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# Managing Iron Deficiency Anemia With IV Iron Therapy to Optimize Outcomes in Patient-Centered Care

## INTRODUCTION

Repletion of iron in patients with iron deficiency anemia (IDA) is important for the function of many biological processes.<sup>1,2</sup> Iron repletion through intravenous (IV) treatment is safe and effective for many patients.<sup>1,2</sup> The choice of an IV iron (IVI) product may be based on a combination of considerations including cost, patient and provider preference, and availability.<sup>1</sup> These products vary in recommended dosage, infusion time, and number of infusions needed for repletion as well as risk of certain adverse events (AEs).<sup>1,3-8</sup>

Adherence to recommended treatment dosing tends to decline as the number of separate recommended infusion visits increases.<sup>9-13,\*</sup> Treatment nonadherence may lead to clinical and economic consequences, and patients prescribed multiple IVI infusions often prefer a single-dose option.<sup>14-18</sup> Ferric derisomaltose injection, solution (FDI) (Monoferric; Pharmacosmos Therapeutics Inc) is an IVI product that can be infused as a single 1000-mg dose; dosing can be repeated if IDA recurs.<sup>8</sup>

## BACKGROUND ON IDA

IDA is common worldwide; patients with this chronic disease may experience negatively impacted health and activities of daily living (ADLs).<sup>1,2,16,19</sup> Iron is important for enzymatic processes, DNA and hemoglobin synthesis, oxygen transport, mitochondrial energy generation, and many other cellular functions.<sup>1,2,20</sup> Reduced oxygen levels may lead to symptoms including fatigue,

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## IMPORTANT SAFETY INFORMATION INDICATIONS

Monoferric is indicated for the treatment of iron deficiency anemia (IDA) in adult patients:

- who have intolerance to oral iron or have had unsatisfactory response to oral iron
- who have non-hemodialysis dependent chronic kidney disease (NDD-CKD)

## CONTRAINDICATIONS

Monoferric is contraindicated in patients with a history of serious hypersensitivity to Monoferric or any of its components. Reactions have included shock, clinically significant hypotension, loss of consciousness, and/or collapse.

Please see accompanying Important Safety Information throughout.  
Please see accompanying Full Prescribing Information or visit [Monoferric.com](https://www.monoferric.com).

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Mike Hennessy Sr | 1960-2021

**AJMC**  
THE AMERICAN JOURNAL OF MANAGED CARE

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lethargy, shortness of breath, and cardiac dysfunction.<sup>1</sup> Downstream complications can also include malabsorption, nausea, weight loss, abdominal pain, headaches, restless leg syndrome, pica, cognitive impairment, and, in children, developmental delays.<sup>1,15,21,22</sup>

In absolute iron deficiency, iron stores in the body are depleted; in functional iron deficiency, total iron stores in the body are adequate, but iron cannot be mobilized easily for erythropoiesis.<sup>2,20,23</sup> IDA may be asymptomatic, and it can occur consequent to many chronic inflammatory diseases with overlapping symptoms that complicate its diagnosis and appropriate management.<sup>1,2</sup> Gaps in care and delayed treatment of IDA can lead to exacerbation of comorbid conditions.<sup>1</sup> Furthermore, untreated IDA carries cost implications, such as emergency hospitalization and the need for blood transfusions.<sup>1</sup>

### Comorbidities and Contributing Disease States

Increased iron requirements (eg, during pregnancy), decreased iron intake or absorption (eg, resulting from malnutrition or malabsorption), chronic inflammation, loss of healthy blood cells and bone marrow, or some combination of these factors can lead to IDA (Figure<sup>23</sup>).<sup>1,2,20</sup> IDA may be associated with surgical procedures due to associated blood loss and inflammation.<sup>20</sup> IDA also can occur due to increased demand for iron in female patients with abnormal uterine bleeding (AUB) or in pregnant patients as a result of chronic blood loss or maternal and fetal growth, respectively.<sup>2,20,24</sup> In patients with cancer, IDA may develop as a result of chemotherapy, malnutrition, malabsorption, systemic inflammation, chronic blood loss, or blood loss after surgery.<sup>20,23</sup> Further, IDA is common in individuals with inflammatory bowel disease (IBD) as a result of impaired nutrient absorption by chronically inflamed bowels, chronic blood loss, or surgical resection.<sup>1,2,20</sup> IDA can occur in patients with chronic kidney disease (CKD) due to reduced gastrointestinal (GI) iron absorption, inflammation, dialysis-associated poor nutrition and blood loss, recurrent blood sampling, and use of certain drugs (eg, proton-pump inhibitors, anticoagulants).<sup>1,2,20</sup> Additionally, IDA is often associated with heart failure (HF) due to several factors including reduced appetite, increased GI blood loss due to antiplatelet or anticoagulation medication, inflammation, and edema-associated reductions in GI iron absorption.<sup>1,2,20,25</sup>

