Approved Revision: Do Not Implement Until 4/2/21

Eculizumab

NDC CODE(S) 25682-0001-XX - Soliris 10MG/ML Solution (ALEXION PHARMACEUTICALS)

DESCRIPTION

Eculizumab, a recombinant monoclonal antibody, binds to the complement protein C5 and inhibits its cleavage to C5a and C5b, preventing the generation of terminal complement complex C5b-9. The complement system of proteins, which is part of the immune system, destroys abnormal red blood cells. Eculizumab prevents destruction of red blood cells that are deficient in terminal complement inhibitors.

POLICY

- Eculizumab for the treatment of the following is considered ***medically necessary*** if the medical appropriateness criteria are met: **(See Medical Appropriateness below.)**
  - Atypical hemolytic uremic syndrome (aHUS)
  - Generalized Myasthenia Gravis (gMG)
  - Neuromyelitis Optica Spectrum Disorder (NMOSD)
  - Paroxysmal nocturnal hemoglobinuria
- Eculizumab for the treatment of other conditions/diseases is considered ***investigational.***

MEDICAL APPROPRIATENESS

INITIAL APPROVAL

- Eculizumab is considered **medically appropriate** if **ALL** of the following criteria are met:
  - Individual is 18 years of age or older unless otherwise specified
  - Individual is free from unresolved serious systemic infection including Neisseria meningitidis infection
  - Individual immunized against Neisseria meningitidis at minimum 2 weeks before beginning treatment and revaccinated according to current medical guidelines for vaccine use (*Note: If urgent eculizumab therapy is indicated in an unvaccinated patient, administer meningococcal vaccine(s) as soon as possible and provide patients with two weeks of antibacterial drug prophylaxis.*)
  - Prescriber is enrolled in the Soliris REMS (Risk Evaluation Mitigation Strategy) program
  - Will not be used in combination with other complement-inhibitor therapy (e.g., ravulizumab-cwvz)
  - **BCBST requirement:** Prior trial and failure of ravulizumab-cwvz is required for the treatment of **ANY ONE** of the following:
    - Atypical Hemolytic Uremic Syndrome (aHUS)
    - Paroxysmal Nocturnal Hemoglobinuria
  - Diagnosis of **ANY ONE** of the following:
    - Atypical hemolytic uremic syndrome (aHUS) diagnosis if individual is **ALL** of the following:
      - Individual is 2 months of age or older
      - Thrombotic Thrombocytopenic Purpura (TTP) has been ruled out by evaluating ADAMTS-13 level (ADAMTS-13 activity level >10%)
      - Shiga toxin E. coli- related hemolytic uremic syndrome (STEC-HUS) is ruled out
      - Other hemolytic causes have been ruled out such as coexisting diseases or conditions (e.g. bone marrow transplantation, solid organ transplantation, malignancy, autoimmune disorder, drug-induced, malignant hypertension, HIV infection, etc.), Streptococcus pneumoniae or Influenza A (H1N1) infection, or cobalamin deficiency
      - Documented baseline values for **ANY ONE** or more of the following (necessary for renewal):
        - Serum lactate dehydrogenase (LDH)
        - Serum creatinine/eGFR (estimated glomerular filtration rate)
        - Platelet count

