Medical and Behavioral Health Policy Activity

Policies Effective: June 3, 2024 Notification Posted: April 1, 2024

Policies Developed

- **Exagamglogene autotemcel (Casgevy), II-293**

I. <u>Initial Review for Exagamglogene Autotemcel (Casgevy™) for Sickle Cell Disease</u>

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

- Age 12 years or older; **AND**
- Diagnosis of sickle cell disease (includes genotypes β^S/β^S, β^S/β^0, or β^S/β^+) as confirmed by genetic testing by HBB sequence gene analysis showing biallelic pathogenic variants; **AND**
- ONE of the following:
  - Symptomatic disease despite treatment with hydroxyurea and add-on therapy (e.g., crizanlizumab, voxelotor, etc.); OR
  - Previously tried and failed hydroxyurea and add-on therapy (e.g., crizanlizumab, voxelotor, etc.); OR
  - Documented intolerance, FDA labeled contraindication, or hypersensitivity to hydroxyurea and add-on therapy (e.g., crizanlizumab, voxelotor, etc.);

  AND
- At least 4 vaso-occlusive crises (VOCs) in the prior 24 months while adhering to treatment; **AND**
- VOCs require a visit to a medical facility for evaluation AND BOTH of the following:
  - Require subsequent interventions such as opioid pain management, non-steroidal anti-inflammatory drugs, RBC transfusion, etc.; AND
  - VOCs manifest as ONE OR MORE of the following:
    - Acute pain; OR
    - Acute chest syndrome; OR
    - Acute splenic sequestration; OR
    - Acute hepatic sequestration; OR
    - Priapism lasting >2 hours;

  AND
- Candidate for an autologous hematopoietic stem cell transplantation; **AND**
- Screened and found negative for hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus 1 & 2 (HIV-1/HIV-2); **AND**
- No serious concomitant illness (e.g., advanced liver disease, uncorrected bleeding disorder, prior or current malignancy, myeloproliferative and/or immunodeficiency disorder); **AND**
- Not previously treated with exagamglogene autotemcel or other gene therapies (e.g., lovotibeglogene autotemcel [Lyfgenia®]); **AND**
- No previous hematopoietic stem cell transplantation; **AND**
- Prescribed by, or in consultation with, a hematologist or transplant specialist; **AND**
- No FDA labeled contraindications to therapy (see table 1 below).

II. <u>Initial Review for Exagamglogene Autotemcel (Casgevy™) for Transfusion-Dependent Beta Thalassemia</u>

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

- Age 12 years or older; **AND**

- Diagnosis of beta thalassemia (includes homozygous beta thalassemia or compound heterozygous beta thalassemia including beta thalassemia/hemoglobin E [HbE]) as confirmed by genetic testing by HBB sequence gene analysis showing biallelic pathogenic variants; **AND**
- Absence of sickle cell beta thalassemia or alpha thalassemia; **AND**
- Transfusion dependent disease (i.e., Hb <70 g/L on 2 occasions at least 2 weeks apart AND/OR presence of clinical criteria irrespective of Hb level, including poor growth/ failure to thrive, significant symptomatic anemia, complications from excessive intramedullary hematopoiesis, or clinically significant extramedullary hematopoiesis); **AND**
- ONE of the following:
  - T2*-weighted magnetic resonance imaging [MRI] measurements of myocardial iron greater than 10 msec; OR
  - Left ventricular ejection fraction (LVEF) greater than 45% by echocardiogram;

  AND
- Candidate for an autologous hematopoietic stem cell transplantation; **AND**
- Screened and found negative for hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus 1 & 2 (HIV-1/HIV-2); **AND**
- No serious concomitant illness (e.g., advanced liver disease, uncorrected bleeding disorder, prior or current malignancy, myeloproliferative and/or immunodeficiency disorder, uncontrolled seizure disorder); **AND**
- Not previously treated with exagamglogene autotemcel or other gene therapies (e.g., lovotibeglogene autotemcel [Lyfgenia®]); **AND**
- No previous hematopoietic stem cell transplantation; **AND**
- Prescribed by, or in consultation with, a hematologist or transplant specialist; **AND**
- No FDA labeled contraindications to therapy (see table 1 below).

