Medical and Behavioral Health Policy Activity

Policies Effective: April 1, 2024. Notification Posted: February 1, 2024.

Policies Developed

- **Avacincaptad pegol (Izervay), II-290**

I. Initial Review for Avacincaptad Pegol (Izervay™)

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

- Diagnosis of geographic atrophy of the macula secondary to age-related macular degeneration (AMD) and BOTH of the following:
  - Confirmed by imaging testing (e.g., optical coherence tomography, fluorescein angiography, fundus photography, fundus autofluorescence [FAF]); AND
  - Physical findings attributable to geographic atrophy of the macula (e.g., a phenotype of central geographic atrophy having 1 or more zones of well-demarcated retinal pigment epithelium (RPE) and/or choriocapillaris atrophy);

  AND
- Geographic atrophy is not secondary to a condition other than AMD (e.g., Stargardt disease, cone rod dystrophy, toxic maculopathies); **AND**
- Not used in combination with other intravitreal complement inhibitor therapies; **AND**
- Prescribed by, or in consultation with, an ophthalmologist; **AND**
- No FDA labeled contraindications to therapy (see table 1 below); **AND**
- The dose is within the FDA labeled dose (see table 2 below).

II. Renewal Review for Avacincaptad Pegol (Izervay™)

Avacincaptad pegol 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**
- A total of 12 consecutive months (i.e., 12 doses per each eye) of therapy has not been received; **AND**
- Continued positive clinical response to avacincaptad pegol therapy (e.g., slowing GA lesion growth, stabilization and/or slowing of disease progression, or decrease in symptom severity and/or frequency); **AND**
- Prescribed by, or in consultation with, an ophthalmologist; **AND**
- No FDA labeled contraindications to therapy (see table 1 below); **AND**
- The dose is within the FDA labeled dose for the indication (see table 2 below).

III. Experimental / Investigative Uses

All other uses of avacincaptad pegol, including but not limited to treatment duration greater than 12 consecutive months (i.e., 12 doses per each eye), 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

Avacincaptad pegol	Ocular or periocular infections. Active intraocular inflammation.

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
Geographic atrophy secondary to age-related macular degeneration	2 mg (0.1 mL of 20 mg/mL solution) administered by intravitreal injection to each affected eye once monthly (approximately 28 ± 7 days) for up to 12 consecutive months.

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. Documentation of imaging testing confirming geographic atrophy of the macula secondary to age-related macular degeneration (AMD).
4. The dose being requested. 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.

Renewal Review

1. Documentation of prior approval for avacincaptad pegol through the initial review process.
2. Documentation, since most recent approval, supporting continued positive clinical response (e.g., slowing of GA lesion growth, 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. 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.

- **External Upper Limb Tremor Stimulator, II-291**
  External upper limb tremor stimulator therapy is considered **EXPERIMENTAL/INVESTIGATIVE** for all indications, including but not limited to the treatment of essential tremor of the hands and Parkinson's disease, due to the lack of evidence demonstrating an impact on improved health outcomes.

Policies Revised

- **Efgartigimod alfa (Vyvgart), II-260**

I. Initial Review for Efgartigimod Alfa (Vyvgart®) and Efgartigimod Alfa and Hyaluronidase (Vyvgart® Hytrulo)

Efgartigimod alfa (Vyvgart®) or efgartigimod alfa and hyaluronidase (Vyvgart® Hytrulo) 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**
- Positive serological test for anti-acetylcholine receptor (AChR) antibodies; **AND**
- Myasthenia Gravis Foundation of America (MGFA) clinical classification II-IV; **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

- Prescribed by or in consultation with a specialist in the patient's disease; **AND**
- No FDA labeled contraindications to efgartigimod alfa or efgartigimod alfa and hyaluronidase (see table 1 below); **AND**
- The dose is within the FDA labeled dose (see table 2 below); **AND**
- For commercial health plan members only, efgartigimod alfa and efgartigimod alfa hyaluronidase are 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 Efgartigimod Alfa (Vyvgart®) and Efgartigimod Alfa and Hyaluronidase (Vyvgart ® Hytrulo)

