional capacity?

The American Heart Association (AHA)/American College of Cardiology (ACC)/Heart Failure Society of America (HFSA) Guideline[3] states iron tests to diagnose ID in HF are a Class 1 recommendation[3]:

Class 1 – recommendation (strong), benefit >>> risk
Routine baseline assessment of all patients with HF should include iron studies

ID in HF is usually defined as ferritin level <100 ng/mL or 100 ng/mL to 300 ng/mL, if the TSAT is <20%

CB. We continue to prioritize guideline-directed medical therapy (GDMT), and United States' guidelines emphasize the importance of iron testing.[3] That's something we can't afford to overlook, because improving how patients are managed keeps them engaged with their care. While we follow the 2022 AHA/ACC/HFSA Guideline closely, we've gone a step further by taking a more proactive approach to routine iron assessment.

CV. In our clinic, we follow the 2022 AHA/ACC/HFSA and related guidelines, which clearly recommend routine iron testing as a Class 1 recommendation for patients with HF.[3] It's a core part of our intake and ongoing monitoring process. If you're iron deficient, let's try to help improve your functional capacity.

While we follow the 2022 AHA/ACC/HFSA Guideline closely, we've gone a step further by taking a more proactive approach to routine iron assessment.
– Dr. Craig Beavers, clinical pharmacist

Optimizing Diagnosis on ID in HF (cont'd)

How does inflammation interfere with iron regulation in chronic conditions, such as HF and CKD, and how can this complicate treatment?

CB. Many HF patients have poor perfusion, including to the gastrointestinal (GI) tract, and when you combine that with inflammation and hepcidin dysregulation, oral iron just isn't absorbed effectively.[7,8,20,21] The data backs this up. Across multiple studies, oral iron consistently falls short of expectations in this population.[22,23,24]

CV. We rely a lot on patient-reported symptoms and use targeted labs to guide our next steps. Inflammation plays a big role, especially when HF is accompanied by chronic conditions like CKD, diabetes, or even untreated sleep apnea.[1,7] Managing these comorbidities is critical, because when left unaddressed, they fuel inflammation, complicate iron metabolism, and make it harder to reach our treatment goals.[5,7]

> ***Managing these comorbidities is critical, because when left unaddressed, they fuel inflammation, complicate iron metabolism, and make it harder to reach our treatment goals.***
> **– Cassie Vorgang, nurse practitioner**

How do you monitor iron levels in patients with chronic inflammatory conditions, given the potential for inflammation to mask lab values?

CV. We understand that inflammation can mask lab values[7], and we take that into account when evaluating patients with HF. It's part of the clinical landscape we manage every day. While we don't dive into the technical details with patients, it's one of many factors that guides our decision-making behind the scenes.

CB. Ferritin levels <100 ng/mL are a well-established threshold[3], but we have to remember that ferritin is an acute phase reactant, so it can be influenced by inflammation.[25] That's why transferrin saturation, or TSAT, has emerged as the more reliable marker.[25] Ultimately, iron assessment needs to be embedded into HF workflows, especially in heart failure with reduced ejection fraction (HFrEF). The guidelines are clear: it's something we must prioritize.[3]

ID in HF and IDA can be diagnosed by testing for 3 key indices[26,27]:

NORMAL LEVELS IN HEALTHY ADULT PATIENTS*	
Hb[28]	**M:** 13.5 g/dL-17.5 g/dL **F:** 12.0 g/dL-15.5 g/dL
Ferritin[29]	**M:** 40 ng/mL-300 ng/mL **F:** 20 ng/mL-200 ng/mL
TSAT[30]	**M:** 20%-50%† **F:** 20%-50%†

*Normal lab values may vary based on patient characteristics/comorbidities and by laboratory.

† Injectafer is not indicated to treat patients with CKD who are on dialysis or patients with anemia of chronic disease. For adult patients with CKD and anemia, guidelines issued by National Kidney Foundation (NKF) recommend IV iron for patients with a TSAT ≤30% and ferritin ≤500 ng/mL. Consult the NKF guidelines for a complete list of recommendations for lab values when starting treatment.[6]

FROM ORAL IRON TO IV: MAKING THE SWITCH

How do the limitations of oral iron inform your decision to transition patients to IV iron therapies like Injectafer? What factors guide that timing and choice?

