Corporate Medical Policy

Eculizumab (Soliris®)

File Name: eculizumab_soliris
Origination: 8/2014
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Next CAP Review: 4/2021
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Description of Procedure or Service

Paroxysmal nocturnal hemoglobinuria

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare clonal hematopoietic stem cell disorder clinically characterized by chronic complement-mediated hemolysis, thrombosis, and bone marrow failure. Thrombosis, the major cause of death in PNH, is observed in approximately 40% of patients. The symptoms associated with this disorder, including fatigue, pain, esophageal spasm, and erectile dysfunction, are often severe and disabling.

Hemolytic-uremic syndrome

Hemolytic-uremic syndrome (HUS) is characterized by hemolytic anemia, thrombocytopenia, and renal failure caused by platelet thrombi in the microcirculation of the kidney and other organs. Typical (acquired) HUS is triggered by infectious agents such as strains of E. coli (Stx-E. coli) that produce powerful Shiga-like exotoxins, whereas atypical HUS (aHUS) can be genetic, acquired, or idiopathic (of unknown cause). Onset of atypical HUS ranges from prenatal to adulthood. Individuals with genetic atypical HUS frequently experience relapse even after complete recovery following the presenting episode. Sixty percent of genetic aHUS progresses to end-stage renal disease (ESRD).

Myasthenia gravis

Myasthenia gravis (MG) is a debilitating, chronic and progressive autoimmune neuromuscular disease. It can occur at any age and is characterized by muscle weakness that typically begins with difficulty controlling eye movement. The disease often progresses to the more severe and generalized form, known as generalized myasthenia gravis (gMG) that includes weakness of the head, neck, trunk, limb and respiratory muscles. Individuals with anti-acetylcholine receptor (AchR) antibody-positive MG produce antibodies against AchR, a receptor located on muscle cells at the neuromuscular junction. As a result, the communication between nerve and muscle is impaired causing a loss of normal muscle function. This loss of function can lead to further complication, exacerbations and myasthenic crises which can be life-threatening.

First-line treatment typically includes symptomatic management with anticholinesterase agents, such as pyridostigmine, and may be the only therapy needed for some patients. However, most myasthenia gravis patients require further treatment with or addition of corticosteroids (prednisone) and/or chronic immunomodulating therapy at some point during the disease process.

The approach to therapy with chronic immunomodulating drugs is usually highly individualized for each patient and will depend upon patient age, disease severity and rate of disease progression. There are a number of chronic immunomodulating drugs that are used to treat MG, with proposed treatment algorithms involving different lines of therapy. In general, commonly used first-line immunotherapies for long-term control are azathioprine and mycophenolate mofetil. Second-line agents include cyclosporine and tacrolimus. Immunomodulating agents generally reserved for treatment-refractory MG include rituximab, methotrexate and cyclophosphamide.

Periodic intravenous immune globulin (IVIG) or plasmapheresis offer rapid treatment with short duration of action, and are typically reserved for treatment of myasthenic crisis, bridge therapy during initiation of slow acting immunotherapies, preoperatively prior to thymectomies, or as an adjuvant to other immunomodulators in refractory patients.

Surgical treatment with thymectomy serves beneficial to patients with nonthymomatous, generalized acetylcholine receptor antibody-associated myasthenia gravis; however, benefits from such treatment may take months or years to demonstrate effect.

Neuromyelitis optica spectrum disorder

Neuromyelitis optica spectrum disorder (NMOSD) is a relapsing, inflammatory disease of the central nervous system (CNS) that is characterized by severe, immune-mediated demyelination and axonal damage typically affecting the optic nerves and spinal cord. NMOSD presents as recurrent attacks of optic neuritis and myelitis, and such attacks are often associated with poor recovery. Approximately 50% of patients with NMOSD have permanent visual impairment and paralysis caused by NMOSD attacks. The aquaporin-4 (AQP4) autoantibody is a specific biomarker for NMOSD that has been shown to correlate with clinical disease activity and is associated with complement-mediated damage to the CNS. Due to the characteristic progressive deterioration of NMOSD, long-term immunosuppressive therapy (e.g. azathioprine, rituximab, mycophenolate mofetil, mitoxantrone, oral glucocorticoids) is indicated as relapse prevention directly following diagnosis; however, 25-60% of patients continue to have recurrent attacks while receiving these treatments.

