Medical and Behavioral Health Policy Activity

Policies Effective: February 5, 2024 Notification Posted: December 1, 2023

Policies Developed

- **Digital Therapeutics for Amblyopia, II-288**
  The use of digital therapeutic systems for the treatment of amblyopia is considered **EXPERIMENTAL/INVESTIGATIVE** due to the lack of clinical evidence demonstrating an impact on improved health outcomes.

- **Digital Therapeutics for Diagnostic Applications, II-289**
  The use of prescription digital therapeutics for diagnostic applications is considered **EXPERIMENTAL/INVESTIGATIVE** for all indications due to the lack of clinical evidence demonstrating an impact on improved health outcomes.

- **Rozanolixizumab, II-287**

I. Initial Review for Rozanolixizumab (Rystiggo®)

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

- Age 18 years or older; **AND**
- Diagnosis of generalized myasthenia gravis (gMG); **AND**
- ONE of the following:
  - Positive serological test for anti-acetylcholine receptor (AChR) antibodies; OR
  - Positive serological test for anti-muscle-specific tyrosine kinase (MuSK) antibodies;

  AND
- Myasthenia Gravis Foundation of America (MGFA) clinical classification II-IV; **AND**
- Myasthenia Gravis Activities of Daily Living (MG-ADL) total score ≥3; **AND**
- Patient has tried and failed treatment within the past 12 months with ONE of the following:
  - At least 2 or more immunosuppressive therapies (e.g., azathioprine, cyclosporine, mycophenolate mofetil, tacrolimus, methotrexate, cyclophosphamide, corticosteroids) either in combination or as monotherapy; OR
  - At least 1 immunosuppressive therapy (e.g., azathioprine, cyclosporine, mycophenolate mofetil, tacrolimus, methotrexate, cyclophosphamide, corticosteroids) AND ONE of the following:
    - Chronic intravenous immunoglobulin (IVIG); OR
    - Plasmapheresis/plasma exchange given at least weekly for a minimum of 4 weeks without symptom control;

    OR
  - Documented intolerance, FDA labeled contraindication, or hypersensitivity to immunosuppressive therapies, IVIG, and plasmapheresis/plasma exchange;

  AND
- Not used in combination with another biologic immunomodulator (e.g., eculizumab [Soliris®], ravulizumab [Ultomiris®], efgartigimod alfa [Vyvgart®], efgartigimod alfa and hyaluronidase [Vyvgart Hytrulo®], rituximab [Rituxan®]); **AND**
- Prescribed by, or in consultation with, a specialist in the patient's disease (e.g., neurologist); **AND**
- No FDA labeled contraindications to rozanolixizumab (see table 1 below); **AND**
- The dose is within the FDA labeled dose (see table 2 below); **AND**
- For commercial health plan members only, rozanolixizumab is administered in accordance with site of service criteria (see policy XI-06); **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 Rozanolixizumab (Rystiggo®)

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

- Previously approved for rozanolixizumab through the initial review process; **AND**
- Continued positive clinical response to rozanolixizumab therapy (e.g., stabilization and/or slowing of disease progression or decrease in symptom severity and/or frequency); **AND**
- Not used in combination with another biologic immunomodulator (e.g., eculizumab [Soliris®], ravulizumab [Ultomiris®], efgartigimod alfa [Vyvgart®], efgartigimod alfa and hyaluronidase [Vyvgart Hytrulo®], rituximab [Rituxan®]); **AND**
- Prescribed by, or in consultation with, a specialist in the patient's disease (e.g., neurologist); **AND**
- No FDA labeled contraindications to rozanolixizumab (see table 1 below); **AND**
- The dose is within the FDA labeled dose (see table 2 below); **AND**
- For commercial health plan members only, rozanolixizumab is administered in accordance with site of service criteria (see policy XI-06).

III. Experimental/Investigative Uses

All other uses of rozanolixizumab, including but not limited to initiating subsequent treatment cycles prior to 63 days from the start of the previous treatment cycle, 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
Rozanolixizumab	None

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>FDA Labeled Indications</th><th>Dosing</th></tr>
<tr><td>Generalized myasthenia gravis</td><td>Administer via subcutaneous infusion once weekly for 6 weeks.

Administer based upon body weight:
<table>
<tr><th>Body Weight</th><th>Dose</th><th>Volume to be Infused</th></tr>
<tr><td>Less than 50 kg</td><td>420 mg</td><td>3 mL</td></tr>
<tr><td>50 kg to less than 100 kg</td><td>560 mg</td><td>4 mL</td></tr>
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	100 kg and above	840 mg	6 mL
	Administer subsequent treatment cycles based on clinical evaluation. The safety of initiating subsequent cycles prior to 63 days from the start of the previous treatment cycle has not been established.		

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. Clinical notes describing current and past treatments for the diagnosis, including response to the treatments.
3. The dose being requested, including the patient's weight if the diagnosis requires 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.
4. For commercial health plan members only, the site of service for rozanolixizumab administration is specified, including CMS place of service code (see policy XI-06). If rozanolixizumab is administered in a hospital outpatient facility, a clear explanation for the medical necessity of the site of service MUST be submitted, including documentation for one or more of the site of service criteria provided in policy XI-06.
5. 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).

Renewal Review

1. Documentation of prior approval for rozanolixizumab through the initial review process.
2. Documentation, since most recent approval, supporting continued positive clinical response with rozanolixizumab therapy (e.g., stabilization and/or slowing of disease progression or decrease in symptom severity and/or frequency).
3. The dose being requested, including the patient's weight if the diagnosis requires 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.
4. For commercial health plan members only, the site of service for rozanolixizumab administration is specified, including CMS place of service code (see policy XI-06). If rozanolixizumab is administered in a hospital outpatient facility, a clear explanation for the medical necessity of the site of service MUST be submitted, including documentation for one or more of the site of service criteria provided in policy XI-06.