III. Renewal Review for Exagamglogene Autotemcel (Casgevy™)

Use of exagamglogene autotemcel for more than one treatment course (i.e., one dose) is considered **EXPERIMENTAL/INVESTIGATIVE** due to the lack of clinical evidence demonstrating an impact on improved health outcomes.

IV. Experimental/Investigative Uses

All other uses of exagamglogene autotemcel 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
Exagamglogene autotemcel	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 for Sickle Cell Disease

1. Clinical notes describing the diagnosis and clinical features of the diagnosis.
2. Laboratory documentation confirming diagnosis of sickle cell disease by HBB sequence gene analysis showing biallelic pathogenic variants.
3. Documentation of at least 4 VOCs in the prior 24 months.

4. Documentation that the patient is clinically stable and able to undergo a hematopoietic stem cell transplant.
5. Clinical notes describing current and past medications for the diagnosis, including response to the medications.

Initial Review for Transfusion-Dependent Beta Thalassemia

1. Clinical notes describing the diagnosis and clinical features of the diagnosis.
2. Laboratory documentation confirming diagnosis of beta thalassemia by HBB sequence gene analysis showing biallelic pathogenic variants.
3. Documentation of transfusion dependent disease (i.e., Hb <70 g/L on 2 occasions at least 2 weeks apart AND/OR presence of clinical criteria irrespective of Hb level, including poor growth/ failure to thrive, significant symptomatic anemia, complications from excessive intramedullary hematopoiesis, or clinically significant extramedullary hematopoiesis).
4. Documentation of T2*-weighted MRI measurements of myocardial iron greater than 10 msec (confirming absence of severe iron overload) or LVEF greater than 45% by echocardiogram.
5. Documentation that the patient is clinically stable and able to undergo a hematopoietic stem cell transplant.
6. Clinical notes describing current and past medications for the diagnosis, including response to the medications.

- **Lovotibeglogene autotemcel (Lyfgenia), II-294**

I. Initial Review for Lovotibeglogene Autotemcel (Lyfgenia®)

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

- Age 12 years or older; **AND**
- Diagnosis of sickle cell disease (includes genotypes β^S/β^S, β^S/β^0, or β^S/β^+) as confirmed by genetic testing by HBB sequence gene analysis showing BOTH of the following:
  - Biallelic pathogenic variants; AND
  - Not more than 2 alpha-globin gene deletions;

  AND
- ONE of the following:
  - Symptomatic disease despite treatment with hydroxyurea and add-on therapy (e.g., crizanlizumab, voxelotor, etc.); OR
  - Previously tried and failed hydroxyurea and add-on therapy (e.g., crizanlizumab, voxelotor, etc.); OR
  - Documented intolerance, FDA labeled contraindication, or hypersensitivity to hydroxyurea and add-on therapy (e.g., crizanlizumab, voxelotor, etc.);

  AND
- At least 4 vaso-occlusive crises (VOCs) in the prior 24 months while adhering to treatment; **AND**
- VOCs require a visit to a medical facility for evaluation AND BOTH of the following:
  - Require subsequent interventions such as opioid pain management, non-steroidal anti-inflammatory drugs, RBC transfusion, etc.; AND
  - VOCs manifest as ONE OR MORE of the following:
    - Acute pain; OR
    - Acute chest syndrome; OR
    - Acute splenic sequestration; OR
    - Acute hepatic sequestration; OR
    - Priapism lasting >2 hours;

  AND
- Candidate for an autologous hematopoietic stem cell transplantation; **AND**
- Screened and found negative for hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus 1 & 2 (HIV-1/HIV-2); **AND**

- No serious concomitant illness (e.g., advanced liver disease, uncorrected bleeding disorder, prior or current malignancy, immunodeficiency disorder); **AND**
- Not previously treated with lovotibeglogene autotemcel or other gene therapies (e.g., exagamglogene autotemcel [Casgevy™]); **AND**
- No previous hematopoietic stem cell transplantation; **AND**
- Prescribed by, or in consultation with, a hematologist or transplant specialist; **AND**
- No FDA labeled contraindications to therapy (see table 1 below).

II. Renewal Review for Lovotibeglogene Autotemcel (Lyfgenia®)

Use of lovotibeglogene autotemcel for more than one treatment course (i.e., one dose) is considered **EXPERIMENTAL/INVESTIGATIVE** due to the lack of clinical evidence demonstrating an impact on improved health outcomes.