- Plasma exchange/infusion requirement
- Generalized Myasthenia Gravis (gMG) if **ALL** of the following:
  - Diagnosed with Myasthenia Gravis Foundation of America (MGFA) Clinical Classification of Class II to IV disease
  - Positive serologic test for anti-acetylcholine receptor (AchR) antibodies
  - Physician has assessed the baseline Quantitative Myasthenia Gravis (QMG) score
  - MG-Activities of Daily Living (MG-ADL) total score of ≥ 6
  - Inadequate response after minimum of 1 year with **ANY ONE** of the following:
    - Minimum of 2 immunosuppressive therapies (e.g. azathioprine, cyclosporine, mycophenolate, etc.)
    - Minimum of 1 immunosuppressive therapy and required chronic plasmapheresis, plasma exchange (PE) or intravenous immunoglobulin (IVIG)
- Neuromyelitis Optica Spectrum Disorder (NMOSD) if individual has **ALL** of the following:
  - Diagnosis confirmed by **ALL** of the following:
    - Seropositive for aquaporin-4 (AQP4) IgG antibodies*
    - Found to have **ANY ONE** of the following core clinical characteristics of NMOSD:
      - Optic neuritis
      - Acute myelitis
      - Area postrema syndrome (episode of otherwise unexplained hiccups or nausea and vomiting)
      - Acute brainstem syndrome
      - Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions
      - Symptomatic cerebral syndrome with NMOSD-typical brain lesions
    - Alternative diagnoses have been excluded (e.g., multiple sclerosis, sarcoidosis, cancer, chronic infection, etc.)

  ****Important Note:** *Sensitivity of the AQP4-IgG antibodies laboratory test should be* **≥ 77% (e.g., AQP4 FACS [M23 isoform]).** *With a negative or inconclusive result from a less sensitive test* **ONLY**, *at least* **two core clinical characteristics must be met**, *one being either* **optic neuritis**, **acute myelitis** *with longitudinally extensive transverse myelitis lesions or* **area postrema syndrome** *with additional MRI requirements (see chart below). After meeting these requirements, a diagnosis of NMOSD for the use of eculizumab can be confirmed.*

  - History of minimum of 2 relapses in the last 12 months OR 3 relapses in the last 24 months, with at least 1 relapse in the last 12 months
  - Expanded Disability Status Score (EDSS) of ≤ 7.0 (consistent with the presence of at least limited ambulation with aid
  - Individual is receiving concurrent corticosteroid therapy of 20 mg per day or less and those receiving immunosuppressive therapy (e.g. azathioprine, glucocorticoids, mycophenolate, etc) are on a stable dose regimen
  - Individual has/will **ALL** of the following
    - NOT received therapy with rituximab or mitoxantrone in the last 3 months
    - NOT received intravenous immune globulin (IVIG) in the last 3 weeks
    - NOT concomitantly receive therapy with **ANY ONE** of the following:
      - IL6-inhibitor (e.g., satralizumab)
      - Anti-CD20-directed antibody (e.g., rituximab)
      - Anti-CD19-directed antibody (e.g., inebilizumab)
- Paroxysmal nocturnal hemoglobinuria (PNH) diagnosis with **ALL** of the following:
  - Diagnosis must be accompanied by detection of PNH clones of at least 10% by flow cytometry diagnostic testing

- Demonstrate the presence of at least 2 different GPI protein (glycosylphosphatidylinositol) deficiencies (e.g., CD55, CD59, etc.) within at least 2 different cell lines (granulocytes, monocytes, erythrocytes)
- Individual has/is **ANY ONE** of the following indications for therapy:
  - Presence of a thrombotic event
  - Presence of organ damage secondary to chronic hemolysis
  - Pregnant and potential benefit outweighs potential fetal risk
  - Is transfusion dependent
  - High LDH activity (defined as ≥1.5 x ULN) with clinical symptoms
- Documented baseline values for **ANY ONE** or more of the following (necessary for renewal):
  - Serum lactate dehydrogenase (LDH)
  - Hemoglobin level
  - Packed RBC transfusion requirement