Policies Revised

- **Posterior Tibial Nerve Stimulation, IV-135**
  - **I.** Percutaneous posterior tibial nerve stimulation may be considered **MEDICALLY NECESSARY AND APPROPRIATE** for the treatment of urinary dysfunction (i.e., incontinence, urgency frequency, and non-obstructive urinary retention) in patients who meet **ALL** the following criteria:
    - Absence of neurologic disease associated with detrusor hyperreflexia; **AND**

- Absence of outlet obstruction; **AND**
- Symptoms have resulted in significant disability (e.g., the frequency and/or severity of leakages are limiting the patient's ability to work or participate in activities outside the home); **AND**
- Trial and failure of conservative forms of treatment, including BOTH of the following:
  - Behavioral therapy (e.g., bladder training, bladder control strategies, pelvic floor muscle training, fluid management) following 12 weeks of treatment without meeting treatment goals; **AND**
  - Pharmacologic therapy following 8 weeks of treatment without meeting treatment goals OR inability to tolerate pharmacologic therapy.

II. The use of percutaneous posterior tibial nerve stimulation for any other indication is considered **EXPERIMENTAL/INVESTIGATIVE** due to a lack of clinical evidence demonstrating an impact on improved health outcomes.

III. Posterior tibial nerve stimulation by any other means (e.g., subcutaneous, transcutaneous, implantable) is considered **EXPERIMENTAL/INVESTIGATIVE** for all indications due to a lack of clinical evidence demonstrating an impact on improved health outcomes.

- **Hematopoietic Stem Cell Transplantation for Genetic Diseases and Acquired Anemias, II-129**

I. **Allogeneic Hematopoietic Stem-Cell Transplantation**

- Allogeneic hematopoietic stem-cell transplantation may be considered **MEDICALLY NECESSARY AND APPROPRIATE** for selected patients with the following disorders:
  - Hemoglobinopathies
    - Sickle cell anemia in children or young adults with either a history of prior stroke or at increased risk of stroke or end-organ damage
    - Homozygous beta-thalassemia (i.e., thalassemia major)
  - Bone marrow failure syndromes including but not limited to:
    - Acquired aplastic anemia
    - Diamond-Blackfan anemia
    - Dyskeratosis congenita
    - Fanconi anemia
    - Shwachman-Diamond anemia
  - Primary immunodeficiencies
    - Lymphocyte immunodeficiencies
      - Adenosine deaminase deficiency
      - Artemis deficiency
      - Calcium channel deficiency
      - CD40 ligand deficiency
      - Cernunnos/X-linked lymphoproliferative disease deficiency
      - CHARGE syndrome with immune deficiency
      - Common gamma chain deficiency
      - Deficiencies in CD45, CD3, CD8
      - DiGeorge syndrome
      - DNA ligase IV
      - Interleukin-7 receptor alpha deficiency
      - Janus-associated kinase 3 (JAK3) deficiency
      - Major histocompatibility class II deficiency
      - Omenn syndrome
      - Purine nucleoside phosphorylase deficiency
      - Recombinase-activating gene (RAG) 1/2 deficiency

- Reticular dysgenesis
- Severe combined immunodeficiency (SCID)
- Winged helix deficiency
- Wiskott-Aldrich syndrome
- X-linked lymphoproliferative disease
- Zeta-chain-associated protein-70 (ZAP-70) deficiency

▪ Phagocytic deficiencies
- Chediak-Higashi syndrome
- Chronic granulomatous disease
- Hemophagocytic lymphohistiocytosis
- Griscelli syndrome, type 2
- Interferon-gamma receptor deficiencies
- Leukocyte adhesion deficiency
- Severe congenital neutropenia

▪ Other immunodeficiencies
- Autoimmune lymphoproliferative syndrome
- Cartilage hair hypoplasia
- CD25 deficiency
- Hyper IgD and IgE syndromes
- Immunodeficiency, centromeric instability, and facial dysmorphism syndrome (ICF syndrome)
- Immunodysregulation polyendocrinopathy enteropathy X-linked syndrome (IPEX syndrome)
- NEMO deficiency syndrome
- NF-κB inhibitor, alpha (IκB-alpha) deficiency
- Nijmegen breakage syndrome

○ Genetic disorders affecting skeletal tissue
▪ Infantile malignant osteopetrosis (Albers-Schonberg disease or marble bone disease)

○ Inherited metabolic disease
▪ Alpha-mannosidosis
▪ Aspartylglucosaminuria.
▪ Childhood-onset cerebral X-linked adrenoleukodystrophy
▪ Globoid-cell leukodystrophy
▪ Hurler syndrome
▪ Maroteaux-Lamy syndrome
▪ Metachromatic leukodystrophy
▪ Sly syndrome

- Allogeneic hematopoietic stem-cell transplantation is considered **EXPERIMENTAL/INVESTIGATIVE** for treatment of Hunter, Sanfilippo and Morquio syndromes due to a lack of evidence demonstrating an impact on improved health outcomes.

II. Autologous Hematopoietic Stem-Cell Transplantation

- Autologous hematopoietic stem-cell transplantation is considered **EXPERIMENTAL/INVESTIGATIVE** for treatment of genetic diseases and acquired anemias due to a lack of clinical evidence demonstrating an impact on improved health outcomes.

III. Repeat Transplant

- A second (allogeneic or autologous) hematopoietic stem-cell transplantation (HSCT) is considered **EXPERIMENTAL/INVESTIGATIVE** for all indications, due to the lack of clinical evidence demonstrating an impact on improved health outcomes.