CB. Oral iron comes with well-known adherence issues, such as unpleasant taste, GI side effects, and frequent dosing.[21,23] While it's inexpensive, it's not the most effective choice in HF.[21,22] There's still a gap in awareness, but within the ID in HF population, we have strong data supporting IV iron and far less for oral formulations.[22,31]

CV. Many patients come to us already on oral iron, so I make it a point to talk through its limitations, especially in HF. We discuss how reduced cardiac output limits gut absorption, making oral iron less effective.[7,8] I'll reference studies showing that even after months of oral therapy, iron stores often remain low.[32] We also review common side effects like black stools and constipation.[33] I frame it as: what can we do now to help you feel better? That short-term benefit tends to resonate with patients more than distant outcomes.

What considerations do you look for when assessing the suitability of Injectafer in the patients seen in your practice?

CV. Before starting IV iron, we always confirm the patient has an HF diagnosis. We also pay close attention to patient logistics. Our clinic serves a wide area across the DC metro region, and we have patients traveling from places like West Virginia or southern Maryland. For them, even one visit can be a real hurdle. That's why the higher dose of Injectafer is so helpful: it limits the number of infusions, which really matters for patients balancing long travel distances. It's also been very well tolerated.[6,34,35]

CB. One of the key advantages of Injectafer is its ability to deliver higher doses in fewer administrations. That makes it more convenient for both patients and facilities.[6,34,35] That improvement plays a big role in patient acceptance and overall comfort with the treatment.

"One of the key advantages of Injectafer is its ability to deliver higher doses in fewer administrations. That makes it more convenient for both patients and facilities. That improvement plays a big role in patient acceptance and overall comfort with the treatment."

– Dr. Craig Beavers, clinical pharmacist

SELECTED SAFETY INFORMATION

CONTRAINDICATIONS

Injectafer is contraindicated in patients with hypersensitivity to Injectafer or any of its inactive components.

WARNINGS AND PRECAUTIONS

Symptomatic Hypophosphatemia

Symptomatic hypophosphatemia with serious outcomes including osteomalacia and fractures requiring clinical intervention has been reported in patients treated with Injectafer in the post-marketing setting. These cases have occurred mostly after repeated exposure to Injectafer in patients with no reported history of renal impairment. However, symptomatic hypophosphatemia has been reported after one dose. Possible risk factors for hypophosphatemia include a history of gastrointestinal disorders associated with malabsorption of fat-soluble vitamins or phosphate, inflammatory bowel disease, concurrent or prior use of medications that affect proximal renal tubular function, hyperparathyroidism, vitamin D deficiency, malnutrition, and hereditary hemorrhagic telangiectasia (HHT or Osler-Weber-Rendu syndrome). In most cases, hypophosphatemia resolved within three months.

Correct pre-existing hypophosphatemia prior to initiating therapy with Injectafer. Monitor serum phosphate levels in patients at risk for chronic low serum phosphate. Check serum phosphate levels prior to a repeat course of treatment in patients at risk for low serum phosphate and in any patient who receives a second course of therapy within three months. Treat hypophosphatemia as medically indicated.

FROM ORAL IRON TO IV: MAKING THE SWITCH (CONT'D)

Injectafer has been studied in more than 8800 patients enrolled in more than 40 clinical trials, making it the most-studied IV iron therapy. Over 3 million patients in the US have been treated with Injectafer since its FDA approval in 2013.[36]

Injectafer is indicated for the treatment of IDA in[6]:

- Adults and pediatric patients 1 year of age and older who have either intolerance to oral iron or an unsatisfactory response to oral iron
- Adult patients who have non-dialysis-dependent chronic kidney disease

Injectafer is indicated for the treatment of ID in[6]:

- Adult patients with heart failure and New York Heart Association class II/III to improve exercise capacity

Injectafer is available as a 750 mg iron/15 mL single-dose vial and 100 mg iron/2 mL single-dose vial[6]

How frequently do you reassess iron levels in patients undergoing treatment, and what indicators guide your follow-up?

