Injectafer® (ferric carboxymaltose injection) Receives FDA Approval for Single Dose Option for the Treatment of Adult Patients with Iron Deficiency Anemia

For patients weighing 50 kg (110 lb) or more, Injectafer may now be administered as a 1000 mg single dose for IDA treatment[1]

Basking Ridge, N.J. and Shirley, N.Y. (May 6, 2021) – Daiichi Sankyo, Inc. and American Regent, Inc., a Daiichi Sankyo Group company, today announced that the U.S. Food and Drug Administration (FDA) has approved a single 1000 mg dose option of Injectafer® (ferric carboxymaltose injection), an iron replacement product, for the treatment of iron deficiency anemia (IDA) in adult patients who have intolerance to oral iron, have had unsatisfactory response to oral iron, or have non-dialysis dependent chronic kidney disease (CKD).[1]

"We are pleased to build on the proven, mainstay Injectafer 1500 mg two-dose course of treatment with the approval of this new 1000 mg single dose option," said Linda Mundy, Chief Medical Officer at American Regent, Inc. "More than 1.7 million patients have been treated with Injectafer in the U.S. and healthcare providers now have an additional dosing option for adult patients with IDA who may not be appropriate for oral iron or who have non-dialysis dependent CKD."

Injectafer was first approved by the FDA in 2013 as a 1500 mg course of treatment, administered as two doses up to 750 mg each separated by seven days. The 1500 mg regimen is the recommended dosage for patients weighing 50 kg (110 lb) or more, administered in two doses separated by at least 7 days.[1] This dosage remains the proven course of treatment for evidence-based full iron repletion available for adult patients with IDA.

The safety and efficacy of Injectafer for treatment of IDA were established in four randomized, open-label, controlled clinical trials. In Trial 1 and 2, evaluating safety and efficacy, Injectafer was administered at a dose of 15 mg/kg 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. In Trial 3 and 4, evaluating safety and tolerability, for patients weighing 50 kg or more, Injectafer 15 mg/kg to a maximum of 1000 mg was administered as a single dose per course.[1]

Injectafer has been studied in more than 40 clinical trials that included over 8,800 patients worldwide.[2] Injectafer has been approved in 75 countries since initial European Union (EU) approval in 2007[3] and is the most extensively studied intravenous iron.[4]

Daiichi Sankyo, Inc. anticipates the single 1000 mg dose option of Injectafer will be available in the coming weeks.

About Injectafer®

Injectafer® (ferric carboxymaltose injection) is an iron replacement product and is given intravenously (into the vein) by a healthcare provider. For patients weighing 50 kg (110 lb) or more, Injectafer is administered in two doses of 750 mg separated by at least 7 days for a total cumulative dose of 1500 mg of iron per course. For patients weighing less than 50 kg (110 lb), each dose is administered as 15 mg/kg body weight. Alternatively, for patients weighing 50 kg (110 lb) or more, Injectafer may be administered as a single 1000 mg dose.

Injectafer is manufactured and marketed under the name of Ferinject® (Ferric Carboxymaltose) by Vifor Pharma (Switzerland) outside of North America.

U.S. Important Safety Information for INJECTAFER

INDICATIONS
Injectafer® (ferric carboxymaltose injection) 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, or who have non-dialysis dependent chronic kidney disease.

IMPORTANT SAFETY INFORMATION

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

WARNINGS AND PRECAUTIONS
Symptomatic hypophosphatemia requiring clinical intervention has been reported in patients at risk of low serum phosphate in the postmarketing setting. These cases have occurred mostly after repeated exposure to Injectafer in patients with no reported history of renal impairment. Possible risk factors for hypophosphatemia include a history of gastrointestinal disorders associated with malabsorption of fat-soluble vitamins or phosphate, concurrent or prior use of medications that affect proximal renal tubular function, hyperparathyroidism, vitamin D deficiency and malnutrition. In most cases, hypophosphatemia resolved within three months.

Monitor serum phosphate levels in patients at risk for low serum phosphate who require a repeat course of treatment.

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.

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.

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
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%); dizziness (2.1%); and vomiting (2%).

Pooled data from two Phase 3 studies 1VIT09030 (NCT00981045) and 1VIT09031 (NCT00982007) with a dosing regimen of Injectafer 15 mg/kg up to a maximum of 750 mg x 2 doses to a cumulative dose of 1500 mg of iron were analyzed to compare rates of adverse reactions in two Phase 3 parallel group studies 1VIT07017 (NCT00548860) and 1VIT07018 (NCT00548691) with a dosing regimen of Injectafer 15 mg/kg up to a maximum of 1000 mg single dose. Adverse reactions reported by ≥2% of Injectafer-treated patients were injection site reactions (4%) and injection site extravasation (2%) in 1VIT07017 and 1VIT07018.

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 (rarely reported event); *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.

About Daiichi Sankyo
Daiichi Sankyo is dedicated to creating new modalities and innovative medicines by leveraging our world-class science and technology for our purpose “to contribute to the enrichment of quality of life around the world.” In addition to our current portfolio of medicines for cancer and cardiovascular disease, Daiichi Sankyo is primarily focused on developing novel therapies for people with cancer as well as other diseases with high unmet medical needs. With more than

100 years of scientific expertise and a presence in more than 20 countries, Daiichi Sankyo and its 16,000 employees around the world draw upon a rich legacy of innovation to realize our 2030 Vision to become an "Innovative Global Healthcare Company Contributing to the Sustainable Development of Society." For more information, please visit www.daiichisankyo.com. Daiichi Sankyo, Inc., headquartered in Basking Ridge, New Jersey, is a member of the Daiichi Sankyo Group. For more information on Daiichi Sankyo, Inc., please visit: www.dsi.com.

About American Regent, Inc.
American Regent, Inc., a Daiichi Sankyo Group company, is a top-10 injectable manufacturer. For over 50 years, American Regent has been developing, manufacturing, and supplying quality generic and branded injectables for healthcare providers. For nearly 20 years, we have been a leader in IV iron therapy. American Regent is committed to U.S.-based manufacturing. In 2018, more than 99% of units supplied were formulated, filled, and finished at our U.S.-based facilities, making us uniquely positioned to quickly mobilize to respond to shortages or changes in market needs. Speed counts. Flexibility matters. Reliability and quality are paramount. Because patients should never have to wait for the medications they need. For more information, please visit www.americanregent.com.

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[1] Injectafer [package insert]. Shirley, NY: American Regent, Inc.; April 2021.
[2] Data on file. PSUR (Periodic Safety Update Report), January 2017. Luitpold Pharmaceuticals, Inc., Shirley, NY.
[3] Data on file. Injectafer approvals as of Dec 2017. Daiichi Sankyo Inc., Basking Ridge, NJ.
[4] Data on file. Injectafer Studies. Daiichi Sankyo Inc., Basking Ridge, NJ.