Medical and Behavioral Health Policy Activity

Policies Effective: November 6, 2023 Notification Posted: September 1, 2023

Policies Developed

- **Teclistamab, II-282**

I. Initial Review for Teclistamab (Tecvayli®)

Teclistamab may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ALL** of the following criteria are met:

- Age 18 years or older; **AND**
- Diagnosis of multiple myeloma; **AND**
- Relapsed or refractory disease after four or more prior lines of therapy, including ALL of the following:
  - An immunomodulatory agent;
  - A proteasome inhibitor;
  - An anti-CD38 monoclonal antibody;

  AND
- ONE of the following:
  - Eastern Cooperative Oncology Group (ECOG) Performance Status grade of 0 or 1; OR
  - Karnofsky Performance Status ≥ 70;

  AND
- Not previously treated with chimeric antigen receptor (CAR) T-cell therapy or other gene therapy; **AND**
- No previous or concurrent therapy with a treatment targeted to B-cell maturation antigen (BCMA) (e.g., belantamab mafodotin [Blenrep®]); **AND**
- Screened for hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) infection and has begun therapy if appropriate; **AND**
- Does not have ANY of the following:
  - Central nervous system (CNS) involvement;
  - History or presence of clinically relevant CNS pathology (e.g., stroke with CNS sequelae, dementia);
  - History of allogeneic stem cell transplant within the previous 6 months;
  - History of autologous stem cell transplant within the previous 12 weeks;

  AND
- No FDA labeled contraindications to teclistamab (see table 1 below); **AND**
- For commercial health plan members only, step therapy supplement criteria may apply for select conditions (see policy II-242: Step Therapy Supplement).

II. Renewal Review for Teclistamab (Tecvayli®)

Teclistamab may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ALL** of the following criteria are met:

- Previously approved for teclistamab through the initial review process; **AND**
- Continued positive clinical response to teclistamab therapy (e.g., stabilization and/or slowing of disease progression or decrease in symptom severity and/or frequency, decrease in size of tumor or tumor spread); **AND**
- No previous or concurrent therapy with a treatment targeted to B-cell maturation antigen (BCMA) (e.g., belantamab mafodotin [Blenrep®]); **AND**
- No FDA labeled contraindications to teclistamab (see table 1 below).

III. Experimental/Investigative Uses

All other uses of teclistamab are considered **EXPERIMENTAL/INVESTIGATIVE** due to the lack of clinical evidence demonstrating an impact on improved health outcomes.

Table 1. FDA Labeled Contraindications

Agent	FDA Labeled Contraindications
Teclistamab	None

Documentation Submission:

Documentation supporting the medical necessity criteria described in the policy must be included in the prior authorization, when prior authorization is required. In addition, the following documentation must also be submitted:

Initial Review

1. Clinical notes describing the diagnosis and clinical features of the diagnosis.
2. Laboratory results for HBV, HCV, and HIV screening.
3. Clinical notes describing current and past treatments for the diagnosis, including response to the treatments.
4. Clinical notes documenting absence of central nervous system (CNS) involvement, allogeneic stem cell transplant within the previous 6 months, and autologous stem cell transplant within the previous 12 weeks.
5. For commercial health plan members only, when step therapy requirements apply for the requested indication, documentation for one or more of the step therapy supplement criteria MUST be provided (see policy II-242).

Renewal Review

1. Documentation of prior approval for teclistamab through the initial review process.
2. Documentation, since most recent approval, supporting continued positive clinical response with teclistamab therapy (e.g., stabilization and/or slowing of disease progression or decrease in symptom severity and/or frequency, decrease in size of tumor or tumor spread).
3. Clinical notes describing current and past medications for the diagnosis, including response to the medications.