CV. If a patient has a history of ID and presents with fatigue or declining activity tolerance, that's a clear sign to recheck iron labs. In our clinic, we've added a dedicated bullet in the assessment and plan to document the last ferritin, TSAT, and any prior treatment. Since nurse practitioners often see patients more frequently than physicians, we've really taken ownership of that follow-up. When I talk to patients about starting iron infusions, I let them know they may start regaining some exercise capacity within about 30 days of their last injection[6,19,37,38]

Consider testing your patients beginning 14-30 days after starting oral iron to see if they are having an adequate response[39,40]

CB. It's also critical to consider where patients are on their journeys overall. Even when GDMT is optimized, lingering symptoms or hospitalization could point to untreated ID. Checking iron levels in those cases can be revealing. We've traditionally used thresholds adapted from CKD, like ferritin ≤100 ng/mL to ≤300 ng/mL and TSAT <20%, which remain applicable in HF, given its inflammatory nature.[3,7] As the evidence base grows, we're getting better at targeting those who will benefit most.

> ***If a patient has a history of ID or IDA and presents with fatigue or declining activity tolerance, that's a clear sign to recheck iron labs…Nurse practitioners often see patients more frequently than physicians, we've really taken ownership of that follow-up.***
> **– Cassie Vorgang, nurse practitioner**

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IMPACT THROUGH INJECTAFER: FRONTLINE PERSPECTIVES ON MANAGING ID IN HF

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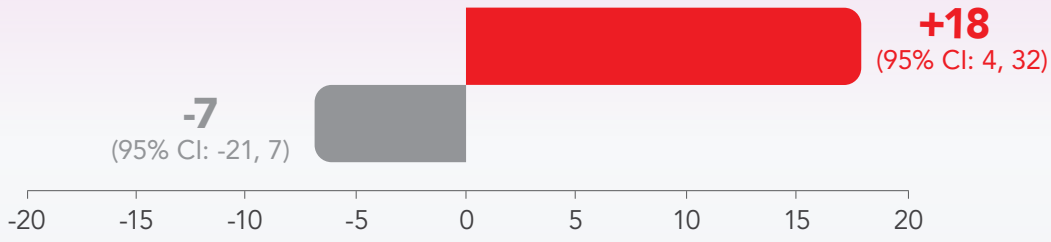
What key insights from Injectafer's pivotal trial CONFIRM-HF have influenced patient care in your practice?

CB. Clinical trial evidence is essential, but we also have to weigh physical outcomes, like 6-minute walk test (6MWT) performance. Both domains matter. It's not just about major cardiac events; it's about how patients feel and function in daily life. These real-world outcomes are critical to engagement and adherence. Sometimes we focus too heavily on hard endpoints, but functional improvement is just as important. Injectafer has demonstrated benefits in this space, particularly in improving 6MWT distance.[6,38]

CV. We tell patients that full iron repletion with IV therapy like Injectafer isn't just about improving lab values, it's about helping them increase their exercise capacity. We've seen measurable gains, like distance improvements in 6MWT.[6,38] Allowing patients to improve their exercise capacity, even if it just means something as simple as being able to play catch in the backyard, makes patients invested in their treatment because they see the results in their ability to exercise.

"We've seen measurable gains, like distance improvements in 6MWT....When they can walk farther, that's when they know their treatment is working."
– Cassie Vorgang, nurse practitioner

Improvements in 6MWT at 24 weeks[6,38]



25 m
(~82 ft) difference in 6MWT was seen with Injectafer vs placebo (95% CI: 7, 43) *P*=0.007

Changes in 6MWT distance from baseline (meters): mean (SD)

Injectafer Placebo

SELECTED SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONT'D)

Hypersensitivity Reactions

Serious hypersensitivity reactions, including anaphylactic-type reactions, some of which have been life-threatening and fatal, have been reported in patients receiving Injectafer. Patients may present with shock, clinically significant hypotension, loss of consciousness, and/or collapse. Monitor patients for signs and symptoms of hypersensitivity during and after Injectafer administration for at least 30 minutes and until clinically stable following completion of the infusion. Only administer Injectafer when personnel and therapies are immediately available for the treatment of serious hypersensitivity reactions. In clinical trials, serious anaphylactic/anaphylactoid reactions were reported in 0.1% (2/1775) of subjects receiving Injectafer. Other serious or severe adverse reactions potentially associated with hypersensitivity which included, but were not limited to, pruritus, rash, urticaria, wheezing, or hypotension were reported in 1.5% (26/1775) of these subjects.

