Medical and Behavioral Health Policy Activity

Policies Effective: December 4, 2023 Notification Posted: October 1, 2023

Policies Developed

- **Delandistrogene moxeparvovec, II-284**
  All uses of delandistrogene moxeparvovec, including but not limited to treatment of Duchenne muscular dystrophy (DMD), are considered **EXPERIMENTAL/INVESTIGATIVE** due to the lack of evidence demonstrating an impact on improved health outcomes.

- **Valoctocogene roxaparvovec, II-286**
  NOTE: When factor prophylaxis therapy will be used, please refer to the applicable pharmacy benefit plan.

I. Valoctocogene roxaparvovec (Roctavian®) may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ALL** of the following criteria are met:

- Age ≥ 18 years; **AND**
- Diagnosis of severe hemophilia A (congenital factor VIII deficiency) as evidenced by documentation of past or current factor VIII levels < 1 IU/dL; **AND**
- Evidence of any bleeding disorder not related to hemophilia A has been ruled out; **AND**
- Currently on prophylactic factor VIII replacement therapy for ≥ 12 months; **AND**
- Patient has been tested for anti-adeno-associated virus serotype 5 (AAV5) antibodies and is deemed a suitable candidate for treatment; **AND**
- Laboratory testing confirms absence of factor VIII inhibitor; **AND**
- Prescribed by or in consultation with a hematologist affiliated with a federally recognized hemophilia treatment center (HTC); **AND**
- Absence of ALL of the following:
  - Liver cirrhosis of any etiology; AND
  - Untreated or unresolved Hepatitis B or C; AND
  - Alanine transaminase (ALT) >2 times the upper limit of normal; AND
  - Bilirubin >2 times the upper limit of normal; AND
  - Alkaline phosphatase >2 times the upper limit of normal;

  AND
- No other serious concomitant illness; **AND**
- Not previously treated with valoctocogene roxaparvovec or other gene therapies; **AND**
- No FDA labeled contraindications to valoctocogene roxaparvovec (see table 1 below).

II. All other uses of valoctocogene roxaparvovec are considered **EXPERIMENTAL/INVESTIGATIVE**, including but not limited to treatment of hemophilia A not meeting the criteria above and repeat infusions, due to the lack of clinical evidence demonstrating an impact on improved health outcomes.

Table 1. FDA Labeled Contraindications

Agent	FDA Labeled Contraindications
Valoctocogene roxaparvovec (Roctavian®)	Active infections, either acute or uncontrolled chronic. Known significant hepatic fibrosis (stage 3 or 4) or

	cirrhosis. Known hypersensitivity to mannitol.

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. Documentation confirming severe hemophilia A and past or current factor VIII levels < 1 IU/dL.
3. Documentation confirming prophylactic factor VIII replacement therapy.
4. Laboratory testing confirms anti-adeno-associated virus serotype 5 (AAV5) antibody titer testing and absence of factor VIII inhibitor.
5. Clinical notes describing current and past medications for the diagnosis when applicable, including response to the medications.

Policies Revised

- **Vagus Nerve Stimulation, IV-131**

I. Implantable vagus nerve stimulation may be considered **MEDICALLY NECESSARY AND APPROPRIATE** for the treatment of medically refractory or intractable epileptic seizures, defined as failure of at least two antiepileptic drugs.

II. Repeat/ revision of an implantable vagus nerve stimulator may be considered **MEDICALLY NECESSARY AND APPROPRIATE** for a non-functioning stimulator and/or lead migration.

III. Implantable vagus nerve stimulation is considered **EXPERIMENTAL/INVESTIGATIVE** for all other indications, due to a lack of evidence demonstrating an impact on improved health outcomes. Those indications include, but are not limited to, the following:

- Chronic or recurrent depression
- Essential tremor
- Headache (including but not limited to cluster and migraine headache)
- Obesity
- Fibromyalgia
- Congestive heart failure
- Tinnitus
- Traumatic brain injury (TBI)
- Post-traumatic stress disorder (PTSD)
- Upper-limb impairment due to stroke

IV. Non-implantable transcutaneous vagus nerve stimulation is considered **EXPERIMENTAL/INVESTIGATIVE** for all indications due to the lack of clinical evidence demonstrating an impact on improved health outcomes.

- **Islet Cell Transplantation and Cellular Therapy, IV-09**

I. Autologous islet cell transplantation may be considered **MEDICALLY NECESSARY AND APPROPRIATE** as an adjunct to a total or near total pancreatectomy in patients with chronic pancreatitis.