### Epidemiology

Iron deficiency is not the only cause of anemia (defined as low blood hemoglobin); further, anemia, iron deficiency, and IDA are often conflated.<sup>1,20,24</sup> Diagnostic criteria vary, and testing for anemia as a proxy for iron deficiency or IDA can result in early-stage iron deficiency going undiagnosed and untreated.<sup>24</sup> There is a dearth of epidemiologic data on iron deficiency, and a lack of consensus and updated guidelines on biomarkers and diagnostic thresholds further complicates identification of IDA.<sup>24</sup> However, over 5% of the US population is estimated to have anemia, and iron deficiency is the leading cause of anemia.<sup>2,24,26</sup>

### Treatment Recommendations

The aim of treatment for IDA involves provision of supplemental iron to replenish iron stores and normalize blood hemoglobin levels via oral or IV routes or through red blood cell (RBC) transfusion.<sup>1,2</sup>

Oral iron supplementation is an inexpensive treatment for IDA, however, 3 to 6 months of treatment are required for iron repletion, and long-term use is limited by the occurrence of GI AEs that may impact patient adherence and lead to treatment cessation.<sup>1,2</sup> Use of different dosing regimens or formulations can decrease AEs associated with oral iron treatment.<sup>1</sup>

Oral iron treatment may not be effective for certain patients including those with malabsorption, chronic blood loss, active IBD, or intolerance or unsatisfactory response to oral iron therapy.<sup>2,20</sup> In these patients, IVI therapy is recommended due to its rapid increase of hemoglobin levels compared with oral treatment.<sup>1,2</sup> In addition, IVI shows an improved safety profile as it bypasses the GI tract and avoids mucosal aggravation and inflammation.<sup>1</sup> IVI treatment is also indicated in patients with cancer or CKD who are treated with erythropoiesis-stimulating agents (ESAs), as iron enhances the effect of ESAs, and iron deficiency cannot support normal erythropoiesis.<sup>2</sup> IVI treatment may be associated with transient nausea, vomiting, pruritis, headache, and muscle and joint pain; rarer reactions include hypersensitivity, skin discoloration, and, occasionally, hypophosphatemia.<sup>1,2</sup>

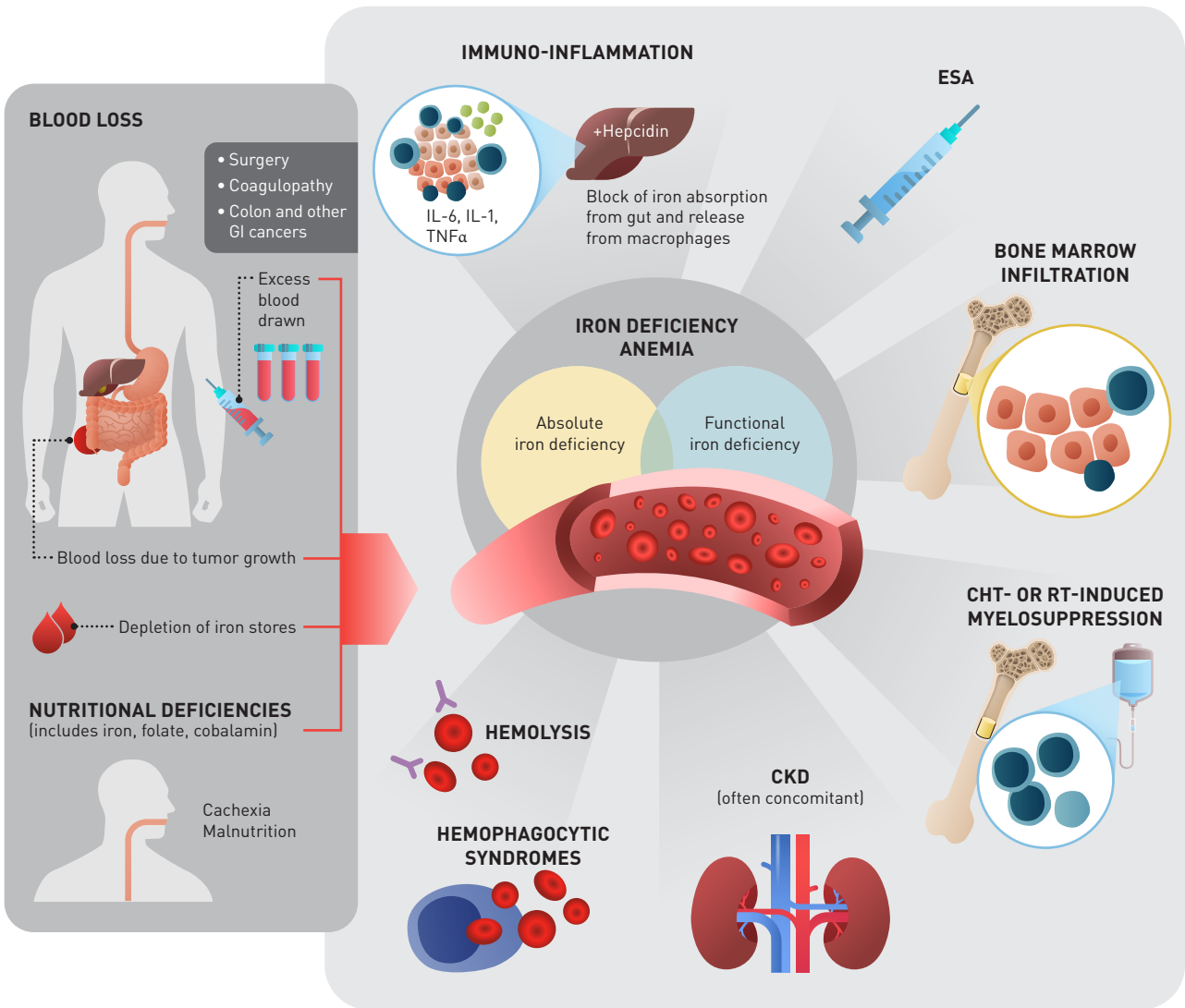
There are a variety of IVI agents available; cost, patient and provider preference, and product availability factor into treatment decision-making.<sup>1</sup> Products differ in formulation, infusion time, and number of infusions needed, but there generally is a consensus that the overall target dose should be 1000 mg of iron.<sup>1-8,21</sup>