Regulatory status

On March 16, 2007, Eculizumab (Soliris®; Alexion Pharmaceuticals, Inc. Cheshire, CT), a humanized monoclonal antibody that binds to the human C5 complement protein, received accelerated approval by the U.S. Food and Drug Administration for the treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis.

On September 23, 2011 the U.S. Food and Drug Administration (FDA) approved Eculizumab (Soliris®) for the treatment of all pediatric and adult patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement mediated thrombotic microangiopathy.

On October 23, 2017, the U.S. Food and Drug Administration approved Eculizumab (Soliris®) for the treatment of adult patients with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AchR) antibody-positive.

Eculizumab (Soliris®)

On June 27, 2019, The U.S. Food and Drug Administration approved Eculizumab (Soliris®) for the treatment of adult patients with neuromyelitis optica spectrum disorder (NMOSD) who are anti-aquaporin-4 (AQP4) antibody positive.

******Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

Related Medical Policies:
Inebilizumab-cdon (Uplizna™)
Place of Service for Medical Infusion
Ravulizumab-cwvz (Ultomiris™)

Related Pharmacy Policies:
Enspryng™

Policy

BCBSNC will provide coverage for Eculizumab (Soliris®) when it is determined to be medically necessary because the medical criteria and guidelines noted below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Eculizumab (Soliris®) is covered

Paroxysmal Nocturnal Hemoglobinuria (PNH)

Initial Therapy

Eculizumab may be considered medically necessary for the treatment of **Paroxysmal Nocturnal Hemoglobinuria (PNH)** when the following criteria are met:

- The patient has a diagnosis of paroxysmal nocturnal hemoglobinuria (PNH); **AND**
- The patient is transfusion-dependent (i.e., has at least 1 transfusion in the 24 months prior to initiation of eculizumab due to documented hemoglobin less than 7 g/dL in persons without anemic symptoms or less than 9 g/dL in persons with symptoms from anemia) prior to initiation of eculizumab treatment; **OR** the member has a documented history of major adverse vascular events from thromboembolism; **AND**
- The patient has been administered a meningococcal vaccine at least two weeks prior to initiation of eculizumab therapy; **AND**
- The patient is revaccinated according to current medical guidelines for vaccine use while on eculizumab therapy; **AND**
- The patient will not receive eculizumab concurrently with other complement inhibitors used to treat PNH (e.g., ravulizumab).

Initial authorization: 6 months

Continuation Therapy

Continuation of treatment with eculizumab beyond 6 months after initiation of therapy, and every 12 months thereafter, may be considered medically necessary for the treatment of paroxysmal nocturnal hemoglobinuria (PNH) when the following criteria are met:

- The patient has been receiving eculizumab treatment, and continues to meet or would have met initial criteria at the time of therapy initiation; **AND**
- The patient has had either stabilization or improvement of symptoms from baseline while on eculizumab therapy; **AND**
- The patient will not receive eculizumab concurrently with other complement inhibitors used to treat PNH (e.g., ravulizumab).

Atypical Hemolytic Uremic Syndrome (aHUS)

Initial Therapy

Eculizumab may be considered medically necessary for the treatment of **Atypical Hemolytic Uremic Syndrome (aHUS)** when the following criteria are met:

- The patient has a diagnosis of Atypical Hemolytic Uremic Syndrome (aHUS); **AND**
- The patient has been administered a meningococcal vaccine at least two weeks prior to initiation of eculizumab therapy; **AND**
- The patient is revaccinated according to current medical guidelines for vaccine use while on eculizumab therapy; **AND**
- The patient will not receive eculizumab concurrently with other complement inhibitors used to treat aHUS (e.g., ravulizumab).

Initial authorization: 6 months

Continuation Therapy

Continuation of treatment with eculizumab beyond 6 months after initiation of therapy, and every 12 months thereafter, may be considered medically necessary for the treatment of atypical hemolytic uremic syndrome (aHUS) when the following criteria are met:

- The patient has been receiving eculizumab treatment, and continues to meet or would have met initial criteria at the time of therapy initiation; **AND**
- The patient has had a positive clinical response as measured by hematological parameters or thrombotic microangiopathy (TMA) response while on eculizumab therapy; **AND**
- The patient will not receive eculizumab concurrently with other complement inhibitors used to treat aHUS (e.g., ravulizumab).