III. Experimental/Investigative Uses

All other uses of lovotibeglogene autotemcel 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
Lovotibeglogene autotemcel	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 documentation confirming diagnosis of sickle cell disease by HBB sequence gene analysis showing biallelic pathogenic variants AND not more than 2 alpha-globin gene deletions.
3. Documentation of at least 4 VOCs in the prior 24 months.
4. Documentation that the patient is clinically stable and able to undergo a hematopoietic stem cell transplant.
5. Clinical notes describing current and past medications for the diagnosis, including response to the medications.

Policies Revised

- **Spinal Manipulation Under Anesthesia, II- 116**

NOTE: This policy does not address manipulation under anesthesia for fractures, completely dislocated joints, adhesive capsulitis (e.g., frozen shoulder), and/or fibrosis of a joint that may occur following total joint replacement.

All forms of spinal manipulation under anesthesia (SMUA) (including spinal manipulation under joint anesthesia [SMUJA] and spinal manipulation after epidural anesthesia and corticosteroid injection [SMUESI]) are considered **EXPERIMENTAL/INVESTIGATIVE** for the treatment of chronic spinal (i.e., cranial, cervical, thoracic, lumbar) pain and chronic sacroiliac and pelvic pain due to a lack of clinical evidence demonstrating an impact on improved health outcomes.

- **Percutaneous Electrical Nerve Stimulation, Percutaneous Neuromodulation Therapy, and Restorative Neurostimulation Therapy, II-81**

  Percutaneous electrical nerve stimulation is considered **EXPERIMENTAL/ INVESTIGATIVE** for all indications due to the lack of clinical evidence demonstrating an impact on improved health outcomes.

  Percutaneous neuromodulation therapy is considered **EXPERIMENTAL/ INVESTIGATIVE** for all indications due to the lack of clinical evidence demonstrating an impact on improved health outcomes.

  Percutaneous electrical nerve field stimulation is considered **EXPERIMENTAL/ INVESTIGATIVE** for all indications due to the lack of clinical evidence demonstrating an impact on improved health outcomes.

  Restorative neurostimulation therapy (e.g., ReActiv8) is considered **EXPERIMENTAL/ INVESTIGATIVE** for all indications due to the lack of clinical evidence demonstrating an impact on improved health outcomes.

- **Axial (Percutaneous) Lumbar Interbody Fusion, IV- 91**

  Axial (percutaneous) lumbar interbody fusion is considered **EXPERIMENTAL/ INVESTIGATIVE** for all indications, including but not limited to pseudoarthrosis, spinal stenosis, and spondylolisthesis, due to the lack of clinical evidence demonstrating an impact on improved health outcomes.

- **Evinacumab (Evkeeza), II-250**

I. Initial Review for Evinacumab (Evkeeza®)

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

- Age 5 or older; **AND**
- Diagnosis of homozygous familial hypercholesterolemia (HoFH) as indicated by ONE of the following:
  - Genetic testing confirming confirmation of two mutant alleles at the LDL-R, APOB, PCSK9, or LDLRAP1 genes; OR
  - Untreated total cholesterol > 500 mg/dL (12.93 mmol/L) and ONE of the following;
    - LDL-C > 250 mg/dL (6.47 mmol/L) in both parents (untreated); or
    - Cutaneous or tendinous xanthoma before the age of 10 years;

  AND
- Used as an adjunct to a low-fat or heart-healthy diet; **AND**
- Receiving stable background lipid lowering therapy for at least 4 weeks; **AND**
- Evinacumab will be used in conjunction with other LDL-lowering therapies (e.g., statins, ezetimibe, PCSK9 inhibitors, LDL apheresis); **AND**
- Patient has tried and failed at least a 3-month trial of adherent therapy with BOTH of the following:
  - Ezetimibe used in combination with the highest available (or maximally tolerated) dose of atorvastatin OR rosuvastatin, unless contraindicated; AND
  - Combination therapy consisting of the highest available (or maximally tolerated) dose of atorvastatin OR rosuvastatin, ezetimibe, AND a PSCK9 inhibitor indicated for HoFH (e.g., evolocumab), unless contraindicated;

  AND
- Despite pharmacological treatment with a PCSK9 inhibitor, statin, and ezetimibe, unless contraindicated, the patient's LDL cholesterol ≥ 100 mg/dL (or ≥ 70 mg/dL for patients with clinical atherosclerotic cardiovascular disease [ASCVD]); **AND**
- Prescribed by or in consultation with a specialist (e.g., endocrinologist, cardiologist); **AND**
- No FDA labeled contraindications to evinacumab (see table 1 below); **AND**

- Requested dose is within the FDA labeled dose for the labeled indication (see table 2 below).