IMPACT THROUGH INJECTAFER: FRONTLINE PERSPECTIVES ON MANAGING ID IN HF (CONT'D)

In clinical trials evaluating Injectafer in adult patients with iron deficiency and heart failure (1016 patients received Injectafer vs 857 received placebo), the overall safety was consistent across the studied indications.[6]

Adverse events (AE) in CONFIRM-HF[38]

Safety endpoint or event	Injectafer (n=152) n (%) events	Placebo (n=152) n (%) events
Subject with at least one drug-related AE	14 (9.2) 24	5 (3.3) 7
General disorders and administration site conditions	9 (5.9) 9	2 (1.3) 2
Skin and subcutaneous tissue disorders	4 (2.6) 4	0 (0.0) 0
Nervous system disorders	2 (1.3) 3	1 (0.7) 1
Gastrointestinal disorders	2 (1.3) 3	0 (0.0) 0
Vascular disorders	1 (0.7) 2	1 (0.7) 1
Investigations	1 (0.7) 1	2 (1.3) 2
Ear and labyrinth disorders	1 (0.7) 1	0 (0.0) 0
Injury, poisoning and procedural complications	1 (0.7) 1	0 (0.0) 0
Cardiac disorders	0 (0.0) 0	1 (0.7) 1

How has your experience with Injectafer affected your practice, particularly for patients with HF and ID in areas like exercise tolerance/capacity?

CB. Injectafer has significantly improved our management of HF patients with ID, particularly in improving exercise capacity.[6,38] By adopting a proactive approach to screening and treatment, we've been able to identify and address ID early, often before it exacerbates symptoms like fatigue and functional decline. The robust clinical evidence supporting Injectafer, including improvements in 6MWT outcomes[6], has made it a preferred option in our practice. Injectafer has become an essential part of our strategy to improve patient outcomes and engagement in their HF care journey.

CV. Most of our patients come in feeling terrible, so anything that offers meaningful improvement in exercise capacity really resonates. When they can walk farther, that's when they know their treatment is working.

> ***"The robust clinical evidence supporting Injectafer, including improvements in 6MWT outcomes, has made it a preferred option in our practice."***
> **– Dr. Craig Beavers, clinical pharmacist**

SELECTED SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONT'D)

Hypertension

In clinical studies, hypertension was reported in 4% (67/1775) of subjects in clinical trials 1 and 2. Transient elevations in systolic blood pressure, sometimes occurring with facial flushing, dizziness, or nausea were observed in 6% (106/1775) of subjects in these two clinical trials. These elevations generally occurred immediately after dosing and resolved within 30 minutes. Monitor patients for signs and symptoms of hypertension following each Injectafer administration.

Laboratory Test Alterations

In the 24 hours following administration of Injectafer, laboratory assays may overestimate serum iron and transferrin bound iron by also measuring the iron in Injectafer.

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IMPACT THROUGH INJECTAFER: FRONTLINE PERSPECTIVES ON MANAGING ID IN HF (CONT'D)

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What best practices can you share about utilizing electronic health record (EHR) systems to streamline patient referrals and treatment workflows, assuming your institution has one in place?

CV. Our Epic system triggers best-practice advisories for every HFrEF patient, prompting us to confirm they're on all 4 pillars of GDMT across both inpatient and outpatient settings. While iron testing and cardiac rehab aren't part of those alerts yet, the reminders are still incredibly useful. They push us to ask, "Why isn't this patient on this therapy?" and take immediate action. It's a streamlined system that reinforces adherence to guidelines without creating alert fatigue.

Streamlined care

Electronic health record (EHR) solutions allow providers to receive the latest evidence-based information directly at the point of care. Contact your DSI representative if interested in EHR implementation.

- **Embed dosing and administration details for Injectafer into order sets for IDA.**
- **Embed blood tests for iron deficiency directly into your HF order set.**
- **Set up clinical alerts at point of care to test for iron deficiency in appropriate HF patients.**

Makes it easy for you to order lab tests for your patients with ID in HF or IDA.