Myasthenia Gravis

Initial Therapy

Eculizumab may be considered medically necessary for the treatment of refractory **Myasthenia Gravis** in adults when the following criteria are met:

- The patient has a diagnosis of generalized Myasthenia Gravis (gMG) with class II to IV disease per Myasthenia Gravis Foundation of America (MGFA) classification system (see Policy Guidelines); **AND**
- The patient is anti-acetylcholine receptor (AchR) antibody positive; **AND**
- The patient has impaired activities of daily living defined by a Myasthenia Gravis Activities of Daily Living (MG-ADL) score of at least 6 or higher (see Policy Guidelines); **AND**
- The patient has had an inadequate response or intolerance to at least three previous lines of non-steroidal chronic immunomodulating therapies used alone or in combination, for at least one year; **AND**
- The patient is revaccinated according to current medical guidelines for vaccine use while on eculizumab therapy.

Initial authorization: 6 months

Continuation Therapy

Continuation of treatment with eculizumab beyond 6 months after initiation of therapy, and every 12 months thereafter, may be considered medically necessary for the treatment of refractory myasthenia gravis when the following criteria are met:

- The patient has been receiving eculizumab treatment, and continues to meet or would have met initial criteria at the time of therapy initiation; **AND**
- The patient has had either stabilization or improvement of symptoms (i.e., MG-ADL score) from baseline while on eculizumab therapy.

Neuromyelitis Optica Spectrum Disorder (NMOSD)

Initial Therapy

Eculizumab may be considered medically necessary for the treatment of N**euromyelitis Optica Spectrum Disorder (NMOSD)** in adults when the following criteria are met:

- The patient has a diagnosis of NMOSD (see Policy Guidelines); **AND**
- The patient is anti-aquaporin-4 (AQP4) antibody seropositive; **AND**
- The patient has not received rituximab or mitoxantrone during the previous 3 months, or intravenous immune globulin (IVIG) duing the previous 3 weeks; **AND**
- The patient is revaccinated according to current medical guidelines for vaccine use while on eculizumab therapy; **AND**
- The patient will not receive eculizumab concurrently with other biologics used to treat NMOSD (e.g., inebilizumab, satralizumab); **AND**
- The patient has tried and had an inadequate response to inebilizumab (Uplizna) AND satralizumab (Enspryng); **OR**
- The patient has a clinical contraindication or intolerance to both inebilizumab (Uplizna) and satralizumab (Enspryng).

Initial authorization: 6 months

Continuation Therapy

Continuation of treatment with eculizumab beyond 6 months after initiation of therapy, and every 12 months thereafter, may be considered medically necessary for the treatment of Neuromyelitis Optica Spectrum Disorder (NMOSD) when the following criteria are met:

- The patient has been receiving eculizumab treatment, and continues to meet or would have met initial criteria at the time of therapy initiation; **AND**
- The patient has had clinical benefit (i.e., reduction of relapses or disease stabilization) while on eculizumab treatment; **AND**
- The patient will not receive eculizumab concurrently with other biologics used to treat NMOSD (e.g., inebilizumab, satralizumab).

When Eculizumab (Soliris®) is not covered

Eculizumab is considered **investigational** and therefore not covered when the above criteria are not met, and for treatment of conditions other than aHUS, PNH, gMG, or NMOSD**.**

Use of Eculizumab as treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS) is considered **investigational.**

Continued use of Eculizumab as a treatment of PNH is considered not medically necessary when transfusion requirements are not significantly reduced.

Continued use of Eculizumab as a treatment of PNH is considered not medically necessary when thromboembolism events persist despite treatment.

Policy Guidelines

FDA Approved Indications

Paroxysmal Nocturnal Hemoglobinuria (PNH)

Soliris® is indicated for the treatment of patients with PNH to reduce hemolysis.

The recommended dosing regimen for eculizumab for PHN consists of:

- 600 mg every seven days for the first four weeks followed by
- 900 mg for the fifth dose seven days later, then
- 900 mg every 14 days thereafter.

Eculizumab should be administered at the recommended dosage regimen time points, or within two days of these time points.

Atypical Hemolytic Uremic Syndrome (aHUS)

Soliris® is indicated for the treatment of patients with aHUS to inhibit complement-mediated thrombotic microangiopathy

There is no history or evidence of injection drug abuse that might be associated with atypical HUS or TTP (specifically Opana).