- **Hematopoietic Stem Cell Transplantation for Autoimmune Diseases, II-121**

I. Systemic Sclerosis/Scleroderma

- Autologous hematopoietic stem cell transplantation may be considered **MEDICALLY NECESSARY AND APPROPRIATE** for treatment of systemic sclerosis/scleroderma when all of the following are met:
  - Adult patients age 18 to 69 years; **AND**
  - Disease duration ≤ 4 years; **AND**
  - Rapidly progressing systemic sclerosis/scleroderma at risk of organ failure; **AND**
  - ONE of the following:
    - Patient meets transplanting institution's selection criteria for HSCT in treatment of systemic sclerosis/scleroderma;
      OR
    - If center does not have selection criteria for this condition, **NONE** of the following comorbid conditions are present:
      1. Cardiac disease: left ventricular ejection fraction (LVEF) of less than 50%
      2. Pulmonary arterial hypertension: mean pulmonary artery pressure > 20 mm Hg
      3. Renal disease: creatinine clearance of less than 40 mL/min
- Allogeneic hematopoietic stem cell transplantation as a treatment of systemic sclerosis/scleroderma is considered **EXPERIMENTAL/INVESTIGATIVE** due to a lack of evidence demonstrating an impact on improved health outcomes.

II. Other Autoimmune Conditions

Autologous or allogeneic hematopoietic stem cell transplantation is considered **EXPERIMENTAL/ INVESTIGATIVE** as a treatment of all other autoimmune diseases, including but not limited to the following, due to a lack of evidence demonstrating an impact on improved health outcomes:

- Multiple sclerosis (MS);
- Rheumatoid arthritis (RA);
- Juvenile idiopathic arthritis;
- Systemic lupus erythematosus (SLE);
- Type 1 diabetes mellitus;
- Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP).

III. Repeat Transplant

A second (allogeneic or autologous) hematopoietic stem-cell transplantation (HSCT) is considered **EXPERIMENTAL/INVESTIGATIVE** for all indications, due to the lack of clinical evidence demonstrating an impact on improved health outcomes.

- **Intravitreal Angiogenesis Inhibitors for Treatment of Retinal & Choroidal Vascular Conditions, II-71**

I. Initial Review for Bevacizumab (Avastin®)

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

- Diagnosis of ONE of the following:
  - Diabetic macular edema; OR
  - Diabetic retinopathy; OR
  - Neovascular (wet) age-related macular degeneration or choroidal neovascularization; OR
  - Macular edema (e.g., cystoid) following retinal vein occlusion; OR
  - Neovascular glaucoma; OR
  - Rubeosis (i.e., neovascularization of the iris); OR
  - Retinopathy of prematurity;

  AND
- Prescribed by or in consultation with an ophthalmologist; **AND**
- Not used in combination with intravitreal corticosteroids or verteporfin photodynamic therapy; **AND**
- No concomitant use of another anti-VEGF agent in the same eye; **AND**
- No FDA labeled contraindications to bevacizumab (see table 1 below).

II. <u>Initial Review for Ranibizumab (Lucentis®, Byooviz™, Cimerli™)</u>

Intravitreal injection of ranibizumab (Lucentis®, Byooviz™, Cimerli™) may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ALL** of the following criteria are met:

- ONE of the following:
  - Diagnosis of diabetic macular edema, with or without diabetic retinopathy; OR
  - BOTH of the following:
    1. Diagnosis of ONE of the following:
       - Diabetic retinopathy without diabetic macular edema; OR
       - Neovascular (wet) age-related macular degeneration or choroidal neovascularization; OR
       - Macular edema (e.g., cystoid) following retinal vein occlusion; AND
    2. ONE of the following:
       - Previously tried and failed intravitreal bevacizumab; OR
       - Documented intolerance, FDA labeled contraindication, or hypersensitivity to intravitreal bevacizumab;

  AND
- Prescribed by or in consultation with an ophthalmologist; **AND**
- Not used in combination with intravitreal corticosteroids or verteporfin photodynamic therapy; **AND**
- No concomitant use of another anti-VEGF agent in the same eye; **AND**
- No FDA labeled contraindications to ranibizumab (see table 1 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).

III. <u>Initial Review for Ranibizumab (Susvimo™)</u>

Intravitreal injection of ranibizumab (Susvimo™) via ocular implant may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ALL** of the following criteria are met:

- Diagnosis of neovascular (wet) age-related macular degeneration or choroidal neovascularization; **AND**
- ONE of the following:
  - Previously tried and failed intravitreal bevacizumab; OR
  - Documented intolerance, FDA labeled contraindication, or hypersensitivity to intravitreal bevacizumab;

  AND
- Previously responded to at least two intravitreal injections of ranibizumab (e.g., Lucentis®, Byooviz™); **AND**
- Prescribed by or in consultation with an ophthalmologist; **AND**

- Not used in combination with intravitreal corticosteroids or verteporfin photodynamic therapy; **AND**
- No concomitant use of another anti-VEGF agent in the same eye; **AND**
- No FDA labeled contraindications to ranibizumab (see table 1 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).

IV. Initial Review for Aflibercept (Eylea®)

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

- ONE of the following:
  - Diagnosis of diabetic macular edema, with or without diabetic retinopathy; OR
  - Diagnosis of retinopathy of prematurity (ROP) AND ONE of the following:
    1. Type I ROP (i.e., ROP zone I stage 1+, 2+, 3, 3+ OR ROP zone II stage 2+, 3+); OR
    2. Aggressive posterior ROP (AP-ROP);

    OR
  - BOTH of the following:
    1. Diagnosis of ONE of the following:
       - Diabetic retinopathy without diabetic macular edema; OR
       - Neovascular (wet) age-related macular degeneration or choroidal neovascularization; OR
       - Macular edema (e.g., cystoid) following retinal vein occlusion;

       AND
    2. ONE of the following:
       - Previously tried and failed intravitreal bevacizumab; OR
       - Documented intolerance, FDA labeled contraindication, or hypersensitivity to intravitreal bevacizumab;

  AND
- Prescribed by or in consultation with an ophthalmologist; **AND**
- Not used in combination with intravitreal corticosteroids or verteporfin photodynamic therapy; **AND**
- No concomitant use of another anti-VEGF agent in the same eye; **AND**
- No FDA labeled contraindications to aflibercept (see table 1 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).