- An alert prompts you to test your patients with ID in HF or IDA and directs you to the order set where lab tests are embedded
- This reminder allows you to focus on patient care and takes the burden off you and your team to remember to routinely test HF patients for iron deficiency

Order set and alert guides include step-by-step instructions that make these updates easy to implement. Updating your EHR can have a powerful impact on how you care for patients.

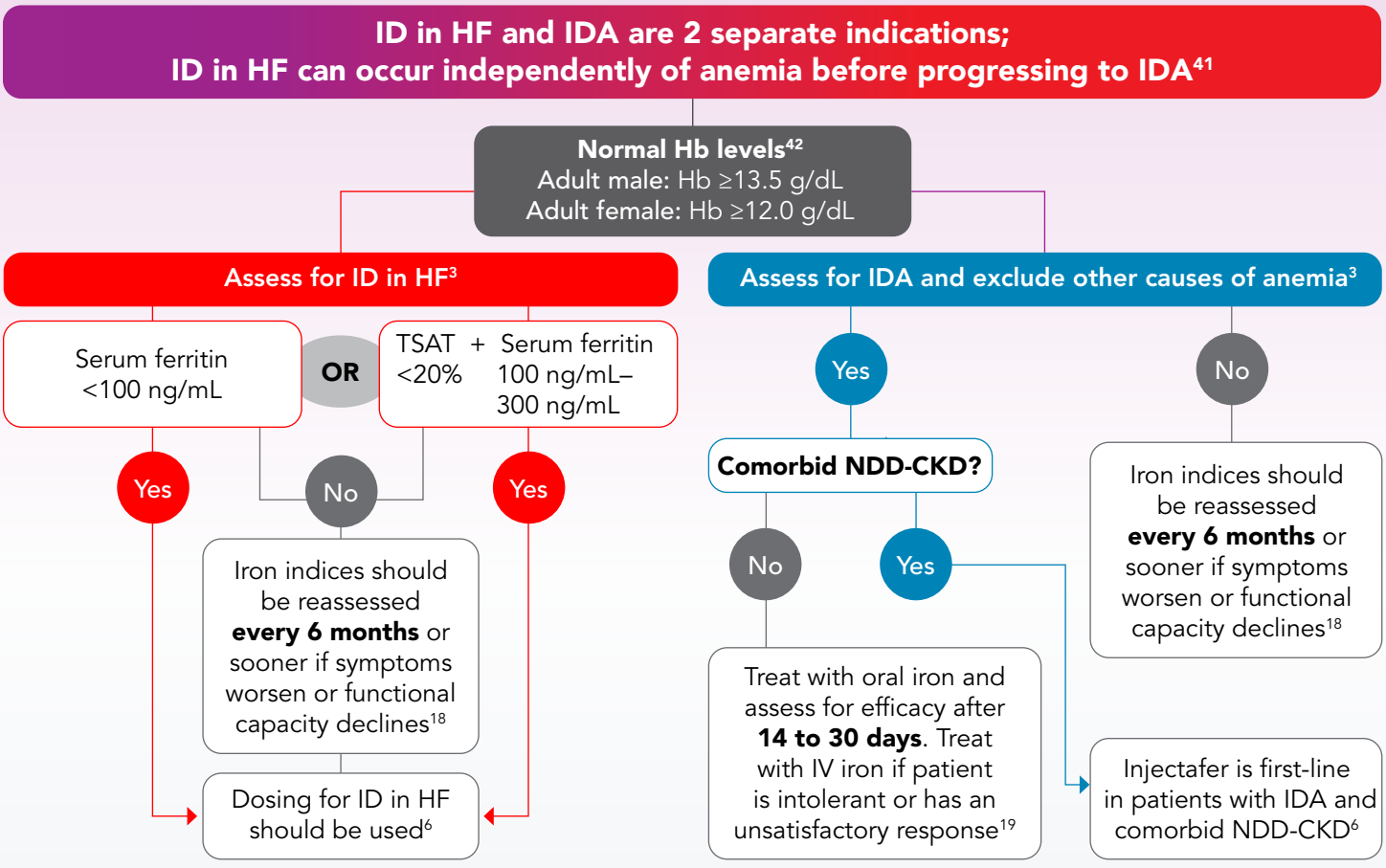
Does your institution employ protocols for incorporating IV iron into HF management? If possible, can you share personal experiences with protocol use?