- **Epcoritamab, II-283**

I. Initial Review for Epcoritamab (Epkinly™)

Epcoritamab may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ALL** of the following criteria are met:

- Age 18 years or older; **AND**
- ONE of the following:
  - Diagnosis of ANY of the following Non-Hodgkin Lymphoma (NHL):
    - Diffuse Large B-cell lymphoma (DLBCL), not otherwise specified; or
    - High-grade B-cell lymphoma; or
    - Histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma; or
    - HHV8-positive diffuse large B-cell lymphoma; or
    - HIV-related diffuse large B-cell lymphoma; or
    - Monomorphic post-transplant lymphoproliferative disorders (PTLD), B-cell type; or
    - Primary effusion lymphoma;

AND

- Disease is refractory or relapsed after TWO or more lines of systemic therapy. Examples include the following:
  - No response to last line of therapy, defined by progressive disease as best response to most recent therapy regimen; OR
  - No response to last line of therapy, defined by stable disease as best response to most recent therapy with duration ≤6 months from last dose of therapy; OR
  - Disease progression or relapsed ≤12 months post-autologous stem cell transplantation (ASCT); OR
  - If salvage therapy is given post-ASCT, no response to or relapsed after the last line of therapy;

AND

- Patient must have received adequate prior therapy, including the following:
  - An anthracycline-containing chemotherapy regimen; AND
  - Anti-CD20 monoclonal antibody (e.g., rituximab) unless tumor is CD20-negative;

AND

- ONE of the following:
  - Eastern Cooperative Oncology Group (ECOG) Performance Status grade of 0-2; OR
  - Karnofsky Performance Status ≥ 50;

AND

- No concurrent therapy with chimeric antigen receptor (CAR) T-cell therapy or other gene therapy; **AND**
- No FDA labeled contraindications to epcoritamab (see table 1); **AND**
- Screened for hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) infection and has begun therapy if appropriate; **AND**
- Does not have ANY of the following:
  - Active infection;
  - Primary central nervous system (CNS) lymphoma or CNS involvement by lymphoma;
  - Known past or current malignancy;
  - Current autoimmune disease, or other disease, requiring permanent immunosuppressive therapy;

AND

- For commercial health plan members only, step therapy supplement criteria may apply for select conditions (see policy II-242: Step Therapy Supplement).

II. Renewal Review for Epcoritamab (Epkinly™)

Epcoritamab may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ALL** of the following criteria are met:

- Previously approved for epcoritamab through the initial review process; **AND**
- Continued positive clinical response to epcoritamab therapy (e.g., stabilization and/or slowing of disease progression or decrease in symptom severity and/or frequency); **AND**
- No concurrent therapy with chimeric antigen receptor (CAR) T-cell therapy or other gene therapy;
- No FDA labeled contraindications to epcoritamab (see table 1 below).

III. Experimental/ Investigative Uses

All other uses of epcoritamab are considered **EXPERIMENTAL/ INVESTIGATIVE** due to the lack of clinical evidence demonstrating an impact on improved health outcomes.

Table 1. FDA Labeled Contraindications

Agent	FDA Labeled Contraindications

Epcoritamab (Epkinly™)	None

Documentation Submission:

Documentation supporting the medical necessity criteria described in the policy must be included in the prior authorization, when prior authorization is required. In addition, the following documentation must also be submitted:

Initial Review

1. Clinical notes describing the diagnosis and clinical features of the diagnosis.
2. Laboratory results for HBV, HCV, and HIV screening.
3. Clinical notes describing current and past treatments for the diagnosis, including response to the treatments.
4. Clinical notes documenting absence of active infection, primary CNS lymphoma or NCS involvement by lymphoma, known past or current malignancy, and disease requiring permanent immunosuppressive therapy.
5. For commercial health plan members only, when step therapy requirements apply for the requested indication, documentation for one or more of the step therapy supplement criteria MUST be provided (see policy II-242).

Renewal Review

1. Documentation of prior approval for epcoritamab through the initial review process.
2. Documentation, since most recent approval, supporting continued positive clinical response with epcoritamab therapy (e.g., stabilization and/or slowing of disease progression or decrease in symptom severity and/or frequency.)
3. Clinical notes describing current and past medications for the diagnosis, including response to the medications.

Policies Revised

- **Risk-Reducing Mastectomy, IV-27**
  NOTE:
  - **The policy does NOT address Gender Affirming Procedures for Gender Dysphoria (IV-123)**
  - **Coverage may be subject to legislative mandates, including but not limited to the following, which apply prior to the policy statements:**
    - **Federal Women's Health and Cancer Rights Act (WHCRA)**
    - **Minnesota Statute 62A.25 Reconstructive Surgery**

I. Risk-Reducing mastectomy may be considered **MEDICALLY NECESSARY AND APPROPRIATE** in individuals meeting **ANY** of the following criteria:

A. Bilateral or unilateral (i.e., contralateral prophylactic mastectomy) for individuals with a personal history of breast cancer; **OR**