## IMPORTANT SAFETY INFORMATION (CONTINUED) WARNINGS AND PRECAUTIONS

### Hypersensitivity

Serious hypersensitivity reactions, including anaphylactic-type reactions, some of which have been life-threatening and fatal, have been reported in patients receiving Monoferric. 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 Monoferric administration for at least 30 minutes and until clinically stable following completion of the infusion. Only administer Monoferric when personnel and therapies are immediately available for the treatment of serious hypersensitivity reactions. Monoferric is contraindicated in patients with prior serious hypersensitivity reactions to Monoferric or any of its components. In clinical trials in patients with IDA and CKD, serious or severe hypersensitivity were reported in 0.3% (6/2008) of the Monoferric treated subjects. These included 3 events of hypersensitivity in 3 patients; 2 events of infusion-related reactions in 2 patients and 1 event of asthma in one patient.

**Figure.** Etiologic Factors Associated With IDA<sup>23</sup>



Dee-sign / FARBA / KP Arts / mast3r - stock.adobe.com (Modified by Julianne Costello)

CHT, chemotherapy; CKD, chronic kidney disease; ESA, erythropoiesis-stimulating agent; GI, gastrointestinal; IDA, iron deficiency anemia; IL, interleukin; RT, radiotherapy.

**IMPORTANT SAFETY INFORMATION (CONTINUED)  
WARNINGS AND PRECAUTIONS (cont'd)**

**Iron Overload**

Excessive therapy with parenteral iron can lead to excess iron storage and possibly iatrogenic hemosiderosis or hemochromatosis. Monitor the hematologic response (hemoglobin and hematocrit) and iron parameters (serum ferritin and transferrin saturation) during parenteral iron therapy. Do not administer Monoferric to patients with iron overload.

However, limited data on comparative safety and efficacy from large head-to-head trials are available.<sup>1,2</sup>

The third treatment option for IDA—RBC transfusion—is only recommended for patients with severe anemia, insufficient blood flow, cardiovascular symptoms, and associated comorbidities.<sup>1,2</sup> This treatment acts rapidly to resolve hypoxia and iron deficiency.<sup>2</sup> Nevertheless, patients will often need further iron supplementation, and the procedure is associated with risks including transfusion-related reactions and infection transmission.<sup>1</sup>