The recommended dosing regimen for eculizumab in aHUS for patients 18 years of age and older consists of:

- 900 mg every seven days for the first four weeks, followed by
- 1200 mg for the fifth dose seven days later, then
- 1200 mg every 14 days thereafter.

The recommended dosing regimen for eculizumab in aHUS for patients less than 18 years of age is weight based.

The FDA issued a Black Box Warning for Soliris® regarding serious meningococcal infection risk. Therefore, patients should receive a meningococcal vaccination at least 2 weeks prior to receiving the first eculizumab treatment and have revaccination according to current medical guidelines. Patients must be monitored and evaluated immediately for early signs of meningococcal infections and treated with antibiotics as indicated.

Eculizumab (Soliris®) is being studied in a variety of conditions. There is insufficient evidence regarding safety and efficacy, therefore treatment of conditions other than aHUS, PNH, myasthenia gravis, or NMOSD are considered investigational.

Eculizumab is not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS). While the few studies available demonstrate possible efficacy of eculizumab in treating Shiga toxin E. coli-related hemolytic uremic syndrome, further studies are needed to demonstrate that it is both safe and effective for this indication.
Plasma therapy should be initiated quickly in any patient in whom noninfectious HUS is suspected while awaiting the results of complement testing and genotyping. If not initiated, irreversible renal lesions may develop within a few days. Plasma therapy may need to continue until complement genotyping is completed.

Generalized Myasthenia Gravis (gMG)

There are many effective chronic immunomodulating agents available for use in MG. The choice of which agent to use depends on many factors, including relative contraindications to glucocorticoids, desired time for response onset, leukopenia and liver or kidney disease precluding the use of certain agents. The use of eculizumab should be reserved for use in patients who have tried and failed first and second line immuomodulating as well as one of the agents

usually reserved for refractory disease. Refractory disease is defined by unchanged or worsened status after treatment with corticosteroids and at least two other immunosuppressant agents, used in adequate doses for a sufficient duration, with persistent symptoms or side effects limiting function. The three lines of therapy to which the policy statement refers may have been used with or without prednisone.

Eculizumab (Soliris®) is indicated for the treatment of patients with generalized myasthenia gravis who are anti-acetylcholine receptor antibody positive.

Dosing and Administration

The recommended dosing regimen for eculizumab (Soliris®) in gMG for members 18 years of age and older consists of:

- 900 mg every seven days for the first four weeks followed by
- 1200 mg for the fifth dose seven days later, then
- 1200 mg every 14 days thereafter.

Administer eculizumab (Soliris®) at the recommended dosage regimen time points, or within two days of these time points.

Clinical Trial Evidence

The efficacy and safety of eculizumab in the treatment of generalized myasthenia gravis was evaluated by the REGAIN study. This phase 3, randomized, double-blind, placebo-controlled, multicenter clinical trial included 125 adult patients with anti-acetylcholine receptor antibody-positive refractory generalized myasthenia gravis. Patients were required to have Myasthenia Gravis Foundation of America (MGFA) class II-IV disease with a Myasthenia Gravis-Activities of Daily Living (MG-ADL) score of 6 or greater (scale: 0-24), and previous treatment with at least two immunosuppressant drugs or at least one immunosuppressant drug and chronic intravenous immune globulin (IVIG) or plasma exchange given at least four times per year, for a duration of 12 months without symptom control. Patients were randomized to receive either intravenous eculizumab (n=62) or intravenous matched placebo (n=63) for a total of 26 weeks. Prior to enrollment, over half of patients (52%) had tried three or more immunosuppressive treatments, 28% had previous long-term IVIG therapy, and 11% had previous long-term plasma exchange therapy. Patients were maintained on existing myasthenia gravis therapies if acceptable. The primary efficacy endpoint was change from baseline to week 26 in MG-ADL total score. In the 26-week trial, change in MG-ADL total score was not statistically significant between the eculizumab and placebo groups as measured by pre-specified worst-rank analysis (least-squares mean rank 56.6 [SEM 4.5] vs. 68.3 [4.5]; rank-based treatment difference -11.7 [95% CI -24.3 to 0.96]; p=0.0698). However, eculizumab significantly improved the secondary efficacy outcomes compared with placebo.