B. Bilateral mastectomy in individuals without a personal history of breast cancer with **any** of the following:
- Presence of **one or more** known genetic variant(s) associated with high risk of breast cancer, confirmed by genetic testing. These include **any** the following:
  - *BRCA1* or *BRCA2* (Hereditary breast and ovarian cancer syndrome)
  - *CDH1*
  - PALB2
  - *PTEN* (Cowden syndrome, PTEN hamartoma syndrome)

- *STK11*
- *TP53* (Li-Fraumeni syndrome); **OR**

- Strong family history of breast cancer as indicated by one of the following:
  - One first- or second-degree blood relative with two or more breast cancer primaries
  - Two or more blood relatives on the same side of the family with breast cancer primaries with at least one diagnosed at 50 years of age or younger
  - One first-degree or second-degree blood relative with breast cancer before the age of 45 years
  - One first- or second-degree male blood relative with breast cancer
  - One first-degree **AND** 2 or more second- or third-degree blood relatives on the same side of the family with breast cancer
  - Three or more first- or second-degree blood relatives on the same side of the family with breast cancer
  - One first- or second-degree blood relative with breast cancer **AND** 1 first-degree blood relative with ovarian, fallopian tube or primary peritoneal cancer
  - Two third-degree blood relatives on the same side of the family with breast cancer **AND** 1 first- or second-degree blood relative with ovarian, fallopian tube or primary peritoneal cancer
  - Background ethnicity is known to be associated with a higher incidence of breast cancer (e.g., Ashkenazi Jewish) **AND** 1 or more blood relative with a history of breast, ovarian, fallopian tube, primary peritoneal or pancreatic cancer; **OR**
- History of thoracic radiation at less than 30 years of age (e.g., radiation for Hodgkin's lymphoma);

AND

- Patient is a never-smoker OR has abstained from smoking, use of smokeless tobacco and/or nicotine products, and/or nicotine replacement therapy for a minimum of 6 weeks prior to surgery

II. Risk-Reducing unilateral or bilateral mastectomy is considered **EXPERIMENTAL/INVESTIGATIVE** in all other situations, including but not limited to treatment of breast pain (mastodynia/mastalgia) or fibrocystic breast changes in the absence of risk factors listed above, due to a lack of clinical evidence demonstrating an impact on health outcomes.

- **Hematopoietic Stem Cell Transplantation in the Treatment of Germ-Cell Tumors, II-114**

Note: HSCT for epithelial ovarian cancer are addressed in a separate policy: II-123 Hematopoietic Stem Cell Transplantation for Miscellaneous Solid Tumors in Adults

I. <u>Autologous Hematopoietic Stem Cell Transplantation</u>

Single autologous hematopoietic stem cell transplantation

- Single autologous hematopoietic stem cell transplantation may be considered **MEDICALLY NECESSARY AND APPROPRIATE** as salvage therapy for germ-cell tumors in the following situations:
  - In patients with favorable prognostic factors (i.e., those with a testis or retroperitoneal primary site, a complete response to initial chemotherapy, low levels of serum markers, and low volume disease) who have failed a previous course of conventional-dose salvage chemotherapy; **OR**
  - In patients with unfavorable factors (i.e., incomplete response to initial therapy or relapsing mediastinal nonseminomatous germ-cell tumors) as initial treatment of first relapse (i.e., without a course of conventional-dose salvage chemotherapy) and in patients with platinum-refractory disease.

Complex autologous hematopoietic stem cell transplant therapies

- Autologous hematopoietic stem cell transplantation may be considered **MEDICALLY NECESSARY AND APPROPRIATE** for the treatment of testicular tumors either as salvage therapy or with platinum-refractory disease, in the following situations:
  - As tandem autologous hematopoietic stem cell transplantation; OR
  - With sequential high-dose chemotherapy.

- Autologous hematopoietic stem cell transplantation may be considered **MEDICALLY NECESSARY AND APPROPRIATE** for the treatment of ovarian germ-cell tumors, in the following situations:
  - With sequential high-dose chemotherapy for recurrent disease that was responsive to standard chemotherapy; OR
  - With sequential high-dose chemotherapy for persistent disease.