V. Initial Review for Aflibercept (Eylea® HD)

Intravitreal injection of 8mg aflibercept may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ALL** of the following criteria are met:

- ONE of the following:
  - Diagnosis of diabetic macular edema, with or without diabetic retinopathy; OR
  - Neovascular (wet) age-related macular degeneration;

  AND
- ONE of the following:
  - Previously tried and failed intravitreal bevacizumab; OR
  - Documented intolerance, FDA labeled contraindication, or hypersensitivity to intravitreal bevacizumab;

  AND
- Prescribed by or in consultation with an ophthalmologist; **AND**
- Not used in combination with intravitreal corticosteroids or verteporfin photodynamic therapy; **AND**
- No concomitant use of another anti-VEGF agent in the same eye; **AND**

- No FDA labeled contraindications to aflibercept (see table 1 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).

VI. Initial Review for Pegaptanib (Macugen®)

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

- Diagnosis of neovascular (wet) age-related macular degeneration or choroidal neovascularization; **AND**
- ONE of the following:
  - Previously tried and failed intravitreal bevacizumab; OR
  - Documented intolerance, FDA labeled contraindication, or hypersensitivity to intravitreal bevacizumab;

  AND
- Prescribed by or in consultation with an ophthalmologist; **AND**
- Not used in combination with intravitreal corticosteroids or verteporfin photodynamic therapy; **AND**
- No FDA labeled contraindications to pegaptanib (see table 1 below); **AND**
- No concomitant use of another anti-VEGF agent in the same eye; **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).

VII. Initial Review for Brolucizumab (Beovu®)

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

- Diagnosis of neovascular (wet) age-related macular degeneration or choroidal neovascularization; **AND**
- ONE of the following:
  - Previously tried and failed intravitreal bevacizumab; OR
  - Documented intolerance, FDA labeled contraindication, or hypersensitivity to intravitreal bevacizumab;

  AND
- Prescribed by or in consultation with an ophthalmologist; **AND**
- Not used in combination with intravitreal corticosteroids or verteporfin photodynamic therapy; **AND**
- No concomitant use of another anti-VEGF agent in the same eye; **AND**
- No FDA labeled contraindications to brolucizumab (see table 1 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).

VII. Initial Review for Faricimab (Vabysmo™)

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

- ONE of the following:
  - Diagnosis of diabetic macular edema;

    OR
  - BOTH of the following:

    1. Diagnosis of ONE of the following:
       - Neovascular (wet) age-related macular degeneration; OR
       - Macular edema following retinal vein occlusion;

AND

2. ONE of the following:
   - Previously tried and failed intravitreal bevacizumab; OR
   - Documented intolerance, FDA labeled contraindication, or hypersensitivity to intravitreal bevacizumab

AND

- Prescribed by or in consultation with an ophthalmologist; **AND**
- Not used in combination with intravitreal corticosteroids or verteporfin photodynamic therapy; **AND**
- No concomitant use of another anti-VEGF agent in the same eye; **AND**
- No FDA labeled contraindications to faricimab (see table 1 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).

VIII. Renewal Review for Bevacizumab (Avastin®), Ranibizumab (Lucentis®, Byooviz™, Cimerli™), Ranibizumab (Susvimo™), Aflibercept (Eylea®, Eylea® HD), Pegaptanib (Macugen®), Brolucizumab (Beovu®), or Faricimab (Vabysmo™)

Intravitreal injection of bevacizumab, ranibizumab, aflibercept, pegaptanib, brolucizumab, or faricimab may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ALL** of the following criteria are met:

- Previously approved for the requested agent through the initial review process; **AND**
- Demonstrated positive clinical response to the requested therapy (e.g., improvement or stabilization of visual acuity, macular thickness, subretinal/intraretinal cystic fluid, or subretinal hemorrhage); **AND**
- Prescribed by or in consultation with an ophthalmologist; **AND**
- Not used in combination with intravitreal corticosteroids or verteporfin photodynamic therapy; **AND**
- No concomitant use of another anti-VEGF agent in the same eye; **AND**
- No FDA labeled contraindications to the requested agent (see table 1 below).

IX. Experimental/Investigative Uses

All other uses of ranibizumab, pegaptanib, brolucizumab, or faricimab are considered **EXPERIMENTAL/INVESTIGATIVE** due to the lack of clinical evidence demonstrating an impact on improved health outcomes.

All other non-oncologic uses of bevacizumab and aflibercept 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
Bevacizumab (Avastin®)	None*
Ranibizumab (Lucentis®, Byooviz™, Cimerli™)	Ocular or periocular infection; Known hypersensitivity to ranibizumab or any of its excipients
Ranibizumab (Susvimo™)	Ocular or periocular infections; Known hypersensitivity to ranibizumab products or any of its excipients; Active intraocular inflammation
Aflibercept (Eylea®, Eylea®	Ocular or periocular infection;

HD)	Known hypersensitivity to aflibercept or any of its excipients; Active intraocular inflammation
Pegaptanib (Macugen®)	Ocular or periocular infection; Known hypersensitivity to pegaptanib sodium or any of its excipients
Brolucizumab (Beovu®)	Ocular or periocular infection; Known hypersensitivity to brolucizumab or any of its excipients; Active intraocular inflammation
Faricimab (Vabysmo™)	Ocular or periocular infection; Active intraocular inflammation; Hypersensitivity to faricimab or any of its excipients

*Bevacizumab is not FDA-approved for treatment of ocular conditions; therefore, there are no FDA labeled contraindications related to intravitreal administration.

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. Clinical notes describing current and past medications for the diagnosis, including response to the medications.
3. Clinical notes documenting absence of active ocular or periocular infection.
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).