## IVI LANDSCAPE

All available IVI products are formulated as iron-carbohydrate nanoparticles with an iron-oxyhydroxide core and a carbohydrate coating to increase stability, keep the particles in colloidal suspension, and allow for slow release of elemental iron.<sup>27,28</sup> Older generation IVI products include iron dextran injection (ID) (INFeD; AbbVie), iron sucrose injection (IS) (Venofer; American Regent), and sodium ferric gluconate complex in sucrose injection (SFG) (Ferrlecit; Sanofi); these products are formulated to be infused at lower doses (< 500 mg) over the course of several infusions according to prescribing information (Table 1).<sup>3-8,15</sup> Newer generation iron products are formulated with larger, more complex shells or more stable matrix structures that permit faster infusion of higher doses (≥ 500 mg) in 1 sitting (Table 1).<sup>3-8,15,28</sup> These products include ferric carboxymaltose injection (FCM) (Injectafer; Daiichi-Sankyo), ferumoxylol injection (FXT) (Feraheme; AMAG Pharmaceuticals), and ferric derisomaltose injection, solution (FDI) (Monoferric; Pharmacosmos Therapeutics Inc).<sup>6-8,27</sup>

These newer products also differ in the nature of the carbohydrate moiety, the surface charge, the size of the molecule, and the structure of the iron oxyhydroxide.<sup>27</sup> Furthermore, these products are associated with low and comparable incidence of hypersensitivity reactions.<sup>27,29</sup> FDI, the most recent IVI product to become available in the US, received FDA approval in 2020; it can be infused as a single 1000-mg dose.<sup>8,27</sup>

## THE PATIENT BURDEN

Patients with IDA who are prescribed multiple monthly doses of IVI may still experience clinical symptoms and negatively impacted ADLs.<sup>16,18,30</sup> In a 2023 survey of adults with IDA who received multiple IVI doses, it was found that on average, there was a 1.5-year gap between diagnosis and first IVI treatment.<sup>16</sup> Prior to treatment, patients' commonly reported symptoms included cold hands and feet, dizziness, headache, fatigue, and weakness. After IVI, patients reported symptom improvement and at least 50% improvement in certain ADLs (ie, "caring for myself" and "doing things around the house"). However, worse improvement was seen for other ADLs, and many symptoms remained. Treatment gaps and missed doses may have impacted the improvement of these measures.<sup>16</sup> Among the 193 patients who were prescribed at least 2 infusions per month, over one-third (71/193) missed a prescribed dose.<sup>16-18</sup> Among those patients who missed a dose, the most commonly reported reasons for missed infusions were conflict (45.1%), scheduling difficulties (29.6%), and transportation difficulties (26.7%). In addition, 38.0% were not satisfied with their infusion frequency, 84.5% believed that fewer infusions would improve adherence, and 85.9% would have preferred a single-dose option.<sup>17,30,\*</sup>

Additionally, a total of 71 patients (22%) were treated for AUB and prescribed at least 2 infusions per month. The majority of patients with AUB reported that IVI treatment logistics negatively impacted their productivity and attendance at important events (both > 50%), and over two-thirds reported scheduling their life around treatment. Approximately 37% of these patients missed a dose.<sup>18</sup>

## SINGLE-DOSE IVI

Approval of FDI for treatment of IDA was based on 2 open-label, actively-controlled clinical trials (FERWON-IDA and FERWON-NEPHRO) performed in a total of 3050 patients with IDA of different etiologies who were randomly assigned 2:1 to treatment with FDI

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## IMPORTANT SAFETY INFORMATION (CONTINUED) ADVERSE REACTIONS

Adverse reactions were reported in 8.6% (172/2008) of patients treated with Monoferric. Adverse reactions related to treatment and reported by ≥ 1% of the treated patients were nausea (1.2%) and rash (1%). Adjudicated serious or severe hypersensitivity reactions were reported in 6/2008 (0.3%) patients in the Monoferric group. Hypophosphatemia (serum phosphate < 2.0 mg/dL) was reported in 3.5% of Monoferric-treated patients in Trials 1 & 2.

To report adverse events, please contact Pharmacosmos at 1-888-828-0655. You may also contact the FDA at <http://www.fda.gov/medwatch> or call 1-800-FDA-1088.

**Please see Full Prescribing Information.**

**Table 1.** Comparison of Administration Factors for IVI Products<sup>3-8</sup>

IVI product	Recommended treatment dose per visit <sup>a</sup>	Visits needed for recommended total dose <sup>a</sup>	Infusion time per dose <sup>a</sup>	Total time to treat 100 patients <sup>a,b</sup>	Test dose	Boxed warning
ID	100 mg <sup>c</sup>	 x10	≥ 2 min	33.3 h	Yes	Yes (anaphylaxis)
SFG	125 mg	 x8	≥ 60 min <sup>d</sup>	800 h	No	No
IS	200 mg	 x5	≥ 15 min <sup>d</sup>	125 h	No	No
FXT	510 mg	 x2	≥ 15 min	50 h	No	Yes (anaphylaxis)
FCM	750 mg <sup>e</sup>	 x2	≥ 15 min	50 h	No	No
FDI	1000 mg <sup>f</sup>	 x1	≥ 20 min	33.3 h	No	No

CKD, chronic kidney disease; FCM, ferric carboxymaltose injection; FDI, ferric derisomaltose injection, solution; FXT, ferumoxytol injection; ID, iron dextran injection; IS, iron sucrose injection; IV, intravenously; IVI, intravenous iron; SFG, sodium ferric gluconate complex in sucrose injection.