EXPERIMENTAL/INVESTIGATIVE uses

- Autologous hematopoietic stem cell transplantation is considered **EXPERIMENTAL/INVESTIGATIVE** as a component of first-line treatment for germ-cell tumors.
- Repeat autologous hematopoietic stem cell transplantation (not including tandem indication noted above for treatment of testicular tumors) for persistent or recurrent disease is considered **EXPERIMENTAL/INVESTIGATIVE.**
- For patients not meeting the above medical necessity criteria.

II. Allogeneic Hematopoietic Stem-Cell Transplantation

- Allogeneic hematopoietic stem cell transplantation is considered **EXPERIMENTAL/INVESTIGATIVE** to treat germ-cell tumors, including but not limited to, its use as therapy after prior failed autologous hematopoietic stem cell transplantation.

- **Hematopoietic Stem Cell Transplantation, Updates to Several Policies:**
- **Hematopoietic Stem Cell Transplantation for Chronic Lymphocytic, II-122**

I. Allogeneic Hematopoietic Stem Cell Transplantation

- Allogeneic hematopoietic stem cell transplantation may be considered **MEDICALLY NECESSARY AND APPROPRIATE** to treat chronic lymphocytic leukemia or small lymphocytic lymphoma in patients with histologic transformation or other confirmation of disease progression after standard first-line therapy.
- Allogeneic hematopoietic stem cell transplantation is considered **EXPERIMENTAL/INVESTIGATIVE** to treat chronic lymphocytic leukemia or small lymphocytic lymphoma when the criteria above are not met.

II. Autologous Hematopoietic Stem Cell Transplantation

- Autologous hematopoietic stem cell transplantation is considered **EXPERIMENTAL/INVESTIGATIVE** to treat chronic lymphocytic leukemia or small lymphocytic lymphoma.

III. Repeat Transplant

- Repeat allogeneic hematopoietic stem cell transplantation for persistent or recurrent disease is considered **EXPERIMENTAL/INVESTIGATIVE.**

- **Hematopoietic Stem Cell Transplantation for Central Nervous System (CNS) Embryonal Tumors and Ependymoma, II-130**

Note:

- **Peripheral neuroblastoma and Ewing's sarcoma may be are addressed in policy II-131.**
- **Other CNS tumors include astrocytoma, oligodendroglioma, and glioblastoma multiforme are addressed in policy II-120.**

I. Allogeneic Hematopoietic Stem Cell Transplantation

- Allogeneic hematopoietic stem cell transplantation may be considered **MEDICALLY NECESSARY AND APPROPRIATE** to treat chronic lymphocytic leukemia or small lymphocytic lymphoma in patients with histologic transformation or other confirmation of disease progression after standard first-line therapy.
- Allogeneic hematopoietic stem cell transplantation is considered **EXPERIMENTAL/INVESTIGATIVE** to treat chronic lymphocytic leukemia or small lymphocytic lymphoma when the criteria above are not met.

II. Autologous Hematopoietic Stem Cell Transplantation

- Autologous hematopoietic stem cell transplantation is considered **EXPERIMENTAL/INVESTIGATIVE** to treat chronic lymphocytic leukemia or small lymphocytic lymphoma.

III. Repeat Transplant

- Repeat allogeneic hematopoietic stem cell transplantation for persistent or recurrent disease is considered **EXPERIMENTAL/INVESTIGATIVE.**

- **Hematopoietic Stem Cell Transplantation for Solid Tumors of Childhood, II-131**

I. Autologous Hematopoietic Stem Cell Transplantation

- Autologous hematopoietic stem cell transplantation may be considered **MEDICALLY NECESSARY AND APPROPRIATE** for:
  - Initial treatment of high-risk neuroblastoma;
  - Recurrent or refractory neuroblastoma;
  - Initial treatment of high-risk Ewing's sarcoma;
  - Recurrent or refractory Ewing's sarcoma;
  - Metastatic retinoblastoma
- Tandem autologous hematopoietic stem cell transplantation may be considered **MEDICALLY NECESSARY AND APPROPRIATE** for treatment of high-risk neuroblastoma.
- Autologous hematopoietic stem cell transplantation (single or tandem) is considered **EXPERIMENTAL/INVESTIGATIVE** for treatment of all other solid tumors of childhood, including but not limited to:
  - Initial treatment of low- or intermediate-risk neuroblastoma,
  - Initial treatment of low- or intermediate-risk Ewing's sarcoma,
  - Rhabdomyosarcoma;
  - Wilms tumor;
  - Osteosarcoma;
  - Retinoblastoma without metastasis