CB. We have a clearly defined process for managing HF, including when and how to monitor iron status. Within that system, clinical pharmacists play a key role; they're empowered to order labs, assess disease progression, and evaluate response to IV iron therapy. This ensures treatment plans are implemented effectively and consistently. When evaluating IV iron therapies, we begin with the indication, whether it's new or expanded, and assess the supporting data around efficacy and safety. While formulary processes are fairly standardized, what truly matters is how these therapies fit into a value-based care framework. That's where pharmacists bring both clinical insight and strategic alignment.

CV. When I was the only outpatient HF nurse practitioner in our clinic, I developed a best-practice algorithm to ensure consistency, especially as our team grew. The algorithm includes everything from titrating GDMT to the highest tolerated level, to routinely checking iron levels and identifying the root cause of symptoms. It's helped us turn clinical guidelines and real-world experience into an actionable care model that supports better outcomes.

IMPACT THROUGH INJECTAFER: FRONTLINE PERSPECTIVES ON MANAGING ID IN HF (CONT'D)

Daiichi Sankyo, Inc. created the clinical algorithm tool to provide a clear and consistent approach to managing ID in HF and IDA in patients who are either intolerant or had an unsatisfactory response to oral iron and may help streamline variability in care, ensuring that healthcare professionals are more informed on evidence-based guidelines, leading to more predictable and reliable outcomes. The algorithm can also help disseminate up-to-date clinical knowledge to healthcare providers who may not specialize in ID in HF or IDA, possibly reducing the likelihood of omissions or incorrect steps in diagnosis or treatment. Finally, it can serve as an educational tool for new staff or trainees, promoting rapid acclimatization to clinical protocols.



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– Dr. Craig Beavers, clinical pharmacist

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Click here to see accompanying Full Prescribing Information and see Important Safety Information on pages 14-15.

FINAL THOUGHTS: PEER INSIGHTS AND KEY LEARNINGS

CV: For many of my patients with HF, comorbidities like CKD, diabetes, or obesity complicate their care.[1,7] That's why I emphasize the importance of early recognition of ID, helping patients understand that it's common and treatable.[3,17,19] In our clinic, we reassess iron every 3–6 months, especially in those experiencing fatigue or limited exercise capacity. What resonates most with patients isn't the lab results, it's when they notice improvements, like walking farther after IV iron therapy. The best feedback I get is when a patient tells me, "I went on vacation this summer," or "I got to see my granddaughter graduate." Those are the milestones that matter and helping patients achieve them is the most meaningful outcome I could ask for as a nurse practitioner.

CB: Inflammation and disrupted iron metabolism are central to the progression of HF, yet ID is often overlooked as a driver of symptoms and decreased physical capacity.[7,8] That's why I advocate for structured, guideline-based workflows and pharmacist-driven protocols that ensure routine iron testing and early recognition. In my experience, IV iron, particularly Injectafer, offers both higher dosing efficiency and better tolerability than oral iron, improving 6MWT outcomes for patients while streamlining operations for clinics. When patients report walking farther, it reinforces the real-world value of what we're doing. Seeing the evidence translate into practice, and then into tangible improvement for the patient, is what makes this work meaningful.

Injectafer is contraindicated in patients with hypersensitivity to Injectafer or any of its inactive components. Injectafer can cause serious adverse reactions including hypersensitivity reactions, symptomatic hypophosphatemia, and hypertension.

Please see additional Important Safety Information below. Please see additional Important Safety Information on pages 14-15.

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SELECTED SAFETY INFORMATION

ADVERSE REACTIONS

Adults

In two randomized clinical studies [Studies 1 and 2], a total of 1775 patients were exposed to Injectafer, 15 mg/kg of body weight, up to a maximum single dose of 750 mg of iron on two occasions, separated by at least 7 days, up to a cumulative dose of 1500 mg of iron. Adverse reactions reported by >2% of Injectafer-treated patients were nausea (7.2%); hypertension (4%); flushing (4%); injection site reactions (3%); erythema (3%); hypophosphatemia (2.1%); and dizziness (2.1%).