II. Renewal Review for Evinacumab (Evkeeza®)

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

- Previously approved for evinacumab through the initial review process; **AND**
- Continued positive clinical response to evinacumab (e.g., 30% decrease in LDL-C from baseline at 6 months); **AND**
- Patient continues to adhere to diet and background lipid lowering therapy (e.g., statin, ezetimibe, PCSK9-I, lomitapide, LDL apheresis); **AND**
- Prescribed by or in consultation with a specialist (e.g., endocrinologist, cardiologist); **AND**
- No FDA labeled contraindications to evinacumab (see table 1 below); **AND**
- Requested dose is within the FDA labeled dose for the labeled indication (see table 2 below).

III. Experimental/Investigative Uses

All other uses of evinacumab are considered **EXPERIMENTAL/INVESTIGATIVE,** including but not limited to, treatment of heterozygous familial hypercholesterolemia (HeFH), due to the lack of clinical evidence demonstrating an impact on improved health outcomes.

Table 1. FDA Labeled Contraindications

Agent	FDA Labeled Contraindications
Evinacumab	History of serious hypersensitivity reactions to evinacumab or to any of the excipients in Evkeeza®

Table 2. Dosing

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

FDA Labeled Indications	Dosing
Homozygous familial hypercholesterolemia (HoFH)	15 mg/kg by intravenous (IV) infusion once monthly (every 4 weeks)

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 associated symptoms.

2. Genetic testing and laboratory documentation as required in the policy criteria.
3. Clinical notes describing current and past medications for the diagnosis, including response to the medications.
4. The dose being requested, including the patient's weight.

Renewal Review
1. Documentation of prior approval for evinacumab through the initial review process.
2. Laboratory documentation as required in the policy criteria.
3. Documentation, since most recent approval, supporting continued positive clinical response (e.g., percentage decreased LDL).
4. The dose being requested, including the patient's weight.

- **Teprotumumab (Tepezza), II- 239**

I. Initial Review for Teprotumumab (Tepezza®)

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

- Diagnosis of Graves' disease; **AND**
- Diagnosis of thyroid eye disease; **AND**
- ONE of the following:
  - Active disease AND ONE of the following:
    - Previously tried and failed glucocorticoids; OR
    - Documented intolerance, FDA labeled contraindication, or hypersensitivity to glucocorticoids;

    OR
  - Inactive disease (i.e., stable, chronic);

  AND
- Not previously treated for thyroid eye disease with orbital irradiation or surgery; **AND**
- Prescribed by an ophthalmologist; **AND**
- No FDA labeled contraindications to teprotumumab (see table 1 below); **AND**
- Dose is within the FDA labeled dose for the indication (see table 2 below); **AND**
- For commercial and Medicaid health plan members only, step therapy supplement criteria may apply for select conditions (see policy II-242: Step Therapy Supplement).

II. Renewal Review for Teprotumumab (Tepezza®)

Use of teprotumumab following 8 intravenous infusions is considered **EXPERIMENTAL/ INVESTIGATIVE** due to the lack of clinical evidence demonstrating an impact on improved health outcomes.

III. Experimental/Investigative Uses

All other uses of teprotumumab, including but not limited to restarting an incomplete course of therapy or retreatment, 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
Teprotumumab (Tepezza®)	None

Table 2. Dosing

FDA Labeled Indications	Dosing
Thyroid Eye Disease	10 mg/kg followed by 20 mg/kg every 3 weeks for 7 additional infusions.

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:

1. Clinical notes describing the diagnosis and clinical features of the diagnosis.
2. Clinical notes describing current and past medications for the diagnosis, including response to the medications.
3. The dose being requested.
4. For commercial and Medicaid 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).

Policies Delegated to eviCore
None

Policies Inactivated
None