II. Allogeneic Hematopoietic Stem Cell Transplantation

- Allogeneic (myeloablative or nonmyeloablative) hematopoietic stem cell transplantation for treatment of pediatric solid tumors is considered **EXPERIMENTAL/INVESTIGATIVE** due to a lack of evidence demonstrating an impact on improved health outcomes.
- Salvage allogeneic hematopoietic stem cell transplantation for neuroblastoma or other pediatric solid tumors that relapse after autologous transplantation or fail to respond is considered **EXPERIMENTAL/INVESTIGATIVE** due to a lack of evidence demonstrating an impact on improved health outcomes.

III. Repeat Transplant

- Repeat hematopoietic stem cell transplantation (not including tandem indications above for high-risk neuroblastoma) for persistent or recurrent disease is considered **EXPERIMENTAL/INVESTIGATIVE.**

- **Hematopoietic Stem Cell Transplantation for Myelodysplastic Syndrome and Myeloproliferative Neoplasms, II-133**
  Note: HSCT for acute myeloid leukemia is considered separately in policy number II-115; HSCT for chronic myelogenous leukemia is considered separately in policy number II-136.

  I. Allogeneic Hematopoietic Stem Cell Transplantation

  - Myeloablative allogeneic hematopoietic stem cell transplantation (HSCT) may be considered **MEDICALLY NECESSARY AND APPROPRIATE** as a treatment of:
    - Myelodysplastic syndrome; or
    - Myeloproliferative neoplasms.

  - Reduced-intensity conditioning allogeneic HSCT may be considered **MEDICALLY NECESSARY AND APPROPRIATE** as a treatment of myelodysplastic syndromes or myeloproliferative neoplasms in patients who for medical reasons would be unable to tolerate a myeloablative conditioning regimen.

  II. Repeat Transplant

  - Repeat allogeneic hematopoietic stem cell transplant may be considered **MEDICALLY NECESSARY AND APPROPRIATE** as a treatment of myelodysplastic syndrome/myeloproliferative neoplasm recurrence after prolonged remission (18 months or greater)
  - Repeat allogeneic hematopoietic stem cell transplantation for persistent disease or early recurrent disease is considered **EXPERIMENTAL/INVESTIGATIVE.**

  III. Autologous Hematopoietic Stem Cell Transplantation

  - Autologous hematopoietic stem cell transplantation (HSCT) for the treatment of myelodysplastic syndrome or myeloproliferative neoplasms is considered **EXPERIMENTAL/INVESTIGATIVE.**

- **Hematopoietic Stem Cell Transplantation for Hodgkin Lymphoma, II-135**

  I. Autologous Hematopoietic Stem Cell Transplantation

  - Autologous hematopoietic stem cell transplantation may be considered **MEDICALLY NECESSARY AND APPROPRIATE** in patients with primary refractory or relapsed Hodgkin lymphoma.
  - Tandem autologous hematopoietic stem cell transplantation in patients with Hodgkin lymphoma is considered **EXPERIMENTAL/INVESTIGATIVE** due to the lack of clinical evidence demonstrating an impact on improved health outcomes.

  II. Allogeneic Hematopoietic Stem Cell Transplantation

  - Allogeneic hematopoietic stem cell transplantation using a myeloablative conditioning regimen may be considered **MEDICALLY NECESSARY AND APPROPRIATE** in patients with primary refractory or relapsed Hodgkin lymphoma.
  - Allogeneic hematopoietic stem cell transplantation using a reduced-intensity conditioning (RIC) regimen may be considered **MEDICALLY NECESSARY AND APPROPRIATE** to treat Hodgkin lymphoma in patients:
    1. Who have failed a prior autologous hematopoietic stem cell transplant used to treat primary refractory or relapsed disease; **OR**

2. Who would otherwise qualify for a myeloablative allogeneic transplant, but would be unable to tolerate a standard myeloablative conditioning regimen; **OR**
3. When insufficient stem cells are collected for an autologous hematopoietic stem cell transplant.

III. Investigative Indications

- Other uses of hematopoietic stem cell transplantation in patients with Hodgkin lymphoma are considered **EXPERIMENTAL/INVESTIGATIVE** including, but not limited to, initial therapy for newly diagnosed disease to consolidate a first complete remission, due to the lack of clinical evidence demonstrating an impact on improved health outcomes.