Pediatric

The safety of Injectafer in pediatric patients was evaluated in Study 3. Study 3 was a randomized, active-controlled study in which 40 patients (1 to 12 years of age: 10 patients, 12 to 17 years of age: 30 patients) received Injectafer 15 mg/kg to a maximum single dose of 750 mg (whichever was smaller) on Days 0 and 7 for a maximum total dose of 1500 mg; 38 patients evaluable for safety in the control arm received an age-dependent formulation of oral ferrous sulfate for 28 days. The median age of patients who received Injectafer was 14.5 years (range, 1-17); 83% were female; 88% White and 13% Black. The most common adverse reactions (≥4%) were hypophosphatemia (13%), injection site reactions (8%), rash (8%), headache (5%), and vomiting (5%).

Patients with Iron Deficiency and Heart Failure

The safety of Injectafer was evaluated in adult patients with iron deficiency and heart failure in randomized controlled trials FAIR-HF (NCT00520780), CONFIRM-HF (NCT01453608) and AFFIRM-AHF (NCT02937454) in which 1016 patients received Injectafer versus 857 received placebo. The overall safety profile of Injectafer was consistent across the studied indications.

Post-Marketing Experience

The following adverse reactions have been reported from the post-marketing spontaneous reports with Injectafer: *cardiac disorders*: tachycardia; *general disorders and administration site conditions*: chest discomfort, chills, pyrexia; *metabolism and nutrition disorders*: hypophosphatemia; *musculoskeletal and connective tissue disorders*: arthralgia, back pain, hypophosphatemic osteomalacia; *nervous system disorders*: syncope; *respiratory, thoracic and mediastinal disorders*: dyspnea; *skin and subcutaneous tissue disorders*: angioedema, erythema, pruritus, urticaria; *pregnancy*: fetal bradycardia.

CLINICAL CONSIDERATIONS IN PREGNANCY

Untreated IDA in pregnancy is associated with adverse maternal outcomes such as postpartum anemia. Adverse pregnancy outcomes associated with IDA include increased risk for preterm delivery and low birth weight.

Severe adverse reactions including circulatory failure (severe hypotension, shock including in the context of anaphylactic reaction) may occur in pregnant women with parenteral iron products (such as Injectafer) which may cause fetal bradycardia, especially during the second and third trimester.

You are encouraged to report Adverse Drug Events to American Regent, Inc. at 1-800-734-9236 or to the FDA by visiting www.fda.gov/medwatch or calling 1-800-FDA-1088.

injectafer® ferric carboxymaltose injection

Click here to see accompanying Full Prescribing Information and see Important Safety Information on pages 14-15.

INDICATIONS AND IMPORTANT SAFETY INFORMATION

INDICATIONS

Injectafer® (ferric carboxymaltose injection) is indicated for the treatment of iron deficiency anemia (IDA) in adult and pediatric patients 1 year of age and older who have either intolerance or an unsatisfactory response to oral iron, and in adult patients who have non-dialysis dependent chronic kidney disease. Injectafer is also indicated for iron deficiency in adult patients with heart failure and New York Heart Association class II/III to improve exercise capacity.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

Injectafer is contraindicated in patients with hypersensitivity to Injectafer or any of its inactive components.

WARNINGS AND PRECAUTIONS

Symptomatic Hypophosphatemia

Symptomatic hypophosphatemia with serious outcomes including osteomalacia and fractures requiring clinical intervention has been reported in patients treated with Injectafer in the post-marketing setting. These cases have occurred mostly after repeated exposure to Injectafer in patients with no reported history of renal impairment. However, symptomatic hypophosphatemia has been reported after one dose. Possible risk factors for hypophosphatemia include a history of gastrointestinal disorders associated with malabsorption of fat-soluble vitamins or phosphate, inflammatory bowel disease, concurrent or prior use of medications that affect proximal renal tubular function, hyperparathyroidism, vitamin D deficiency, malnutrition, and hereditary hemorrhagic telangiectasia (HHT or Osler-Weber-Rendu syndrome). In most cases, hypophosphatemia resolved within three months.

Correct pre-existing hypophosphatemia prior to initiating therapy with Injectafer. Monitor serum phosphate levels in patients at risk for chronic low serum phosphate. Check serum phosphate levels prior to a repeat course of treatment in patients at risk for low serum phosphate and in any patient who receives a second course of therapy within three months. Treat hypophosphatemia as medically indicated.