<sup>a</sup>Based on prescribing information indicated for the treatment of IDA in adults who have intolerance to oral iron, an unsatisfactory response to oral iron, or patients with non-hemodialysis dependent CKD

<sup>b</sup>Calculated by multiplying the number of visits needed for the total recommended dose times the infusion time per dose times 100 patients

<sup>c</sup>For patients weighing > 15 kg, the recommended total dosage can be calculated based on the patient's current hemoglobin level in g/dL, the target hemoglobin level in g/dL, and the patient's lean body weight in kg.

<sup>d</sup>Infusion times are for product diluted in 100 mL of 0.9% sodium chloride.

<sup>e</sup>For patients weighing ≥ 50 kg, the recommended dosage is 750 mg IV in 2 doses, separated by at least 7 days, for a total cumulative dose of 1500 mg of iron per course. Alternatively, administer 15 mg/kg to a maximum of 1000 mg as a single-dose treatment course. Patient must weigh ≥ 67 kg to receive a 1000-mg dose of FCM. For patients weighing < 50 kg, the recommended dosage is 15 mg/kg IV in 2 doses separated by at least 7 days per course.

<sup>f</sup>For patients weighing ≥ 50 kg, administer 1000 mg of FDI as an IV infusion. For patients weighing < 50 kg, administer FDI as 20 mg/kg of actual body weight as an IV infusion.

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or IS.<sup>8</sup> In these trials, FDI was shown to be non-inferior to IS for the change in hemoglobin from baseline to week 8.<sup>8</sup> Furthermore, there were no significant differences in serious or severe hypersensitivity reactions between FDI and IS.<sup>31</sup> Hypophosphatemia (defined as serum phosphate level < 2.0 mg/dL) was reported in 3.5% of patients treated with FDI in these trials.<sup>8</sup>

## IVI-ASSOCIATED HYPOPHOSPHATEMIA

Patients with IDA may experience symptoms of disease, and some AEs associated with IVI treatment may mimic symptoms of IDA.<sup>1,16,27</sup> Hypophosphatemia is an AE associated with certain IVI products; symptoms include muscle weakness, fatigue, pain, and respiratory depression.<sup>27</sup> Hypophosphatemia can be associated with long-term bone-related AEs such as osteomalacia and fractures, and real-world evidence indicates that FCM treatment is associated with an increased risk of clinically relevant bone complications and kidney stones.<sup>1,6,27,32</sup> Treatment with FCM is associated with much higher rates and increased severity of hypophosphatemia than is treatment with either FDI or FXT.<sup>27</sup> In multicenter clinical trials comparing treatment with FDI or FCM in adult patients with IDA (PHOSPHARE-IDA), the incidence of hypophosphatemia (defined as serum phosphate level < 2.0 mg/dL, at any time from baseline to day 35) was significantly lower with use of FDI than with FCM therapy (trial A: 7.9% vs 75.0%; adjusted rate difference, -67.0% [95% CI, -77.4% to -51.5%],  $P < .001$ ) (trial B: 8.1% vs 73.7%; adjusted rate difference, -65.8% [95% CI, -76.6% to -49.8%];  $P < .001$ ).<sup>33</sup> Generalizability of these data may be limited due to the high incidence of patients with gynecological causes of IDA, which tend to be associated with higher rates of hypophosphatemia; this may explain the higher than anticipated incidence of hypophosphatemia following treatment with FCM.<sup>33</sup> Furthermore, the trials did not measure clinical outcomes.<sup>33</sup>

Patients may experience severe, symptomatic, and persistent

hypophosphatemia and may be required to discontinue IVI therapy and to receive long-term phosphate and calcitriol supplementation.<sup>27,34</sup> Indeed, among patients treated with FCM, moderate to severe hypophosphatemia is associated with the need for IV phosphate supplementation and with longer hospital stays than needed for mild or no hypophosphatemia.<sup>27</sup> Furthermore, phosphate replacement therapy is often an ineffective management strategy in such cases, as increased renal wasting leads to loss of replaced phosphate.<sup>1</sup>