Renewal Review
1. Documentation of prior approval through the initial review process.
2. Documentation since most recent approval supporting continued positive clinical response (e.g., improvement or stabilization of visual acuity, macular thickness, subretinal/intraretinal cystic fluid).

- **Pharmacologic Therapies for Hereditary Angioedema, II-102**
  NOTE:
  - **C1 esterase inhibitor (Haegarda®), icatibant (Firazyr®, Sajazir®, generic), and berotralstat (Orladeyo®) are self-administered agents; please refer to applicable pharmacy benefit plan.**
  - **Lanadelumab (Takhzyro®) is a self-administered agent for ages 12 years and older; please refer to applicable pharmacy benefit plan.**
  - **When C1 esterase inhibitor (Berinert®, Cinryze®, Ruconest®), will be self-administered, please refer to applicable pharmacy benefit plan.**

I. Initial Review for Berinert®, Ruconest®, or Kalbitor®

C1 esterase inhibitor (Berinert®, Ruconest®), or ecallantide (Kalbitor®) may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ALL** of the following criteria are met:

- Diagnosis of hereditary angioedema (HAE), as evidenced by:
  - BOTH of the following for patients with HAE with C1 inhibitor deficiency/dysfunction (HAE type I or II):

1. C4 level below the lower limit of normal as defined by the laboratory performing the test; AND
2. ONE of the following:
   - C1 inhibitor antigenic level below the lower limit of normal as defined by the laboratory performing the test; or
   - C1 inhibitor functional level below the lower limit of normal as defined by the laboratory performing the test;

OR

- ONE of the following for patients with HAE with normal C1 inhibitor (previously HAE type III):
  1. Mutation in ONE of the following genes associated with HAE:
     - Coagulation factor XII;
     - Plasminogen;
     - Angiopoietin-1;
     - Kininogen 1;
     - Heparan sulfate 3-O-sulfotransferase 6;
     - Myoferlin;

     OR
  2. Family history or personal history of angioedema AND failure to respond to chronic, high-dose antihistamine therapy;

AND

- Used for treatment of acute HAE attacks; **AND**
- Not used in combination with other treatments for acute HAE attacks (e.g., Berinert®, Firazyr®, Sajazir®, Kalbitor®, Ruconest®); **AND**
- Medications known to cause angioedema (i.e., ACE-inhibitors, estrogens, angiotensin II receptor blockers) have been evaluated and discontinued when appropriate; **AND**
- Prescribed by or in consultation with an HAE specialist, such as a hematologist, allergist, or immunologist; **AND**
- No FDA labeled contraindications to therapy (see table 1 below); **AND**
- The dose is within the program quantity limit (see table 2 below); **AND**
- For commercial health plan members only, the drug is administered in accordance with site of service criteria (see policy XI-06); **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 Berinert®, Ruconest®, or Kalbitor®

C1 esterase inhibitor (Berinert®, Ruconest®), or ecallantide (Kalbitor®) may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ALL** of the following criteria are met:

- Previously approved for therapy through the initial review process; **AND**
- Used for treatment of acute HAE attacks; **AND**
- Patient continues to have acute HAE attacks; **AND**
- Not used in combination with other treatments for acute HAE attacks (e.g., Berinert®, Firazyr®, Sajazir®, Kalbitor®, Ruconest®); **AND**
- Prescribed by or in consultation with an HAE specialist, such as a hematologist, allergist, or immunologist; **AND**
- No FDA labeled contraindications to therapy (see table 1 below); **AND**
- The dose is within the program quantity limit (see table 2 below); **AND**
- For commercial health plan members only, the drug is administered in accordance with site of service criteria (see policy XI-06).

III. Initial Review for Cinryze®

C1 esterase inhibitor (Cinryze®) may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ALL** of the following criteria are met:

- Diagnosis of hereditary angioedema (HAE), as evidenced by:
  - BOTH of the following for patients with HAE with C1 inhibitor deficiency/dysfunction (HAE type I or II):
    1. C4 level below the lower limit of normal as defined by the laboratory performing the test; AND
    2. ONE of the following:
       - C1 inhibitor antigenic level below the lower limit of normal as defined by the laboratory performing the test; or
       - C1 inhibitor functional level below the lower limit of normal as defined by the laboratory performing the test;

    OR
  - ONE of the following for patients with HAE with normal C1 inhibitor (previously HAE type III):
    1. Mutation in ONE of the following genes associated with HAE:
       - Coagulation factor XII;
       - Plasminogen;
       - Angiopoietin-1;
       - Kininogen 1;
       - Heparan sulfate 3-O-sulfotransferase 6;
       - Myoferlin;

       OR
    2. Family history or personal history of angioedema AND failure to respond to chronic, high-dose antihistamine therapy;

  AND
- ONE of the following:
  - Used for treatment of acute HAE attacks AND the following:
    1. Not used in combination with other treatments for acute HAE attacks (e.g., Berinert®, Firazyr®, Sajazir®, Kalbitor®, Ruconest®); OR
  - Used for prophylaxis against HAE attacks AND ALL of the following:
    1. Not used in combination with other agents for prophylaxis against HAE attacks (e.g., Haegarda®, Takhzyro®); AND
    2. History of at least 2 acute severe (e.g., swelling of the throat, incapacitating gastrointestinal or cutaneous swelling) attacks per month;

  AND
- Medications known to cause angioedema (i.e., ACE-inhibitors, estrogens, angiotensin II receptor blockers) have been evaluated and discontinued when appropriate; **AND**
- Prescribed by or in consultation with an HAE specialist, such as a hematologist, allergist, or immunologist; **AND**
- No FDA labeled contraindications to therapy (see table 1 below); **AND**
- The dose is within the program quantity limit (see table 2 below); **AND**
- For commercial health plan members only, the drug is administered in accordance with site of service criteria (see policy XI-06); **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).