Hypersensitivity Reactions

Serious hypersensitivity reactions, including anaphylactic-type reactions, some of which have been life-threatening and fatal, have been reported in patients receiving Injectafer. Patients may present with shock, clinically significant hypotension, loss of consciousness, and/or collapse.

Monitor patients for signs and symptoms of hypersensitivity during and after Injectafer administration for at least 30 minutes and until clinically stable following completion of the infusion. Only administer Injectafer when personnel and therapies are immediately available for the treatment of serious hypersensitivity reactions. In clinical trials, serious anaphylactic/anaphylactoid reactions were reported in 0.1% (2/1775) of subjects receiving Injectafer. Other serious or severe adverse reactions potentially associated with hypersensitivity which included, but were not limited to, pruritus, rash, urticaria, wheezing, or hypotension were reported in 1.5% (26/1775) of these subjects.

Hypertension

In clinical studies, hypertension was reported in 4% (67/1775) of subjects in clinical trials 1 and 2. Transient elevations in systolic blood pressure, sometimes occurring with facial flushing, dizziness, or nausea were observed in 6% (106/1775) of subjects in these two clinical trials. These elevations generally occurred immediately after dosing and resolved within 30 minutes. Monitor patients for signs and symptoms of hypertension following each Injectafer administration.

Laboratory Test Alterations

In the 24 hours following administration of Injectafer, laboratory assays may overestimate serum iron and transferrin bound iron by also measuring the iron in Injectafer.

ADVERSE REACTIONS

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ADVERSE REACTIONS (CONT'D)

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Post-Marketing Experience

The following adverse reactions have been identified during post approval use of Injectafer. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

The following adverse reactions have been reported from the post-marketing spontaneous reports with Injectafer: *cardiac disorders*: tachycardia; *general disorders and administration site conditions*: chest discomfort, chills, pyrexia; *metabolism and nutrition disorders*: hypophosphatemia; *musculoskeletal and connective tissue disorders*: arthralgia, back pain, hypophosphatemic osteomalacia; *nervous system disorders*: syncope; *respiratory, thoracic and mediastinal disorders*: dyspnea; *skin and subcutaneous tissue disorders*: angioedema, erythema, pruritus, urticaria; *pregnancy*: fetal bradycardia.

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To learn more about ID in HF, IDA, and Injectafer, please scan the QR code and complete the form on the page.

"IV iron, particularly options like Injectafer that allow for high-dose, efficient administration, make this intervention both practical and impactful.".
– Dr. Craig Beavers, clinical pharmacist

"If we can avoid 5 separate infusions, we reduce IV sticks, infection risk, and logistical burdens. That's the kind of standardized, patient-focused care model we should be aiming for."
– Cassie Vorgang, nurse practitioner

Dr. Craig Beavers, PharmD, FACC, FAHA, FCCP, BCCP, CACP

Dr. Craig Beavers is a nationally recognized cardiovascular clinical pharmacist and healthcare leader. He currently serves as Adjunct Associate Professor at the University of Kentucky (UK) College of Pharmacy.

A Kentucky native, Dr. Beavers completed his PGY-1 and PGY-2 cardiology residencies at UK Chandler Hospital. He is actively involved with national organizations like the American College of Cardiology and the American College of Clinical Pharmacy, helping shape practice standards in cardiovascular care.

In 2025, he received the ACC Distinguished Cardiovascular Team Member Award, recognizing his contributions to patient-centered, team-based care.

Cassie Vorgang, MRN, FNP

Cassie Vorgang is a dedicated family nurse practitioner with over 6 years of experience, currently serving as an advanced HF nurse practitioner at Inova Advanced Heart Failure in Falls Church, VA. She's deeply committed to delivering high-value, patient-centered care.

Beyond her clinical work, Ms. Vorgang thrives as an educator and innovator. She developed an APP-led HF medication titration clinic and a tailored onboarding program for advanced practice providers and nurses, demonstrating her natural leadership and focus on collaborative, sustainable models of care. Forward-thinking and invested in both patients and colleagues, Ms. Vorgang brings expertise and empathy to every aspect of her role.

Click here to see accompanying Full Prescribing Information inside pocket.

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