II. Allogeneic islet cell transplantation is considered **EXPERIMENTAL/INVESTIGATIVE** for the treatment of type I diabetes due to the lack of evidence demonstrating an impact on improved health outcomes.

III. Allogeneic islet cellular suspension therapy (e.g., donislecel) is considered **EXPERIMENTAL/ INVESTIGATIVE** for the treatment of type I diabetes due to the lack of evidence demonstrating clinical benefit and evidence demonstrating significant adverse events.

IV. Autologous and allogeneic islet cell transplantation and allogeneic islet cellular suspension therapy (e.g., donislecel) is considered **EXPERIMENTAL/ INVESTIGATIVE** for all other indications.

- **Hematopoietic Stem Cell Transplantation for Acute Lymphoblastic Leukemia, II-118**

I. Pediatric

Initial Transplant

- **Allogeneic or autologous** hematopoietic stem cell transplantation (HSCT) may be considered **MEDICALLY NECESSARY AND APPROPRIATE** to treat childhood acute lymphoblastic leukemia (ALL) in the following situations:
  - First complete remission, but at high risk of relapse, when the patient has **ONE OR MORE** of the following risk factors for relapse:
    - Poor response to initial therapy including poor response to prednisone prophase (defined as an absolute blast count of 1000/μL or greater), or poor treatment response to induction therapy at 6 weeks with high risk having ≥1% minimal residual disease measured by flow cytometry;
    - T-cell phenotype;
    - Poor prognosis genetic abnormalities;

  OR
  - Second or greater remission; OR
  - In patients with relapsed or refractory ALL.

Repeat Transplant

- A second, repeat allogeneic hematopoietic stem cell transplantation (HSCT) may be considered **MEDICALLY NECESSARY AND APPROPRIATE** to treat childhood acute lymphoblastic leukemia (ALL) for relapsing disease, ≥ 6 months after first HSCT.

Experimental/Investigative

- HSCT (allogeneic or autologous) is considered **EXPERIMENTAL/INVESTIGATIVE** to treat childhood ALL for all other indications due to the lack of clinical evidence demonstrating an impact on improved health outcomes.

II. Adults

Initial Transplant
Allogeneic

- Allogeneic HSCT may be considered **MEDICALLY NECESSARY AND APPROPRIATE** to treat adult ALL in the following situations:
  - First or greater complete remission; OR
  - In patients with relapsed or refractory ALL.

- **Reduced-intensity conditioning (RIC) allogeneic** HSCT may be considered **MEDICALLY NECESSARY AND APPROPRIATE** as a treatment of ALL in patients who are in complete marrow and extramedullary first or second remission and who are unable to tolerate a standard myeloablative conditioning regimen, due to the presence of co-morbid conditions (e.g., liver or kidney dysfunction, generalized debilitation, prior intensive chemotherapy, low Karnofsky Performance Status).

Autologous

- Autologous HSCT may be considered **MEDICALLY NECESSARY AND APPROPRIATE** to treat adult ALL **in the absence of a suitable allogeneic donor** in the following situation:
  - First complete remission but at high risk of relapse when the patient has **ONE OR MORE** of the following risk factors for relapse:
    - Leukocytosis at presentation of ≥30,000/μL (B-cell lineage) OR ≥100,000/μL (T-cell lineage);
    - Poor prognosis genetic abnormalities;
    - Extramedullary disease;
    - Minimal residual disease (MRD) positivity at the end of induction.

Repeat Transplant

- A second, repeat allogeneic transplant for may be considered **MEDICALLY NECESSARY AND APPROPRIATE** to treat relapsing adult ALL > 6 months after first HSCT.

Experimental/Investigative

- HSCT (allogeneic or autologous) is considered **EXPERIMENTAL/INVESTIGATIVE** to treat adult ALL for all other indications due to the lack of clinical evidence demonstrating an impact on improved health outcomes.