Efgartigimod alfa (Vyvgart®) or efgartigimod alfa and hyaluronidase (Vyvgart® Hytrulo) may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ALL** of the following criteria are met:

- Previously approved for efgartigimod alfa (Vyvgart®) or efgartigimod alfa and hyaluronidase (Vyvgart® Hytrulo) through the initial review process; **AND**
- Continued positive clinical response to efgartigimod alfa (Vyvgart®) or efgartigimod alfa and hyaluronidase (Vyvgart® Hytrulo) (e.g., stabilization and/or slowing of disease progression, or decrease in symptom severity and/or frequency); **AND**
- Prescribed by or in consultation with a specialist in the patient's disease; **AND**
- No FDA labeled contraindications to efgartigimod alfa (Vyvgart®) or efgartigimod alfa and hyaluronidase (Vyvgart® Hytrulo) (see table 1 below); **AND**
- The dose is within the FDA labeled dose (see table 2 below); **AND**
- For commercial health plan members only, efgartigimod alfa (Vyvgart®) or efgartigimod alfa and hyaluronidase (Vyvgart® Hytrulo) are administered in accordance with site of service criteria (see policy XI-06).

III. Experimental / Investigative Uses

All other uses of efgartigimod alfa (Vyvgart®) or efgartigimod alfa and hyaluronidase (Vyvgart® Hytrulo) 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
Efgartigimod alfa	None
Efgartigimod alfa and hyaluronidase	None

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
Generalized myasthenia gravis	Efgartigimod alfa 10 mg/kg via IV infusion over one hour once weekly for 4 weeks. In patients weighing 120 kg or more, 1200 mg (3 vials) per infusion. Efgartigimod alfa and hyaluronidase One vial (1,008 mg efgartigimod alfa and 11,200 units hyaluronidase) administered as a subcutaneous injection once weekly for 4 weeks. Administer subsequent treatment cycles based on clinical evaluation. Additional treatment cycles are initiated no sooner than every 50 days from the start of the previous treatment cycle.

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

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, 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 efgartigimod alfa or efgartigimod alfa and hyaluronidase administration is specified, including CMS place of service code (see policy XI-06). If efgartigimod alfa 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 efgartigimod alfa or efgartigimod alfa and hyaluronidase 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. The dose being requested, including the patient's weight if the medication 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 efgartigimod alfa or efgartigimod alfa and hyaluronidase administration is specified, including CMS place of service code (see policy XI-06). If efgartigimod alfa or efgartigimod alfa and hyaluronidase 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.

- **Eculizumab (Soliris), II-196**

I. Initial Review for Eculizumab (Soliris®)

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

- Diagnosis of ONE of the following:
  - **Paroxysmal nocturnal hemoglobinuria (PNH)** AND ALL the following:
    - Confirmation of PNH by flow cytometry, including detection of PNH clones (i.e., PNH type III red cells or glycosylphosphatidylinositol-anchored proteins [GPI-AP]-deficient polymorphonuclear cells); AND
    - ONE of the following:
      - Patient is transfusion dependent (defined as hemoglobin ≤7 g/dL OR hemoglobin ≤9 g/dL in patients with symptoms of anemia); or
      - Patient has high lactate dehydrogenase activity (defined as ≥1.5 times the upper limit of normal); or
      - Presence of organ damage secondary to chronic hemolysis; or
      - Patient is pregnant and potential benefit outweighs potential fetal risk; or
      - Documented history of a major adverse vascular event from thromboembolism;

    OR
  - **Atypical hemolytic uremic syndrome (aHUS)** AND ALL the following:

- Shiga toxin-producing *E. coli*-related hemolytic uremic syndrome (STEC-HUS) has been ruled out (e.g., negative for STEC infection); AND
- Thrombotic thrombocytopenic purpura (TTP) has been ruled out (e.g., normal ADAMTS-13 activity and no evidence of an ADAMTS-13 inhibitor), or if TTP cannot be ruled out by laboratory and clinical evaluation, a trial of plasma exchange did not result in clinical improvement;