IV. Renewal Review for Cinryze®

C1 esterase inhibitor (Cinryze®) may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ALL** of the following criteria are met:

- Previously approved for therapy through the initial review process; **AND**
- ONE of the following:

- Used for treatment of acute HAE attacks AND ALL of the following:
  1. Patient continues to have acute HAE attacks; AND
  2. Not used in combination with other treatments for acute HAE attacks (e.g., Berinert®, Firazyr®, Sajazir®, Kalbitor®, Ruconest®); OR
- Used for prophylaxis against HAE attacks AND ALL of the following:
  1. Patient has had a decrease in the frequency of acute attacks from baseline (prior to treatment); AND
  2. Not used in combination with other agents for prophylaxis against HAE attacks (e.g., Haegarda®, Takhzyro®);

AND

- Prescribed by or in consultation with an HAE specialist, such as a hematologist, allergist, or immunologist; **AND**
- No FDA labeled contraindications to therapy (see table 1 below); **AND**
- The dose is within the program quantity limit (see table 2 below); **AND**
- For commercial health plan members only, the drug is administered in accordance with site of service criteria (see policy XI-06).

V. Initial Review for Takhzyro®

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

- Age 2-11 years; **AND**
- Diagnosis of hereditary angioedema (HAE), as evidenced by:
  - BOTH of the following for patients with HAE with C1 inhibitor deficiency/dysfunction (HAE type I or II):
    1. C4 level below the lower limit of normal as defined by the laboratory performing the test; AND
    2. ONE of the following:
       - C1 inhibitor antigenic level below the lower limit of normal as defined by the laboratory performing the test; or
       - C1 inhibitor functional level below the lower limit of normal as defined by the laboratory performing the test;

    OR
  - ONE of the following for patients with HAE with normal C1 inhibitor (previously HAE type III):
    1. Mutation in ONE of the following genes associated with HAE:
       - Coagulation factor XII;
       - Plasminogen;
       - Angiopoietin-1;
       - Kininogen 1;
       - Heparan sulfate 3-O-sulfotransferase 6;
       - Myoferlin;

       OR
    2. Family history or personal history of angioedema AND failure to respond to chronic, high-dose antihistamine therapy;

  AND
- Used for prophylaxis against HAE attacks AND ALL of the following:
  - Not used in combination with other agents for prophylaxis against HAE attacks (e.g., Cinryze® Haegarda®); AND
  - History of at least 2 acute severe (e.g., swelling of the throat, incapacitating gastrointestinal or cutaneous swelling) attacks per month;

  AND
- Medications known to cause angioedema (i.e., ACE-inhibitors, estrogens, angiotensin II receptor blockers) have been evaluated and discontinued when appropriate; **AND**
- Prescribed by or in consultation with an HAE specialist, such as a hematologist, allergist, or immunologist; **AND**

- No FDA labeled contraindications to therapy (see table 1 below); **AND**
- The dose is within the program quantity limit (see table 2 below); **AND**
- For commercial health plan members only, the drug is administered in accordance with site of service criteria (see policy XI-06); **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).

VI. Renewal Review for Takhzyro®

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

- Previously approved for therapy through the initial review process; **AND**
- Age 2-11 years; **AND**
- Used for prophylaxis against HAE attacks AND ALL of the following:
  - Patient has had a decrease in the frequency of acute attacks from baseline (prior to treatment); AND
  - Not used in combination with other agents for prophylaxis against HAE attacks (e.g., Cinryze® Haegarda®); **AND**
- Prescribed by or in consultation with an HAE specialist, such as a hematologist, allergist, or immunologist; **AND**
- No FDA labeled contraindications to therapy (see table 1 below); **AND**
- The dose is within the program quantity limit (see table 2 below); **AND**
- For commercial health plan members only, the drug is administered in accordance with site of service criteria (see policy XI-06).

VII. Experimental/Investigative Uses

All other uses of C1 esterase inhibitor (Berinert®, Cinryze®, Ruconest®), ~~or~~ ecallantide (Kalbitor®), or lanadelumab (Takhzyro®) 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
C1 esterase inhibitor (Berinert®)	History of life-threatening immediate hypersensitivity reactions, including anaphylaxis, to C1 esterase inhibitor preparations
C1 esterase inhibitor (Cinryze®)	History of life-threatening immediate hypersensitivity reactions, including anaphylaxis, to C1 esterase inhibitor preparations
C1 esterase inhibitor (Ruconest®)	History of allergy to rabbits and rabbit-derived products History of life-threatening immediate hypersensitivity reactions, including anaphylaxis, to C1 esterase inhibitor preparations
Ecallantide (Kalbitor®)	Known clinical hypersensitivity to ecallantide

Lanadelumab (Takhzyro®)	None

Table 2. Quantity Limits

NOTE: See documentation submission requirements below if the requested quantity (dose) is greater than the program quantity limit provided in this table.

Agent	Packaging	Dose	Maximum Quantity Limit	Maximum Billable Unit
C1 esterase inhibitor (Berinert®) 10 Units = 1 billable unit	500 Unit single-use vial	20 Units/kg IV	5,000 Units (10 vials) per 30 days	500 billable units per 30 days*
C1 esterase inhibitor (Cinryze®) 10 Units = 1 billable unit	500 Unit single-use vial	Adult and adolescent Initial dose: 1,000 Units IV every 3 to 4 days Inadequate response to initial dose: Maximum 2,500 Units (not exceeding 100 Units/kg) IV every 3 to 4 days Children 6 to 11 years: 500 Units IV every 3 to 4 days Inadequate response to initial dose: Maximum 1,000 Units every 3 to 4 days	Adult and adolescent: 10,000 Units (20 vials) per 30 days Maximum 25,000 Units (50 vials) per 30 days if inadequate response to initial dosing Children 6 to 11 years: 5,000 Units (10 vials) per 30 days Maximum 10,0000 Units (20 vials) per 30 days if inadequate response to initial dosing	Adult and adolescent: 1,000 billable units per 30 days Maximum 2,500 billable units per 30 days if inadequate response to initial dosing Children 6 to 11 years: 500 billable units per 30 days Maximum 1,000 billable units per 30 days if inadequate response to initial dosing
C1 esterase inhibitor (Ruconest®) 10 Units = 1 billable unit	2,100 Unit single-use vial	<185 lbs (<84 kg): 50 Units/kg IV ≥185 lbs (≥84 kg) or inadequate response to initial dose: Maximum 4,200 Units IV (2 doses in 24 hours)	16,800 Units (8 vials) per 30 days	1,680 billable units per 30 days