## MANAGED CARE CONSIDERATIONS

As previously mentioned, a high percentage of patients with IDA report dissatisfaction with IVI regimens requiring multiple infusions or express a preference for a single-dose option.<sup>30</sup> Patient satisfaction scores are important to health care practices. For hospitals specifically, reimbursement (ie, value-based incentive payment) is affected by public reporting of the Hospital Consumer Assessment of Healthcare Providers and Systems: Patients' Perspectives of Care Survey, which includes data on patients' perceptions of their hospital experiences.<sup>35</sup>

Suboptimal adherence to IVI treatment may be seen in patients using therapies that require several infusions, potentially leading to clinical and economic consequences.<sup>15,\*</sup> IVI treatment effectiveness was assessed in a retrospective analysis of DRG real-world evidence US database claims for 2959 adult patients with anemia who received initial therapy (over 21 days) with IS, ID, SFG, FCM, or FXT between 2015 and 2017.<sup>14,†</sup> The mean baseline iron deficit across all patients was 1001 mg (SD, 312).<sup>14</sup> Within a year of the index dose, normalized serum hemoglobin levels were achieved by a significantly higher percentage of patients who received more than 1000 mg as compared with those receiving up to 1000 mg of iron (56% vs 44%, respectively;  $P < .001$ ). Furthermore, the probability of requiring additional IVI treatment was lower among those who received more than 1000 mg.<sup>14</sup> In addition, compared with patients receiving up to 1000 mg, those

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†The study did not consider inter-product differentiation by clinical safety and efficacy.

## IMPORTANT SAFETY INFORMATION (CONTINUED) WARNINGS AND PRECAUTIONS

### Hypersensitivity

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receiving more than 1000 mg of iron had significantly reduced mean (SE) numbers of all-cause outpatient visits (14 [0.37] vs 11 [0.46] visits, respectively;  $P < .001$ ) and all-cause IVI treatment-related outpatient visits (4 [0.07] vs 3 [0.08] visits;  $P < .001$ ).<sup>14</sup> The study authors noted that in addition to reducing the need to return for further treatment, high iron doses may lower health care resource utilization (HCRU) and minimize the risk of treatment ineffectiveness due to patient nonadherence.<sup>14,\*†</sup>

In a retrospective study of 2016–2019 Magellan Rx Management claims data, the impact of nonadherence with older vs newer IVI formulations on total cost of care was evaluated for 24,736 adult patients with IDA.<sup>15,‡</sup> Nonadherence to therapy was defined as having received less than 1000 mg of iron over 6 weeks.<sup>15</sup> Results showed a higher rate of nonadherence for older generation products (54.8%) than for newer generation products (15.9%).<sup>15</sup> Patients who were nonadherent to any IVI treatment had higher mean inpatient and outpatient hospital costs than did those who were adherent.<sup>15,§</sup> These findings highlight the association between adherence to IVI therapy, HCRU, and costs.

Use of IVI products that require fewer rounds of infusion is associated with a higher rate of adherence and a lower cumulative chance for infusion-related reactions or extravasations.<sup>28</sup> In addition, these products may be associated with decreased HCRU due to the reduced number of office visits and use of medical staff required, potentially increasing efficiency for both physicians and patients.<sup>9,28</sup>

Implementation of payer restrictions has been associated with a decline in adherence; this reduced adherence has separately been associated with decreases in the benefits of newer generation IVI products.<sup>36</sup> While many states have passed step therapy exception bills, not all of them support exceptions based upon the patient's best interest as determined by medical necessity or based on expected inefficacy of the required drug due to characteristics of the patient or therapeutic regimen.<sup>37</sup> The findings above suggest that HCRU and patient satisfaction may be negatively impacted by payer restrictions requiring patients with IDA to receive treatment with older generation IVI products before newer products are covered.

## NONADHERENCE WITH IVI PRODUCTS

Patterns of adherence with different IVI products are similar among patients with IDA across disease states according to a series of retrospective analyses of 2020–2022 Komodo Health medical and pharmacy claims data (Table 2).<sup>9–13</sup> In an internal analysis conducted by Pharmacosmos, rates of IVI treatment nonadherence were analyzed for 144,523 commercially insured adult patients with IDA and a record for IVI but no hemodialysis (average Charleston Comorbidity Index [CCI], 1.3).<sup>9</sup> Across all products, overall nonadherence (defined as receiving < 1000 mg of iron within 6 weeks inclusive of the index date) was 34.5% with the lowest rate of nonadherence seen for FDI (0.4%) and the highest noted for SFG (91.8%).<sup>9</sup>

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†Study limitations include use of claims data from an open network that may not capture out of network health care services and that did not include information on use of over-the-counter oral iron or detailed information on durability iron repletion. Generalizability of findings may be limited due to exclusion of patients without complete serum hemoglobin level data. Furthermore, FDI was not approved until after the study period.<sup>14</sup>

‡The study did not consider inter-product differentiation by clinical safety and efficacy.