OR

- **Generalized myasthenia gravis (gMG)** AND ALL the following:
  - Age 18 years or older; AND
  - Positive serological test for anti-acetylcholine receptor (AchR) antibodies; AND
  - Myasthenia Gravis Foundation of America (MGFA) clinical classification II-IV; AND
  - Myasthenia Gravis Activities of Daily Living (MG-ADL) total score ≥6; 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
  - ONE of the following:
    - Previously tried and failed efgartigimod alfa (Vyvgart®)/ efgartigimod alfa and hyaluronidase (Vyvgart Hytrulo®), rozanolixizumab (Rystiggo®), AND ravulizumab (Ultomiris®); OR
    - Documented intolerance, FDA labeled contraindication, or hypersensitivity to efgartigimod alfa (Vyvgart®)/ efgartigimod alfa and hyaluronidase (Vyvgart Hytrulo®), rozanolixizumab (Rystiggo®), AND ravulizumab (Ultomiris®);

OR

- **Neuromyelitis optica spectrum disorder** (NMOSD) AND ALL the following:
  - Age 18 years or older; AND
  - Positive serological test for aquaporin-4 (AQP4) antibodies; AND
  - Clinical characteristics of NMOSD (e.g., optic neuritis, acute myelitis); AND
  - ONE of the following:
    - History of at least 2 relapses during the previous 12 months prior to initiating eculizumab; or
    - History of at least 3 relapses during the previous 24 months, at least one relapse occurring within the past 12 months prior to initiating eculizumab;

    AND
  - ONE of the following:
    - Previously tried and failed satralizumab (Enspryng®); OR
    - Documented intolerance, FDA labeled contraindication, or hypersensitivity to satralizumab (Enspryng®);

    AND
  - Expanded Disability Status Scale (EDSS) score ≤7.0; AND
  - Not receiving eculizumab in combination with disease modifying therapies for treatment of multiple sclerosis (e.g., beta interferons [Avonex®], fingolimod [Gilenya®], dimethyl fumarate [Tecfidera®]);

AND

- Prescribed by, or in consultation with, a specialist in the patient's disease; **AND**

- Not used in combination with another biologic immunomodulator (e.g., ravulizumab [Ultomiris®], efgartigimod alfa [Vyvgart®], efgartigimod alfa and hyaluronidase [Vyvgart® Hytrulo], rozanolixizumab [Rystiggo®], rituximab [Rituxan®]); **AND**
- Immunized with a meningococcal vaccine at least 2 weeks prior to administration of the first dose of eculizumab (unless the clinical record documents that the risks of delaying eculizumab outweigh the risk of meningococcal infection); **AND**
- No evidence of an active meningococcal infection; **AND**
- No FDA labeled contraindications to eculizumab (see table 1 below); **AND**
- The dose is within the FDA labeled dose (see table 2 below); **AND**
- For commercial health plan members only, eculizumab 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 Eculizumab (Soliris®)

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

- Previously approved for eculizumab through the initial review process; **AND**
- Continued positive clinical response to eculizumab therapy. Examples include:
  - For patients with paroxysmal nocturnal hemoglobinuria (PNH), decreased requirement for transfusions, stabilization of hemoglobin, reduction of lactate dehydrogenase (LDH), stabilization and/or slowing of disease progression;
  - For patients with atypical hemolytic uremic syndrome (aHUS), improved platelet count, reduction of lactate dehydrogenase (LDH), improved renal function, stabilization and/or slowing of disease progression;
  - For patients with generalized myasthenia gravis (gMG), improved MG-ADL total score, quantitative myasthenia gravis total score, stabilization and/or slowing of disease progression;
  - For patients with neuromyelitis optic spectrum disorder (NMOSD), reduced rates of relapses, improvement or stabilization of vision or paralysis, stabilization and/or slowing of disease progression;

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

III. Experimental/Investigative Uses

All other uses of eculizumab 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
Eculizumab (Soliris®)	Patients with unresolved serious *Neisseria meningitidis* infection.

	Patients who are not currently vaccinated against *Neisseria meningitidis*, unless the risks of delaying eculizumab treatment outweigh the risks of developing a meningococcal infection.