Ecallantide (Kalbitor®) 1 mg = 1 billable unit	Three 10 mg/mL single-use vials per kit	30 mg SC in three 10 mg injections Inadequate response to initial dose: Maximum 60 mg SC (2 doses in 24 hours)	120 mg (4 kits) per 30 days	120 billable units per 30 days
Lanadelumab (Takhzyro®) 1 mg = 1 billable unit	150 mg/mL single-use prefilled syringe, 150 mg/mL single-use vial	Children 6 to less than 12 years of age: 150 mg SC every 2 weeks (dosing interval every 4 weeks may be considered in some patients) Children 2 to less than 6 years of age: 150 mg every 4 weeks	300 mg per 30 days	300 billable units per 30 days

IV (Intravenous), SC (subcutaneous)

*Maximum quantity limit calculation based on CDC 90 percentile for weight in adults and averaged for men and women to 238 lbs (108 kg)

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 and laboratory results describing confirmation of hereditary angioedema (HAE).
2. Intended use (treatment or prophylaxis) of the requested HAE agent.
3. The quantity (dose) being requested, including the patient's weight if needed. If the requested quantity is greater than the quantity limits provided in the table above, a clear explanation for the medical necessity of the requested quantity MUST be submitted.
4. For commercial health plan members only, the site of service for the drug administration is specified, including CMS place of service code (see policy XI-06). If the drug is administered in a hospital outpatient facility, a clear explanation for the medical necessity of the site of service MUST be submitted, including documentation for one or more of the site of service criteria provided in policy XI-06.
5. 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).

Renewal Review

1. Documentation of prior approval for the requested HAE agent through the initial review process.
2. Documentation supporting ONE of the following:
   - For treatment of acute HAE attacks, patient continues to have acute HAE attacks.
   - For prophylaxis against HAE attacks, patient has had a decrease in the frequency of acute attacks from baseline (prior to treatment).

3. The quantity (dose) being requested, including the patient's weight if needed. If the requested quantity is greater than the quantity limits provided in the table above, a clear explanation for the medical necessity of the requested quantity MUST be submitted.
4. For commercial health plan members only, the site of service for the drug administration is specified, including CMS place of service code (see policy XI-06). If the drug is administered in a hospital outpatient facility, a clear explanation for the medical necessity of the site of service MUST be submitted, including documentation for one or more of the site of service criteria provided in policy XI-06.

- **Tocilizumab, II-181**

NOTE:

- **When tocilizumab (Actemra®, Tofidence™) will be self-administered by subcutaneous injection, including use for treatment of systemic sclerosis-associated interstitial lung disease, please refer to applicable pharmacy benefit plan.**
- **This policy is not to be used for reviews of tocilizumab (Actemra®, Tofidence™) when administered in an inpatient setting. This includes reviews for hospitalized patients with COVID-19.**

I. <u>Initial and Renewal Review for Tocilizumab (Actemra®, Tofidence™) for Oncologic Indications</u>

Tocilizumab (Actemra®, Tofidence™) may be considered **MEDICALLY NECESSARY AND APPROPRIATE** for **oncologic indication**s when **ALL** of the following criteria are met:

- Diagnosis of **ONE** of the following:
  - Chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome associated with treatment of oncologic indications; OR
  - Castleman's disease (angiofollicular lymph node hyperplasia) **AND ONE** of the following:
    - Tocilizumab will be used as second-line therapy as a single agent for relapsed or refractory unicentric Castleman's disease for patients who are human immunodeficiency virus-negative and human herpesvirus-8-negative; OR
    - Tocilizumab will be used as subsequent therapy as a single agent for multicentric Castleman's disease that has progressed following treatment of relapsed/refractory or progressive disease;

  AND
- No FDA labeled contraindications to tocilizumab (see table 1 below); **AND**
- Requested dose is within the FDA labeled dose for the labeled indications or is supported in the literature for additional indications.

II. <u>Initial Review for Tocilizumab (Actemra®, Tofidence™) for Non-Oncologic Indications</u>

Tocilizumab (Actemra®, Tofidence™) may be considered **MEDICALLY NECESSARY AND APPROPRIATE** for **non-oncologic indications** when **ALL** of the following criteria are met:

- Diagnosis of **ONE** of the following:
  - Moderately to severely active rheumatoid arthritis in a patient 18 years of age or older AND ONE of the following:
    - Previously failed another biologic immunomodulator with FDA approval for the same indication; OR
    - Used one conventional agent prerequisite for the indication (see table 2 below); OR
    - Documented intolerance, FDA labeled contraindication, or hypersensitivity to ALL conventional agents;

    OR
  - Active polyarticular juvenile idiopathic arthritis in a patient 2 years of age or older AND ONE of the following:
    - Previously failed another biologic immunomodulator with FDA approval for the same indication; OR
    - Used one conventional agent prerequisite for the indication (see table 2 below); OR
    - Documented intolerance, FDA labeled contraindication, or hypersensitivity to ALL conventional agents;

OR

- Active systemic juvenile idiopathic arthritis in a patient 2 years of age or older AND ONE of the following:
  - Previously failed another biologic immunomodulator with FDA approval for the same indication; OR
  - Used one conventional agent prerequisite for the indication (see table 2 below); OR
  - Documented intolerance, FDA labeled contraindication, or hypersensitivity to ALL conventional agents;