IV. Repeat Transplant

- Repeat hematopoietic stem cell transplantation for persistent or recurrent disease is considered **EXPERIMENTAL/INVESTIGATIVE** (outside of indication noted above).

- **Hematopoietic Stem Cell Transplantation for Chronic Myelogenous Leukemia, II-136**

I. Allogeneic Hematopoietic Stem Cell Transplantation

- Allogeneic hematopoietic stem cell transplantation using a **myeloablative conditioning** regimen may be considered **MEDICALLY NECESSARY AND APPROPRIATE** as a treatment of chronic myelogenous leukemia.
- Allogeneic hematopoietic stem cell transplantation using a **reduced-intensity conditioning (RIC)** regimen may be considered **MEDICALLY NECESSARY AND APPROPRIATE** as a treatment of chronic myelogenous leukemia in patients who meet clinical criteria for an allogeneic HSCT but who are not considered candidates for a myeloablative conditioning allogeneic HSCT.

II. Autologous Hematopoietic Stem Cell Transplantation

- Autologous hematopoietic stem cell transplantation is considered **EXPERIMENTAL/INVESTIGATIVE** as a treatment of chronic myelogenous leukemia due to a lack of evidence demonstrating an impact on improved health outcomes.

III. Repeat Transplant

- Repeat hematopoietic stem cell transplantation for persistent or recurrent disease is considered **EXPERIMENTAL/INVESTIGATIVE.**

- **IV Iron Replacement Therapy, II-243**

Note:
- **This policy addresses ferumoxytol (Feraheme®), ferric carboxymaltose (Injectafer®), and ferric derisomaltose (Monoferric®) intravenous iron therapies only.**
- **This policy does NOT address intravenous iron replacement therapy for use in patients with chronic kidney disease (CKD) on dialysis.**
- **This policy does NOT address other uses of intravenous iron, including use as a contrast dye.**

I. Initial Review for ferumoxytol (Feraheme®) and ferric derisomaltose (Monoferric®)

Use of ferumoxytol or ferric derisomaltose may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ALL** of the following criteria are met:

- Age 18 years or older; **AND**
- Diagnosis of ONE of the following, including lab values obtained within the past 4 weeks:
  - Iron deficiency anemia (IDA) without chronic kidney disease (CKD), as indicated by ONE of the following:
    - Serum ferritin < 30 ng/mL; or
    - Transferrin saturation (TSAT) < 20%; or
    - Absence of stainable iron in bone marrow;

    OR
  - Iron deficiency anemia (IDA) with chronic kidney disease (CKD) in patients not requiring dialysis, as indicated by ONE of the following:
    - Serum ferritin < 100 ng/mL; or
    - Transferrin saturation (TSAT) < 30%;

  AND
- ONE of the following:
  - Inadequate response to full course of treatment (at least 3 ~~to 6~~ months) of oral iron; or
  - Anatomic or physiologic condition that interferes with oral iron absorption; or
  - Documented intolerance, FDA labeled contraindication, or hypersensitivity to oral iron;

  AND
- ONE of the following:
  - Inadequate response to iron dextran (Infed®), iron sucrose (Venofer®), or ferric gluconate (Ferrlecit®); or
  - Documented intolerance, FDA labeled contraindication, or hypersensitivity to iron dextran (Infed®), iron sucrose (Venofer®), and ferric gluconate (Ferrlecit®);

  AND
- No FDA labeled contraindications to the requested agent (see table 1 below); **AND**
- Requested dose is within the FDA labeled dose for the indication (see table 2 below); **AND**
- For commercial health plan members only, step therapy supplement criteria may apply for select conditions (see policy II-242: Step Therapy Supplement).