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>Paroxysmal nocturnal hemoglobinuria (PNH)</td><td>Patients ≥18 years: 600 mg weekly for the first 4 weeks, then 900 mg for the fifth dose 1 week later, then 900 mg every 2 weeks thereafter.</td></tr>
<tr><td>Atypical hemolytic uremic syndrome (aHUS)</td><td>Patients ≥18 years: 900 mg weekly for 4 weeks, 1200 mg for fifth dose 1 week later, 1200 mg every 2 weeks thereafter.
For patients <18 years, administer based upon body weight:
<table>
<tr><th>Body Weight</th><th>Induction</th><th>Maintenance</th></tr>
<tr><td>5 kg to less than 10 kg</td><td>300 mg weekly for 1 week</td><td>300 mg at week 2; then 300 mg every 3 weeks</td></tr>
<tr><td>10 kg to less than 20 kg</td><td>600 mg weekly for 1 week</td><td>300 mg at week 2; then 300 mg every 2 weeks</td></tr>
<tr><td>20 kg to less than 30 kg</td><td>600 mg weekly for 2 weeks</td><td>600 mg at week 3; then 600 mg every 2 weeks</td></tr>
<tr><td>30 kg to less than 40 kg</td><td>600 mg weekly for 2 weeks</td><td>900 mg at week 3; then 900 mg every 2 weeks</td></tr>
<tr><td>≥40kg</td><td>900 mg weekly for 4 weeks</td><td>1200 mg at week 5; then 1200 mg every 2 weeks</td></tr>
</table></td></tr>
<tr><td>Generalized myasthenia gravis (gMG)</td><td>900 mg weekly for 4 weeks, then 1200 mg for fifth dose 1 week later, then 1200 mg every 2 weeks thereafter.</td></tr>
</table>

Neuromyelitis optica spectrum disorder (NMOSD)	900 mg weekly for 4 weeks, then 1200 mg for fifth dose 1 week later, then 1200 mg every 2 weeks thereafter.

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

1. Clinical notes describing the diagnosis and clinical features of the diagnosis.
2. If treating myasthenia gravis, clinical notes describing current and past medications for the diagnosis, including response to the medications.
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 eculizumab administration is specified, including CMS place of service code (see policy XI-06). If eculizumab 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 eculizumab 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. 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 eculizumab administration is specified, including CMS place of service code (see policy XI-06). If eculizumab 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.

- **Medicare Part B Step Therapy, II-247**

Note:

- **This policy applies to Medicare Advantage and Minnesota Senior Health Options (MSHO) lines of business only.**
- **This policy addresses step therapy requirements through preferred products for selected drugs or drug classes.**
- **See table below for preferred and non-preferred products included in the Medicare Part B Step Therapy program.**

- **Medical necessity of the drug will be separately reviewed against the appropriate criteria.**

  Non-preferred products may be **reasonable and necessary** when ANY of the following criteria are met:

  - Documentation of non-preferred therapy within the past 365 days;

  OR

  - BOTH of the following:
    - Previous trial and failure of all preferred products resulting in minimal clinical response to therapy; AND
    - Documentation from the prescriber that clinical response is expected to be superior with the requested non-preferred product;

  OR

  - ALL of the following:
    - Documented intolerance, FDA-labeled contraindication, or hypersensitivity to all preferred products; AND
    - For patients with a documented intolerance or hypersensitivity, BOTH of the following:
      - Documentation from the prescriber that the same intolerance or adverse event would not be expected to occur with the requested non-preferred product; AND
      - For patients who are unable to tolerate all preferred products, documentation from the prescriber clearly indicates the medical reason why the patient cannot use the preferred products.

Table 1. Preferred Products Included in the Medicare Part B Step Therapy Program

Drug Class	Preferred Products	Non-Preferred Products
Intra-articular hyaluronan injections for osteoarthritis	Synvisc®/ Synvisc-One® and Euflexxa®	All other hyaluronan injection products
Infliximab and biosimilars	Remicade®, unbranded infliximab, Inflectra®, and Renflexis®	Avsola®, Ixifi®
C5 Inhibitors and Neonatal Fc receptor blocker (gMG only)	Vyvgart®/ Vyvgart® Hytrulo, Rystiggo®, and Ultomiris®	Soliris®

Policies Delegated to eviCore
None

Policies Inactivated
None