Myasthenia Gravis Foundation of America (MGFA) Disease Classification

Class	**Clinical Symptoms**
I	Any ocular weakness
II	Mild weakness; possible ocular weakness of any severity
III	Moderate weakness affecting other than ocular muscles; possible ocular muscle weakness of any severity
IV	Severe weakness affecting other than ocular muscles; possible ocular muscle weakness of any severity

V	Defined by intubation, with or without mechanical ventilation, except when employed during routine postoperative management

Myasthenia Gravis-Activities of Daily Living (MG-ADL) Scoring System is a tool assessing the level of function or severity of eight different symptomatic areas including talking, chewing, swallowing, breathing, impairment of ability to brush teeth or comb hair, impairment of ability to arise from a chair, double vision, and eyelid droop. Total scoring of activities of daily living ranges from 0 to 24.

Neuromyelitis Optica Spectrum Disorder (NMOSD)

Diagnostic Criteria

The diagnosis of NMOSD is based on the presence of core clinical characteristics, AQP4 antibody status, and magnetic imaging (MRI) neuroimaging features. There are six core clinical characteristics recognized, as described below:

- 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

The diagnosis of NMOSD in patients with AQP4-immunoglobulin G (IgG) antibodies present requires at least one core clinical characteristic present, a positive AQP4-IgG test using the best available detection method, and exclusion of alternative diagnoses.

Eculizumab (Soliris®) is indicated for the treatment of adult patients with neuromyelitis optica spectrum disorder who are anti-aquaporin-4 antibody positive.

Dosing and Administration

The recommended dosing regimen for eculizumab (Soliris®) in NMOSD for members 18 years of age and older consists of:

- 900 mg every seven days for the first four weeks followed by
- 1200 mg for the fifth dose seven days later, then
- 1200 mg every 14 days thereafter.

Administer eculizumab (Soliris®) at the recommended dosage regimen time points, or within two days of these time points

Clinical Trial Evidence

The efficacy of eculizumab for the treatment of NMOSD was evaluated in a randomized, double-blind, placebo-controlled, time-to-event trial (NCT01892345) assessing 143 adult patients with NMOSD who were anti-AQP4 antibody positive. Patients included in the trial were at least 18 years of age with a history of at least two relapses during the previous 12 months or three relapses during the previous 24 months, at least one of which occurred within the previous 12 months. Eligible patients also had to have an Expanded Disability Status Scale (EDSS) score of 7 or less (consistent with the presence of at least limited ambulation with aid), and patients on

immunosuppressant therapy (IST) for relapse prevention had to be at stable doses. At screening, patients were excluded if treated with mitoxantrone or rituximab during the previous 3 months, or intravenous immune globulin during the previous 3 weeks, and those receiving prednisone doses ≥ 20 mg daily or the equivalent for other glucocorticoids. Patients enrolled in the trial were randomized 2:1 to receive either intravenous eculizumab (n=96) according to the recommended dosing regimen or matched placebo (n=47). During the treatment phase of the trial, 76% of patients received concomitant IST, including chronic corticosteroids, and 24% of patients did not receive concomitant IST or chronic corticosteroids during the trial. The primary endpoint was the time to the first adjudicated on-trial relapse, which occurred in 3% (n=3/96) of patients in the eculizumab group and 43% (n=20/47) of patients in the placebo group (hazard ratio, 0.06; 95% CI, 0.02 to 0.20; p<0.001). The time to the first adjudicated relapse was significantly longer in eculizumab-treated patients (with or without concomitant treatment) as compared to placebo-treated patients. The results suggest that eculizumab was associated with a lower risk of relapse than placebo in patients with anti-AQP4 antibody positive NMOSD.