§Because the claims data analyzed were from commercial health plans, results of the study may not be generalizable to Medicare and Medicaid programs. Furthermore, the study did not evaluate whether IVI treatments were used on or off label. In addition, the total treatment dose of 1000 mg was not made on individual iron needs, but rather product label; therefore, the prescribed dose may have been lower in some patients.<sup>15</sup>

## IMPORTANT SAFETY INFORMATION (CONTINUED) WARNINGS AND PRECAUTIONS (cont'd)

### Iron Overload

Excessive therapy with parenteral iron can lead to excess iron storage and possibly iatrogenic hemosiderosis or hemochromatosis. Monitor the hematologic response (hemoglobin and hematocrit) and iron parameters (serum ferritin and transferrin saturation) during parenteral iron therapy. Do not administer Monoferric to patients with iron overload.

A separate analysis focused on IVI nonadherence among 28,856 commercially insured adult patients with IDA and cancer (average CCI, 3.2).<sup>10,\*</sup> In this population, 6-week nonadherence was 33.4% overall; similarly, the lowest rate of nonadherence was seen for FDI (0.4%), and the highest was noted for SFG (92.3%). The authors wrote that lower adherence was noted among patients receiving IVI treatments requiring more infusions and that undertreatment in patients with cancer- and chemotherapy-induced IDA can adversely impact patient outcomes.<sup>10</sup>

Additionally, nonadherence to IVI treatment among patients with cancer has the potential to negatively impact Medicare reimbursement.<sup>11,23,38</sup>

The Enhancing Oncology Model (EOM) of care is intended to generate cost savings and improve quality of care for patients who are undergoing chemotherapy and who have been diagnosed with

breast cancer, chronic leukemia, small intestine/colorectal cancer, lung cancer, lymphoma, multiple myeloma, or prostate cancer.<sup>11,38</sup> Through retrospective performance-based payments based on care quality and savings, participating practices are incentivized to use high-value treatments throughout the care of patients with cancer; these therapies may include supportive care treatments such as use of IVI.<sup>23,38</sup>

A retrospective analysis of Medicare claims data in 6450 patients with IDA and an EOM tumor type (average CCI, 6.0) found overall 6-week IVI therapy nonadherence to be 32.4%. The lowest rate of nonadherence was associated with FDI (0.0%), and the highest was recorded for SFG (90.8%).<sup>11</sup>

Rates of IVI nonadherence were also examined in 2 separate analyses of Medicare data; one involved data for 6210 patients with non-dialysis dependent CKD and IDA (average CCI, 5.9) but excluded

\*All referenced publications (prior to June 2024) sponsored by Pharmacosmos Therapeutics Inc use the term *concordance* in place of *adherence* to IVI therapy. The terms share the same definition (ie, having received ≥ 1000 mg of iron over 6 weeks).

**Table 2.** Real-World Rates of 6-Week IVI Nonadherence<sup>9-13,a</sup>

Analysis	Disease state	ID	SFG <sup>b</sup>	IS	FXT	FCM	FDI	Overall
Pharmacosmos internal analysis of commercial claims data <sup>9</sup>	IDA	32.3%	91.8%	71.2%	16.1%	16.0%	0.4%	34.5%
AMCP conference abstract analyzing commercial claims data <sup>10</sup>	IDA and cancer	29.6%	92.3%	72.9%	16.1%	18.0%	0.4%	33.4%
ISPOR conference poster analyzing commercial claims data <sup>11</sup>	IDA and cancer (EOM tumor type)	38.9%	90.8%	71.0%	17.1%	24.6%	0.0%	32.4%
AMCP conference abstract analyzing Medicare claims data <sup>12</sup>	IDA and NDD CKD	43.5%	95.7%	70.7%	18.6%	23.1%	2.3%	34.9%
Pharmacosmos internal analysis of Medicare claims data <sup>13</sup>	IDA and HF	40.2%	95.7%	71.9%	19.6%	21.6%	0.0%	34.8%

AMCP, Academy of Managed Care Pharmacy; CKD, chronic kidney disease; EOM, Enhancing Oncology Model; FCM, ferric carboxymaltose injection; FDI, ferric derisomaltose injection, solution; FXT, ferumoxytol injection; HF, heart failure; ID, iron dextran injection; IDA, iron deficiency anemia; IS, iron sucrose injection; ISPOR, The Professional Society for Health Economics and Outcomes Research; IVI, intravenous iron; NDD, non-dialysis dependent; SFG, sodium ferric gluconate complex in sucrose injection.

<sup>a</sup>All data sponsored by Pharmacosmos Therapeutics Inc.