- **Axicabtagene Ciloleucel, II-187**

I. Review for Axicabtagene Ciloleucel (Yescarta®) for Second-Line Therapy or Greater

Axicabtagene ciloleucel (Yescarta®) may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ALL** of the following criteria are met:

- Age 18 years or older (unless otherwise specified); **AND**
- Diagnosis of ANY of the following non-Hodgkin lymphomas (NHL):
  - DLBCL not otherwise specified; OR
  - HHV8-positive DLBCL; OR
  - High-grade B-cell lymphoma; OR
  - HIV-related DLBCL; OR
  - Monomorphic post-transplant lymphoproliferative disorder; OR
  - Primary mediastinal large B-cell lymphoma (adult or pediatric patients);

  AND
- Disease is refractory to first-line chemoimmunotherapy or relapses within 12 months of first-line chemoimmunotherapy; **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; **AND**
- No FDA labeled contraindications to axicabtagene ciloleucel; **AND**
- Screened for hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) infection; **AND**
- Does not have ANY of the following:
  - Active infection;
  - Inflammatory disorders;
  - Primary central nervous system lymphoma.
  - Active central nervous system involvement by malignancy.

  AND

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

II. Review for Axicabtagene Ciloleucel (Yescarta®) for Third-Line Therapy or Greater

Axicabtagene ciloleucel (Yescarta®) may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when ALL of the following criteria are met:

- Age 18 years or older; **AND**
- Diagnosis of ANY of the following non-Hodgkin lymphomas (NHL):
  - DLBCL arising from indolent lymphomas/ follicular lymphoma/ nodal marginal zone lymphoma; OR
  - Follicular lymphoma; OR
  - Gastric malt lymphoma; OR
  - Nodal marginal zone lymphoma; OR
  - Nongastric MALT lymphoma (noncutaneous); OR
  - Splenic marginal zone lymphoma;

  AND
- Disease is refractory or relapsed after TWO or more lines of systemic therapy, including ALL of the following:
  - Anti-CD20 monoclonal antibody (e.g., rituximab) unless tumor is CD20-negative; AND
  - An anthracycline-containing chemotherapy regimen (e.g., doxorubicin, epirubicin, daunorubicin), except for patients with follicular lymphoma; AND
  - For patients with transformed FL, prior chemotherapy for FL and chemorefractory disease after transformation to DLBCL;

  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; **AND**
- No FDA labeled contraindications to axicabtagene ciloleucel; **AND**
- Screened for hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) infection; **AND**
- Does not have ANY of the following:
  - Active infection;
  - Inflammatory disorders;
  - Primary central nervous system lymphoma.
  - Active central nervous system involvement by malignancy.

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

III. Experimental/ Investigative Uses

All other uses of axicabtagene ciloleucel 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
Axicabtagene ciloleucel	None

- **Brexanolone, II-231**

I. Brexanolone (Zulresso™) may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ALL** of the following criteria are met:

- Age ≥ 15 years; **AND**
- ≤ 6 months since childbirth at the time of request; **AND**
- Diagnosis of moderate to severe postpartum depression, including documentation from standardized rating scales that reliably measure depressive symptoms (e.g., Hamilton Rating Scale for Depression, Montgomery-Asberg Depression Rating Scale, or PHQ-9); **AND**
- Onset of depressive episode is between the third trimester of pregnancy through 8 weeks postpartum; **AND**
- ONE of the following:
  - Inadequate response to two or more trials of antidepressants from at least two different therapeutic classes (e.g., selective serotonin reuptake inhibitors [SSRIs], serotonin-norepinephrine reuptake inhibitors [SNRIs], tricyclic antidepressants [TCAs]) in the current depressive episode; or
  - Documented intolerance, FDA labeled contraindication, or hypersensitivity to two or more antidepressants from at least two different therapeutic classes; or
  - Use of other antidepressant medications is deemed unsafe, as determined by the treating physician and supported in the submitted documentation; or
  - Patient shows a potential risk of harm to self and/or others, as determined by the treating physician and supported in the submitted documentation;

  AND
- Prescribed by, or in consultation with, a psychiatrist; **AND**
- Not previously treated with brexanolone in current postpartum period; **AND**
- No FDA labeled contraindications to brexanolone (see table 1 below); **AND**
- The dose is within the FDA labeled dose (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. All other uses of brexanolone 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
Brexanolone (Zulresso™)	None

Table 2. Dosing

FDA Labeled Indications	Dosing

Postpartum depression (PPD)	0-4 hours: 30 mcg/kg/hour 4-24 hours: 60 mcg/kg/hour 24-52 hours: 90 mcg/kg/hour (or 60 mcg/kg/hour for those who do not tolerate 90 mcg/kg/hour) 52-56 hours: 60 mcg/kg/hour 56-60 hours: 30 mcg/kg/hour

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. The dose being requested.
3. 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).

Policies Delegated to eviCore
None

Policies Inactivated
None