II. <u>Initial Review for ferric carboxymaltose (Injectafer®)</u>

Use of ferric carboxymaltose may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ALL** of the following criteria are met:

- ONE of the following:
  - Age 18 years or older and ALL of the following:
    - Diagnosis of ONE of the following, including lab values obtained within the past 4 weeks:
      - Iron deficiency anemia (IDA) without chronic kidney disease (CKD), as indicated by ONE of the following:
        - Serum ferritin < 30 ng/mL; or
        - Transferrin saturation (TSAT) < 20%; or
        - Absence of stainable iron in bone marrow;

        OR
      - Iron deficiency anemia (IDA) with chronic kidney disease (CKD) in patients not requiring dialysis, as indicated by ONE of the following:
        - Serum ferritin < 100 ng/mL; or
        - Transferrin saturation (TSAT) < 30%;

      AND
    - ONE of the following:
      - Inadequate response to full course of treatment (at least 3 months) of oral iron; or
      - Anatomic or physiologic condition that interferes with oral iron absorption; or
      - Documented intolerance, FDA labeled contraindication, or hypersensitivity to oral iron;

AND

- ONE of the following:
  - Inadequate response to iron dextran (Infed®), iron sucrose (Venofer®), or ferric gluconate (Ferrlecit®); or
  - Documented intolerance, FDA labeled contraindication, or hypersensitivity to iron dextran (Infed®), iron sucrose (Venofer®), and ferric gluconate (Ferrlecit®);

OR

- Age 18 years or older and ALL of the following:
  - Diagnosis of iron deficiency (with or without anemia); **AND**
  - New York Heart Association (NYHA) functional class II or III heart failure; **AND**
  - Left ventricular ejection fraction (LVEF) ≤ 45%; **AND**
  - ONE of the following:
    - Serum ferritin < 100 ng/mL; or
    - Serum ferritin 100-300 ng/mL AND transferrin saturation (TSAT) < 20%;

OR

- Age 1 year to ≤ 17 years and ALL of the following:
  - Diagnosis of iron deficiency anemia as indicated by ONE of the following:
    - Serum ferritin < 100 ng/mL; or
    - Transferrin saturation (TSAT) < 20%; or
    - Hemoglobin < 12 g/dL;

    AND
  - ONE of the following:
    - Inadequate response to full course of treatment (at least 3 months) of oral iron; or
    - Anatomic or physiologic condition that interferes with oral iron absorption; or
    - Documented intolerance, FDA labeled contraindication, or hypersensitivity to oral iron;

AND

- No FDA labeled contraindications to the requested agent (see table 1 below); **AND**
- Requested dose is within the FDA labeled dose for the indication (see table 2 below); **AND**
- For commercial health plan members only, step therapy supplement criteria may apply for select conditions (see policy II-242: Step Therapy Supplement).

III. Renewal Review for ferumoxytol (Feraheme®), ferric carboxymaltose (Injectafer®), ferric derisomaltose (Monoferric®)

Use of ferumoxytol, ferric carboxymaltose, or ferric derisomaltose may be considered **MEDICALLY NECESSARY AND APPROPRIATE** for retreatment in adult patients when **ALL** of the following criteria are met:

- Previously approved for the requested agent through the initial review process; **AND**
- Continued positive clinical response to the requested agent (e.g., increased hemoglobin level); **AND**
- Recent laboratory results (within the past 4 weeks) since last administration of the requested agent demonstrating a need for additional therapy; **AND**
- No FDA labeled contraindications to the requested agent (see table 1 below); **AND**
- Requested dose is within the FDA labeled dose for the indication (see table 2 below).

IV. Experimental/Investigative Uses

All other uses of ferumoxytol (Feraheme®) for iron deficiency anemia in patients not requiring dialysis are considered **EXPERIMENTAL/INVESTIGATIVE** due to the lack of evidence demonstrating an impact on improved health outcomes.

All other uses of ferric carboxymaltose (Injectafer®) or ferric derisomaltose (Monoferric®) are considered **EXPERIMENTAL/INVESTIGATIVE** due to the lack of evidence demonstrating an impact on improved health outcomes.

Table 1. FDA Labeled Contraindications

Agent	FDA Labeled Contraindications
Ferumoxytol (Feraheme®)	Known hypersensitivity to Feraheme® or any of its components. History of allergic reaction to any intravenous iron product.
Ferric carboxymaltose (Injectafer®)	Hypersensitivity to Injectafer® or any of its inactive components.
Ferric derisomaltose (Monoferric®)	Serious hypersensitivity to Monoferric® or any of its components.

Table 2. Dosing

NOTE: See documentation submission requirements below if the requested dose is outside of the dosing criteria provided in this table.