<sup>b</sup>Most patients receiving SFG would require 8 dialysis sessions or at least 8 weeks to get a cumulative dose of 1000 mg of elemental iron.

## IMPORTANT SAFETY INFORMATION (CONTINUED) ADVERSE REACTIONS

Adverse reactions were reported in 8.6% (172/2008) of patients treated with Monoferric. Adverse reactions related to treatment and reported by ≥1% of the treated patients were nausea (1.2%) and rash (1%). Adjudicated serious or severe hypersensitivity reactions were reported in 6/2008 (0.3%) patients in the Monoferric group. Hypophosphatemia (serum phosphate <2.0 mg/dL) was reported in 3.5% of Monoferric-treated patients in Trials 1 & 2.

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patients with end-stage renal disease (ESRD) (although 55.5% of patients had stage 3 CKD),<sup>12</sup> and the other was an internal analysis conducted by Pharmacosmos examining data for 5127 adult patients with IDA and HF (average CCI, 5.6) but excluding patients with ESRD and those receiving hemodialysis.<sup>13</sup> Both analyses found that nonadherence was lowest for FDI and highest for SFG.<sup>12,13,\*</sup>

Limitations to these retrospective analyses include those associated with use of highly structured real-world administrative claims data without clinical metrics such as laboratory results or physician notes. These studies were conducted with the Komodo Healthcare Map, and data examined were from either commercial or Medicare health plans; results may not be generalizable to other types of insurance programs. The analyses did not consider inter-product differentiation by clinical safety and efficacy. Furthermore, no statistical analysis was performed, and no adjustments were applied to these metrics; therefore, bias may exist between the different IV iron cohorts. Most patients receiving SFG would require 8 dialysis sessions or at least 8 weeks to get a cumulative dose of 1000 mg of elemental iron. In addition, across studies, the populations given FDI were smaller than were those given other IVI products.

## CONCLUSION

The IDA treatment landscape is evolving. Use of IVI products requiring multiple infusions can burden health care delivery systems, community practices, and patients. Newer generation IVI products offer higher doses of iron delivered in fewer visits and potentially address an unmet need among patients who may struggle to receive several infusions and are dissatisfied with the associated treatment logistics. However, further research is needed to examine the clinical and cost consequences of IVI nonadherence and potential incomplete iron repletion. Payers are encouraged to implement coverage policies that do not restrict the use of certain IVI products based on up-front drug cost alone but that also consider other aspects that can impact treatment such as nonadherence and patient outcomes. •

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## IMPORTANT SAFETY INFORMATION INDICATIONS

Monoferric is indicated for the treatment of iron deficiency anemia (IDA) in adult patients:

- who have intolerance to oral iron or have had unsatisfactory response to oral iron
- who have non-hemodialysis dependent chronic kidney disease (NDD-CKD)

## CONTRAINDICATIONS

Monoferric is contraindicated in patients with a history of serious hypersensitivity to Monoferric or any of its components. Reactions have included shock, clinically significant hypotension, loss of consciousness, and/or collapse.

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## IMPORTANT SAFETY INFORMATION (CONTINUED) WARNINGS AND PRECAUTIONS

### Hypersensitivity

Serious hypersensitivity reactions, including anaphylactic-type reactions, some of which have been life-threatening and fatal, have been reported in patients receiving Monoferric. 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 Monoferric administration for at least 30 minutes and until clinically stable following completion of the infusion. Only administer Monoferric when personnel and therapies are immediately available for the treatment of serious hypersensitivity reactions. Monoferric is contraindicated in patients with prior serious hypersensitivity reactions to Monoferric or any of its components. In clinical trials in patients with IDA and CKD, serious or severe hypersensitivity were reported in 0.3% (6/2008) of the Monoferric treated subjects. These included 3 events of hypersensitivity in 3 patients; 2 events of infusion-related reactions in 2 patients and 1 event of asthma in one patient.

### Iron Overload

Excessive therapy with parenteral iron can lead to excess iron storage and possibly iatrogenic hemosiderosis or hemochromatosis. Monitor the hematologic response (hemoglobin and hematocrit) and iron parameters (serum ferritin and transferrin saturation) during parenteral iron therapy. Do not administer Monoferric to patients with iron overload.

### ADVERSE REACTIONS

Adverse reactions were reported in 8.6% (172/2008) of patients treated with Monoferric. Adverse reactions related to treatment and reported by  $\geq 1\%$  of the treated patients were nausea (1.2%) and rash (1%). Adjudicated serious or severe hypersensitivity reactions were reported in 6/2008 (0.3%) patients in the Monoferric group. Hypophosphatemia (serum phosphate  $< 2.0$  mg/dL) was reported in 3.5% of Monoferric-treated patients in Trials 1 & 2.

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