  OR
- Giant cell arteritis in a patient 18 years of age or older AND ONE of the following:
  - Previously failed another biologic immunomodulator with FDA approval for the same indication; OR
  - Used one conventional agent prerequisite for the indication (see table 2 below); OR
  - Documented intolerance, FDA labeled contraindication, or hypersensitivity to ALL conventional agents;

  OR
- Management of immune checkpoint inhibitor related toxicity AND BOTH of the following:
  - ONE of the following:
    - Used as additional therapy for management of immunotherapy-related giant cell arteritis; OR
    - Used as additional disease modifying antirheumatic therapy for management of moderate or severe immunotherapy-related inflammatory arthritis if no improvement after holding immunotherapy and treating with oral corticosteroids or if unable to taper corticosteroids;

    AND
  - Receiving therapy with an immune checkpoint inhibitor (e.g., cemiplimab, nivolumab, pembrolizumab, atezolizumab, avelumab, durvalumab, ipilimumab, etc.); OR
- **NOTE:** See policy section I for chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome;

AND

- No FDA labeled contraindications to tocilizumab (see table 1 below); **AND**
- Not currently being treated with another biologic immunomodulator; **AND**
- For patients not currently receiving a biologic immunomodulator, the patient has been screened for latent tuberculosis (TB) and started on TB therapy if the patient tests positive; **AND**
- Requested dose is within the FDA labeled dose for the labeled indications (see table 3 below); **AND**
- For commercial health plan members only, tocilizumab is administered in accordance with site of service criteria (see policy XI-06); **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).

III. Renewal Review for Tocilizumab (Actemra®, Tofidence™) for Non-Oncologic Indications

Tocilizumab (Actemra®, Tofidence™) may be considered **MEDICALLY NECESSARY AND APPROPRIATE** for **non-oncologic indications** when **ALL** of the following criteria are met:

- Previously approved for tocilizumab through the initial review process; **AND**
- Continued positive clinical response to tocilizumab therapy (e.g., stabilization and/or slowing of disease progression, or decrease in symptom severity and/or frequency); **AND**
- No FDA labeled contraindications to tocilizumab (see table 1 below); **AND**
- Not currently being treated with another biologic immunomodulator; **AND**
- Requested dose is within the FDA labeled dose for the labeled indications (see table 3 below); **AND**
- For commercial health plan members only, tocilizumab is administered in accordance with site of service criteria (see policy XI-06).

IV. Experimental/Investigative Uses

All other uses of tocilizumab (Actemra®, Tofidence™) 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
Tocilizumab (Actemra®, Tofidence™)	Hypersensitivity

Table 2. Conventional Agent Prerequisites

FDA Labeled Indications	Conventional Agent Prerequisites
Rheumatoid arthritis	methotrexate leflunomide sulfasalazine hydroxychloroquine
Polyarticular juvenile idiopathic arthritis (PJIA)	methotrexate leflunomide sulfasalazine hydroxychloroquine
Psoriatic arthritis (PsA)	methotrexate leflunomide cyclosporine sulfasalazine hydroxychloroquine
Giant cell arteritis (GCA)	systemic corticosteroids (e.g., prednisone, methylprednisolone

Table 3. Dosing for Non-Oncologic Indications

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

FDA Labeled Indications	Dosing
Rheumatoid arthritis	IV: 4 mg/kg every 4 weeks, increase to 8 mg/kg every 4 weeks based on clinical response. SC: 162 mg every other week followed by an increase to every week based on clinical response for those <100 kg; 162 mg every week for those ≥100 kg.
Polyarticular juvenile idiopathic arthritis (PJIA)	IV: 10 mg/kg for those <30 kg every 4 weeks, 8 mg/kg for those ≥30 kg every 4 weeks. SC: 162 mg once every three weeks for those <30 kg, 162 mg once every two weeks for those ≥30 kg.

Systemic juvenile idiopathic arthritis (SJIA)	IV: 12 mg/kg for those <30 kg every 2 weeks, 8 mg/kg for those ≥30 kg every 2 weeks. SC: 162 mg every two weeks for those <30 kg, 162 mg every week for those ≥30 kg.
Giant cell arteritis (GCA)	IV: 6 mg/kg every 4 weeks. SC: 162 mg once every week. Once every other week may be prescribed based on clinical considerations.
Off Label Indications	**Dosing**
Immune checkpoint inhibitor related toxicities	IV: 4 mg/kg one time only.

General Dosing Information: It is recommended that tocilizumab not be initiated in patients with an absolute neutrophil count (ANC) below 2000 per mm^3, platelet count below 100,000 per mm^3, or who have ALT or AST above 1.5 times the upper limit of normal (ULN). IV (intravenous); SC (subcutaneous).

Documentation Submission:

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

Initial Review for Non-Oncologic Indications

1. Clinical notes describing the diagnosis and clinical features of the diagnosis.
2. For patients not currently receiving a biologic immunomodulator, laboratory results for latent tuberculosis (TB) screening. If the test was positive, describe follow-up therapy.
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. 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, the site of service for tocilizumab administration is specified, including CMS place of service code (see policy XI-06). If tocilizumab is administered in a hospital outpatient facility, a clear explanation for the medical necessity of the site of service MUST be submitted, including documentation for one or more of the site of service criteria provided in policy XI-06.
6. 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).

Renewal Review for Non-Oncologic Indications

1. Documentation of prior approval for tocilizumab through the initial review process.
2. Documentation, since most recent approval, supporting continued positive clinical response (e.g., 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.
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.
5. For commercial health plan members only, the site of service for tocilizumab administration is specified, including CMS place of service code (see policy XI-06). If tocilizumab is administered in a hospital outpatient facility, a clear explanation for the medical necessity of the site of service MUST be submitted, including documentation for one or more of the site of service criteria provided in policy XI-06.

Policies Delegated to eviCore
None

Policies Inactivated
None