Market Applicability														
Market	**DC**	**FL & FHK**	**FL MMA**	**FL LTC**	**GA**	**KS**	**KY**	**MD**	**NJ**	**NV**	**NY**	**TN**	**TX**	**WA**
Applicable	X	X	NA	NA	X	NA	X	X	X	X	X	NA	NA	X

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Soliris (eculizumab)

DRUG.00050

Override(s)	Approval Duration
Prior Authorization	1 year

Medications
Soliris (eculizumab)

APPROVAL CRITERIA

Paroxysmal Nocturnal Hemoglobinuria

I. Initiation of Soliris (eculizumab) may be approved for the treatment of an individual with documented paroxysmal nocturnal hemoglobinuria when the following criteria are met:
   A. Paroxysmal nocturnal hemoglobinuria as documented by flow cytometry, including the presence:
      1. Paroxysmal nocturnal hemoglobinuria type III red cells; **OR**
      2. Glycosylphosphatidylinositol-anchored proteins (GPI-AP)-deficient polymorphonuclear cells (PMNs);

   AND

   B. Individual has been immunized with a meningococcal vaccine at least 2 weeks prior to administration of the first dose of Soliris (eculizumab) (unless the clinical record documents that the risks of delaying Soliris (eculizumab) outweigh the risk of meningococcal infection);

   AND

   C. There is NO evidence of an active meningococcal infection;

   AND

   D. Either of the following criteria 1. **OR** 2. are met:
      1. The individual has:
         a. Hemoglobin that is less than or equal to 7 g/dl, or the individual has symptoms of anemia and the hemoglobin is less than or equal to 9 g/dl; **OR**
         b. Lactate dehydrogenase is greater than 1.5 times the upper limit of normal;

      OR

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Applicable	X	X	NA	NA	X	NA	X	X	X	X	X	NA	NA	X

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2. Documented history of a major adverse vascular event from thromboembolism.

II. Continuation of Soliris (eculizumab) may be approved for the treatment of an individual with documented paroxysmal nocturnal hemoglobinuria who is currently receiving treatment with Soliris (eculizumab).

Atypical Hemolytic Uremic Syndrome

III. Soliris (eculizumab) may be approved in an initial 6-week trial for the treatment of atypical hemolytic uremic syndrome when the following criteria are met:
   A. The diagnosis of aHUS is supported by the absence of Shiga toxin-producing E. coli infection; **AND**
   B. Thrombotic thrombocytopenic purpura has been ruled out (for example, normal ADAMTS 13 activity and no evidence of an ADAMTS 13 inhibitor), or if thrombotic thrombocytopenic purpura cannot be ruled out by laboratory and clinical evaluation, a trial of plasma exchange did not result in clinical improvement; **AND**
   C. Individual has been immunized with a meningococcal vaccine at least 2 weeks prior to administration of the first dose of Soliris (eculizumab) (unless the clinical record documents that the risks of delaying Soliris (eculizumab) outweigh the risk of meningococcal infection); **AND**
   D. There is NO evidence of an active meningococcal infection.

IV. Continuation of Soliris (eculizumab) following an initial 6-week trial for the treatment of atypical hemolytic uremic syndrome may be approved when there is clinical improvement after the initial trial (for example, increased platelet count or laboratory evidence of reduced hemolysis) until an individual becomes a candidate for physician-directed cessation as evidenced by the following (A. and B.):
   A. Complete clinical remission has been achieved (that is, resolution of thrombocytopenia and mechanical hemolysis, and normalization or new baseline plateau of renal function) *and* improvement of precipitating illness is clinically apparent; **AND**
   B. Duration of clinical remission has been stable for 2 months.

   Note: Close monitoring after cessation is essential (for example: regular laboratory monitoring including complete blood count, peripheral smear, lactate dehydrogenase, renal function, and urine protein beginning the week of the held

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Applicable	X	X	NA	NA	X	NA	X	X	X	X	X	NA	NA	X

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dose and weekly for 4 weeks, every 2 weeks for 1 month, and then monthly for 3 months at the discretion of the treating clinician).

V. Resumption of Soliris (eculizumab) may be approved when relapse occurs in an individual who has discontinued therapy. Relapse is defined as the occurrence of **any** of the following:
   A. Reduction in platelet count to less than 150,000/mm^3 or greater than 25% from baseline; **OR**
   B. Mechanical hemolysis (having 2 or more features of hemoglobin less than 10 g/dL, lactate dehydrogenase greater than 2 times upper limit of normal, undetectable haptoglobin, or presence of schistocytes on smear); **OR**
   C. Acute kidney injury with serum creatinine increase greater than 15% from baseline levels.