RENEWAL CRITERIA

- Eculizumab is considered **medically appropriate** for renewal if **ALL** of the following criteria are met:
  - Individual continues to meet initial approval criteria
  - Absence of unacceptable toxicity from the drug, e.g., infusion reactions, serious infections, etc.
  - Disease response is indicated by **ANY ONE** of the following:
    - For a diagnosis of Atypical Hemolytic Uremic Syndrome (aHUS), **ANY ONE** of the following:
      - Decrease in serum LDH from pretreatment baseline
      - Stabilization/improvement in serum creatinine/eGFR from pretreatment baseline
      - Increase in platelet count from pretreatment baseline
      - Decrease in plasma exchange/infusion requirement from pretreatment baseline
    - For a diagnosis of Generalized Myasthenia Gravis (gMG), **ANY ONE** of the following:
      - Improvement of at least 3-points from baseline in the Myasthenia Gravis-Specific Activities of Daily Living scale (MG-ADL) total score
      - Improvement of at least 5-points from baseline in the Quantitative Myasthenia Gravis (QMG) total score
    - For a diagnosis of Neuromyelitis Optica Spectrum Disorder (NMOSD), stabilization/improvement of neurologic symptoms as evidenced by a decrease in acute relapses, EDSS, hospitalizations or plasma exchange treatments
    - For a diagnosis of Paroxysmal Nocturnal Hemoglobinuria (PNH), **ANY ONE** of the following:
      - Decrease in serum LDH from pretreatment baseline
      - Stabilization/improvement in hemoglobin level from pretreatment baseline
      - Decrease in packed RBC transfusion requirement from pretreatment baseline

INDICATION(S)	DOSAGE & ADMINISTRATION (Doses should be administered at the following intervals or within two days of these time points)
Paroxysmal nocturnal hemoglobinuria	**Loading dose:** 600mg every 7 days for the first 4 weeks, followed by 900mg for the fifth dose 7 days later and then 900mg every 14 days thereafter (initial loading dose requires a total of 3,300mg over 5 weeks) **Maintenance dose:** 900 mg every 14 days
Atypical hemolytic uremic syndrome	**ADULTS** **Loading dose:** 900 mg intravenously every 7 days for the first 4 weeks, followed by 1,200mg for the fifth dose 7 days later and then 1,200mg every 14 days thereafter (initial loading dose requires a total of

	4,800mg over 5 weeks) **Maintenance dose:** 1200 mg intravenously every 14 days **Pediatric < 18 years:** 5 kg to <10 kg - 300 mg weekly x 1 dose, 300 mg at week 2, then 300 mg every 3 weeks 10 kg to <20 kg - 600 mg weekly x 1 dose, 300 mg at week 2, then 300 mg every 2 weeks 20 kg to <30 kg - 600 mg weekly x 2 doses, 600 mg at week 3, then 600 mg every 2 weeks 30 kg to <40 kg - 600 mg weekly x 2 doses, 900 mg at week 3, then 900 mg every 2 weeks ≥ 40 kg - 900 mg weekly x 4 doses, 1200 mg at week 5, then 1200 mg every 2 weeks
Generalized Myasthenia Gravis (gMG) and Neuromyelitis Optica Spectrum Disorder (NMOSD)	**Loading dose:** 900 mg intravenously every 7 days for the first 4 weeks, followed by 1,200 mg intravenously for the fifth dose 7 days later **Maintenance dose:** 1200 mg intravenously every 14 days

Dose Adjustment for aHUS (adult and pediatric patients), gMG (adult patients) and NMOSD (adult patients) in Case of Plasmapheresis, Plasma Exchange or Fresh Frozen Plasma Infusion

Type of Plasma Exchange	Most Recent Eculizumab Dose	Supplemental Eculizumab With Each Plasma Intervention	Timing of Supplemental Eculizumab Dose
Plasmapheresis or plasma exchange (PE)	300 mg	300 mg per each plasmapheresis or PE	Within 60 minutes after each plasmapheresis or PE
	≥ 600 mg	600 mg per each plasmapheresis or PE	
Fresh frozen plasma infusion (FFP)	≥300 mg	300 mg per each infusion of FFP	60 minutes prior to each infusion of FFP

LENGTH OF AUTHORIZATION

Coverage will be provided for twelve months for paroxysmal nocturnal hemoglobinuria (PNH) and atypical hemolytic uremic syndrome (aHUS) and may be renewed.

For Generalized Myasthenia Gravis and Neuromyelitis Optica Spectrum Disorder, initial coverage will be provided for 6 months and may be renewed annually thereafter.

Refer to **DOSAGE LIMITS** below

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

SOURCES

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EFFECTIVE DATE 4/2/21

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