<table>
<tr><th>Agent</th><th>Dosing</th></tr>
<tr><td>Ferumoxytol (Feraheme®)</td><td>Initial 510 mg dose in intravenous infusion followed by a second 510 mg dose 3 to 8 days later.</td></tr>
<tr><td>Ferric carboxymaltose (Injectafer®) – adults</td><td>Recommended dosage for iron deficiency anemia:
For patients weighing 50 kg (110 lb) or more:
• Two-dose regimen: 750 mg once then second dose of 750 mg after ≥7 days. Maximum dose: 1500 mg per treatment course.
• Single-dose regimen: 15 mg/kg as a single dose. Maximum dose: 1,000 mg.
For patients weighing less than 50 kg (110 lb):
• Two-dose regimen: 15 mg/kg once then second dose of 15 mg/kg after ≥7 days.
Treatment may be repeated if iron deficiency anemia reoccurs.
Recommended dosage for iron deficiency with heart failure:
For patients weighing 70 kg (154 lb) or more:
<table>
<tr><th></th><th>< 10 Hb (g/dL)</th><th>10-14 Hb (g/dL)</th><th>> 14 to <15 Hb (g/dL)</th></tr>
<tr><td>Day 1</td><td>1,000 mg</td><td>1,000 mg</td><td>500 mg</td></tr>
<tr><td>Week 6</td><td>1,000 mg</td><td>500 mg</td><td>No dose</td></tr>
</table>
For patients weighing less than 70 kg (154 lb):</td></tr>
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<tr><th></th><th>< 10 Hb (g/dL)</th><th>10-14 Hb (g/dL)</th><th>> 14 to <15 Hb (g/dL)</th></tr>
<tr><td>Day 1</td><td>1,000 mg</td><td>1,000 mg</td><td>500 mg</td></tr>
<tr><td>Week 6</td><td>500 mg</td><td>No dose</td><td>No dose</td></tr>
</table>
Administer a maintenance dose of 500 mg at 12, 24, and 36 weeks if serum ferritin < 100 ng/mL or serum ferritin 100-300 ng/mL with transferrin saturation <20%. Treatment may be repeated if iron deficiency in heart failure reoccurs.
</td></tr>
<tr><td>Ferric carboxymaltose (Injectafer®) – pediatric</td><td>

Two-dose regimen: IV: 15 mg/kg once then second dose of 15 mg after ≥7 days. Maximum dose: 750 mg/dose.
Single-dose regimen: IV: 15 to 20 mg/kg/dose as a single dose. Maximum dose: 1,000 mg/dose.

Treatment may be repeated if iron deficiency anemia reoccurs.
</td></tr>
<tr><td>Ferric derisomaltose (Monoferric®)</td><td>
For patients weighing 50 kg or more:

Administer 1,000 mg of drug as an intravenous infusion.

For patients weighing less than 50 kg:

Administer drug as 20 mg/kg actual body weight as an intravenous infusion.

Repeat treatment if iron deficiency anemia reoccurs.
</td></tr>
</table>

Documentation Submission:

Documentation supporting the medical necessity criteria described in the policy must be included in the prior authorization when prior authorization is required. In addition, the following documentation must also be submitted:

Initial Review

1. Clinical notes describing the diagnosis and clinical features of the diagnosis.
2. Laboratory values demonstrating treatment failure of oral or intravenous therapy after at least 3 weeks of therapy.
3. Laboratory values should be obtained within 1 to 3 weeks following the last dose of intravenous iron in a treatment course.
4. The dose being requested and patient's weight if requested agent includes weight-based dosing. If the requested dose is outside of the dosing criteria provided in the table above, a clear explanation for the medical necessity of the requested dose MUST be submitted, including prior dosing (strength and frequency) associated with inadequate response.
5. For commercial health plan members only, when step therapy requirements apply for the requested indication, documentation for one or more of the step therapy supplement criteria MUST be provided (see policy II-242).

Renewal Review

1. Documentation of prior approval for the requested agent through the initial review process.
2. Documentation, since most recent approval, supporting continued positive clinical response (e.g., increased hemoglobin level).
3. Laboratory results indicating need for further intravenous iron therapy.

4. The dose being requested, including the patient's weight. If the requested dose is outside of the dosing criteria provided in the table above, a clear explanation for the medical necessity of the requested dose MUST be submitted, including prior dosing (strength and frequency) associated with inadequate response.

Policies Delegated to eviCore
None

Policies Inactivated
None