Administration of eculizumab (Soliris) - Site of Care Eligibility

1. Administration of eculizumab (Soliris) may be given in an inpatient setting if the inpatient setting is medically necessary. An inpatient admission for the sole purpose of eculizumab (Soliris) infusion is not medically necessary, OR
2. Adminisration of eculizumab (Soliris) in a hospital outpatient setting is considered medically necessary if the following criteria are met:
    a. History of mild adverse events that have not been successfully managed through mild pre-medication (diphenhydramine, acetaminophen, steroids, fluids, etc.), OR
    b. Inability to physically and cognitively adhere to the treatment schedule and regimen complexity, OR
    c. First infusion, OR
    d. Less than 3 months since first eculizumab (Soliris) infusion, OR
    e. First infusion after six months of no eculizumab (Soliris) infusions, OR
    f. Requirement of a change in eculizumab (Soliris) product.
3. Members who do not meet the criteria above are appropriate for eculizumab (Soliris) administration in a **home-based infusion** or physician office setting with or without supervision by a certified healthcare professional. Inpatient and hospital outpatient infusion, in the absence of the criteria in #1 or #2 above is considered not medically necessary.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: *J1300*

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

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Specialty Matched Consultant Advisory Panel (Nephrology) review 4/2020

Specialty Matched Consultant Advisory Panel (Neurology) review 5/2020

Medical Director review 10/2020

Blue Cross NC Pharmacy and Therapeutics Committee 1/2021

Medical Director review 2/2021

Policy Implementation/Update Information

8/26/14 New policy developed. BCBSNC will provide coverage for Eculizumab (Soliris®) when it is determined to be medically necessary because the medical criteria and guidelines are met. Medical Director review 8/2014. Policy noticed 8/26/14 for effective date 10/28/14. (mco)

5/26/15 Specialty Matched Consultant Advisory Panel review 4/2015. Medical Director review 4/2015. Policy Statements unchanged. (td)

5/31/16 Specialty Matched Consultant Advisory Panel review 4/2016. Medical Director review 4/2016. (td)

5/26/17 Added statement to Policy Guidelines regarding lack of evidence associating injection drug abuse with atypical HUS and TTP. Specialty Matched Consultant Advisory Panel review 4/2017. References updated. Medical Director review 4/2017. (jd)

12/29/17 Policy Guidelines updated to include guidelines for "Site of Care Eligibility related to infusion of eculizumab (Soliris). Policy notification given 1/1/18, effective 4/1/18.Medical Director review. (jd)

5/11/18 Specialty Matched Consultant Advisory Panel review 4/2018. No change to policy intent. (krc)

10/12/18 Updated Description section, Policy Statement, and Policy Guidelines with indication of eculizumab (Soliris) for refractory generalized myasthenia gravis in adults who are anti-acetylcholine receptor (AchR) antibody-positive. References added. Medical Director review 10/2018. (krc)

4/30/19 Minor typographical changes made throughout policy for clarity. Specialty Matched Consultant Advisory Panel (Nephrology) review 4/2019. No change to policy statements. (krc)

5/28/19 Specialty Matched Consultant Advisory Panel (Neurology) review 5/15/2019. No change to policy statements. (krc)

10/15/19 Updated Description section, Policy Statement, and Policy Guidelines with indication of eculizumab (Soliris) for adults with neuromyelitis optica spectrum disorder (NMOSD) who are anti-aquaporin-4 (AQP4) antibody positive. References added. Medical Director review 10/2019. (krc)

5/12/20 Specialty Matched Consultant Advisory Panel (Nephrology) review 4/15/2020. No change to policy intent. (krc)

6/23/20 Specialty Matched Consultant Advisory Panel (Neurology) review 5/20/2020. No change to policy intent. (krc)

10/27/20 Added continuation criteria in "When Covered" section for all indications. For NMOSD, added the following criteria to "When Covered" section: "The patient will not receive eculizumab concurrently with other biologics used to treat NMOSD (e.g., inebilizumab, satralizumab)," and "the patient has tried and had an inadequate response to inebilizumab (Uplizna) AND satralizumab (Enspryng), OR the patient has a clinical contraindication or intolerance to both inebilizumab and satralizumab." For aHUS and PNH, added the following criteria: "The patient will not receive eculizumab concurrently with other complement inhibitors (e.g., ravulizumab)." Edits made throughout policy to clarify intent. Added reference to the following related medical and pharmacy policies: "Inebilizumab-cdon (Uplizna™)" and "Enspryng™". Medical Director review 10/2020. **Policy notification given 10/27/2020 for effective date 1/1/2021**. (krc)

2/9/21 Removed the following criteria from "When Covered" section: "patient has a history of at least two relapses during the previous 12 months or three relapses during the

previous 24 months (at least one of which has occurred within the previous 12 months)." Blue Cross NC Pharmacy and Therapeutics Committee 1/5/2021. Medical Director review 2/2021. (krc)