Myasthenia Gravis

VI. Initiation of Soliris (eculizumab) may be approved for generalized myasthenia gravis in an individual 18 years of age or older when the following criteria are met:
   A. Individual has Myasthenia Gravis Foundation of America Clinical Classification Class II to IV disease; **AND**
   B. Individual has a documented positive serologic test for binding anti-acetylcholine receptor antibodies (AChR-ab); **AND**
   C. Individual has had an inadequate response to, is intolerant of, **or** has a medical contraindication to two or more immunosuppressive drug agents (such as, azathioprine, cyclosporine, or methotrexate) as monotherapy or in combination therapy for greater than or equal to 12 months; **OR**
   D. Individual has had an inadequate response to, is intolerant of, **or** has a medical contraindication to one or more immunosuppressive drug agents as monotherapy or in combination therapy **and** requires chronic plasma exchange or plasmapheresis **or** intravenous immunoglobulin therapy; **AND**
   E. Individual has been 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 risk of delaying eculizumab outweigh the risk of meningococcal infection); **AND**
   F. There is no evidence of an active meningococcal infection.

VII. Continuation of Soliris (eculizumab) following an initial 26-week trial for the treatment of generalized myasthenia gravis may be approved following the initial trial when there is

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Market	DC	FL & FHK	FL MMA	FL LTC	GA	KS	KY	MD	NJ	NV	NY	TN	TX	WA
Applicable	X	X	NA	NA	X	NA	X	X	X	X	X	NA	NA	X

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documentation of clinical response (that is, a reduction in signs or symptoms that impact daily function).

Note: Discontinuation of Soliris (eculizumab) may be associated with serious adverse clinical events including life threatening thrombosis.

Requests for Soliris (eculizumab) may **not** be approved when the criteria above are not met and for all other indications, including but not limited to treatment of:

I. Antibody mediated rejection in organ transplantation; **OR**
II. Antineutrophil cytoplasmic autoantibody vasculitis; **OR**
III. Antiphospholipid antibody syndrome; **OR**
IV. Dense deposit disease or C3 nephropathy; **OR**
V. Guillain-Barre syndrome; **OR**
VI. Hemolysis elevated liver enzymes and low platelets syndrome in preeclampsia; **OR**
VII. Hemolytic cold agglutinin disease; **OR**
VIII. Neuromyelitis optica; **OR**
IX. Nonexudative (dry) age-related macular degeneration; **OR**
X. Shiga toxin E. coli-related hemolytic uremic syndrome ; **OR**
XI. Systemic lupus erythematosus; **OR**
XII. Thrombotic thrombocytopenic purpura.

Note: Soliris (eculizumab) has a black box warning for serious meningococcal infections. Life threatening and fatal meningococcal infections have been reported with the use of Soliris. Individuals should receive the meningococcal vaccine at least 2 weeks prior to receiving the first dose of Soliris, unless the risks of delaying therapy outweigh the risk of developing a meningococcal infection. The most current Advisory Committee on Immunization Practices (ACIP) recommendations should be complied with in respect to meningococcal vaccination in individuals with complement deficiencies. Soliris is available only through a restricted Risk Evaluation and Mitigation Strategy (REMS) program.

State Specific Mandates		
State name	Date effective	Mandate details (including specific bill if applicable)
N/A	N/A	N/A

Key References:

1. Centers for Disease Control (CDC) and Prevention. Immunization Schedules (2017). Available at: http://www.cdc.gov/vaccines/schedules/. Accessed on June 5, 2018.

Market Applicability														
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Applicable	X	X	NA	NA	X	NA	X	X	X	X	X	NA	NA	X

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2. Loirat C, Fakhouri F, Ariceta G, et al; HUS International. An international consensus approach to the management of atypical hemolytic uremic syndrome in children. Pediatr Nephrol. 2016; 31(1):15-39.
3. Sanders DB, Wolfe GI, Benatar M, et al. International consensus guidance for management of myasthenia gravis: executive summary. Neurology. 2016; 87(4):419-425.
4. Scully M, Hunt BJ, Benjamin S, et al; British Committee for Standards in Haematology. Guidelines on the diagnosis and management of thrombotic thrombocytopenic purpura and other thrombotic microangiopathies. Br J Haematol. 2012; 158(3):323-335.
5. Soliris [Product Information]. Alexion Pharmaceutical, Inc., Cheshire, CT; February 28, 2018. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/125166s426lbl.pdf. Accessed on June 5, 2018.
6. U.S. National Institutes of Health (NIH). ClinicalTrials.gov. ECU-MG-302: an extension trial of ECU-MG-301 to evaluate the safety and efficacy of eculizumab in refractory generalized myasthenia gravis. NLM Identifier: NCT02301624. Last updated August 2017. Available at: https://clinicaltrials.gov/ct2/show/NCT02301624. Accessed on June 5, 2018.