

Soliris® (Eculizumab)

Guideline Number: MMG142.S
Effective Date: April 1, 2024

[➔ Instructions for Use](#)

Table of Contents	Page
Coverage Rationale	1
Applicable Codes	1
Background	2
Benefit Considerations	2
Clinical Evidence	3
U.S. Food and Drug Administration	5
References	5
Guideline History/Revision Information	7
Instructions for Use	7

Related Medical Management Guideline
<ul style="list-style-type: none"> Provider Administered Drugs – Site of Care

Coverage Rationale

[➔ See Benefit Considerations](#)

Soliris® (eculizumab) is proven and/or medically necessary for treatment of:

- Atypical hemolytic uremic syndrome (aHUS)¹
- Paroxysmal nocturnal hemoglobinuria (PNH)^{1,12}
- Generalized myasthenia gravis^{1,9,11}
- Neuromyelitis optica spectrum disorder (NMOSD)^{1,25}

Soliris® (eculizumab) is unproven and not medically necessary for treatment of Shiga toxin E. coli-related hemolytic uremic syndrome (STEC-HUS).

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this guideline does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J1300	Injection, eculizumab, 10 mg

Diagnosis Code	Description
D59.30	Hemolytic-uremic syndrome, unspecified
D59.32	Hereditary hemolytic-uremic syndrome
D59.39	Other hemolytic-uremic syndrome

Diagnosis Code	Description
D59.5	Paroxysmal nocturnal hemoglobinuria [Marchiafava-Micheli]
G36.0	Neuromyelitis optica [Devic]
G70.00	Myasthenia gravis without (acute) exacerbation

Maximum Dosage Requirements

Maximum Allowed Quantities by HCPCS Units

This section provides information about the maximum dosage per administration for omalizumab administered by a medical professional.

Medication Name		Diagnosis	Maximum Dosage per Administration	HCPCS Code	Maximum Allowed
Brand	Generic				
Soliris	eculizumab	aHUS	1200 mg	J1300	120 HCPCS units (10 mg per unit)
		MG/NMOSD	1200 mg	J1300	120 HCPCS units (10 mg per unit)
		PNH	900 mg	J1300	90 HCPCS units (10 mg per unit)

HCPCS Code Based Maximum Dosage Information

Maximum Allowed Quantities by National Drug Code (NDC) Units

The allowed quantities in this section are calculated based upon both the maximum dosage information supplied within this policy as well as the process by which NDC claims are billed. This list may not be inclusive of all available NDC's for each drug product and is subject to change.

Medication Name		Diagnosis	How Supplied	National Drug Code	Maximum Allowed
Brand	Generic				
Soliris	eculizumab	aHUS	300 mg vials	25682-0001-01	4 vials/120 ml
		MG/NMOSD	300 mg vials	25682-0001-01	4 vials/120ml
		PNH	300 mg vials	25682-0001-01	3 vials/90ml

Background

Ecuzumab is a monoclonal antibody that binds with high affinity to compliment protein C5, which inhibits its cleavage to C5a and C5b and prevents the generation of the terminal complement complex C5b-9. In those patients with paroxysmal nocturnal hemoglobinuria (PNH), ecuzumab inhibits terminal complement mediated intravascular hemolysis. In patients with atypical hemolytic uremic syndrome (aHUS), impairment in the regulation of complement activity leads to uncontrolled terminal complement activation, resulting in platelet activation, endothelial cell damage and thrombotic microangiopathy. The precise mechanism by which ecuzumab exerts its therapeutic effect in gMG patients is unknown but is presumed to involve reduction of terminal complement complex C5b-9 deposition at the neuromuscular junction.¹⁻³

Benefit Considerations

Some Certificates of Coverage allow coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy. Benefit coverage for an otherwise unproven service for the treatment of serious rare diseases may occur when certain conditions are met.

****Additional Information:** Clinical coverage in this policy addresses the drug only. It does not address coverage for drug administration in a hospital outpatient department. Refer to the member specific benefit plan document and the Medical Management Guideline titled [Provider Administered Drugs - Site of Care](#) for more information. The member specific benefit plan document determines coverage.

Clinical Evidence

Proven/Medically Necessary

Atypical Hemolytic Uremic Syndrome (aHUS)

Eculizumab is indicated for the treatment of atypical hemolytic uremic syndrome (aHUS).^{1,14,15}

Paroxysmal Nocturnal Hemoglobinuria (PNH)

Eculizumab is indicated for the treatment of paroxysmal nocturnal hemoglobinuria (PNH).¹

Hillmen et al evaluated the long-term safety and efficacy of continuous administration of eculizumab in 195 patients with paroxysmal nocturnal hemoglobinuria (PNH) over 66 months.² Patients previously enrolled in the Phase II pilot study and its extensions, the Phase III TRIUMPH (Transfusion Reduction Efficacy and Safety Clinical Investigation, a Randomized, Multicenter, Double-Blind, Placebo-Controlled, Using Eculizumab in Paroxysmal Nocturnal Hemoglobinuria) study (NCT00122330), or the Phase III SHEPHERD (Safety in Hemolytic PNH Patients Treated With Eculizumab: A Multi-Center Open-Label Research Design) study (NCT00130000) were eligible to participate. All patients had a minimum of 10% PNH red blood cells at enrolment in the parent trials and were vaccinated with a meningococcal vaccine at least 14 days prior to the first eculizumab infusion in the parent studies. Efficacy assessments were performed at least every 2 weeks from the time of initiation of eculizumab therapy in the parent study. Efficacy endpoints included patient survival degree of hemolysis, thrombotic events (TE), mean change from baseline in hemoglobin and the number of units of transfused packed red blood cells (PRBCs) administered. Assessments of renal function were performed over the duration of the study by determining the CKD stage using formulas for estimated glomerular filtration rate (GFR). Safety was assessed through monitoring of adverse events (AEs), clinical laboratory tests and vital signs. Four patient deaths were reported, all unrelated to treatment, resulting in a 3-year survival estimate of 97.6%. All patients showed a reduction in lactate dehydrogenase levels, which was sustained over the course of treatment (median reduction of 86.9% at 36 months). Incidence of TEs decreased by 81.8%, with 96.4% of patients remaining free of TEs. Researchers observed a time-dependent improvement in renal function: 93.1% of patients exhibited improvement or stabilization in CKD score at 36 months. Transfusion independence increased by 90.0% from baseline, with the number of red blood cell units transfused decreasing by 54.7%. The median treatment duration was 30.3 months with a maximum duration of 66 months. Eculizumab was well tolerated, with no evidence of cumulative toxicity and a decreasing occurrence of adverse events over time. Very few patients discontinued treatment. Researchers concluded that long-term treatment with eculizumab resulted in sustained improvement in patient outcomes by rapidly reducing hemolysis and significantly reducing the frequency of severe and life-threatening morbidities, such as TEs and CKD, and thus, improving patient survival.

In 2021, Hillmen et al evaluated the efficacy and safety of pegcetacoplan as compared to eculizumab in adults with PNH and hemoglobin levels below 10.5g/dL despite use of eculizumab for at least 3 months in a phase 3 open label, controlled trial (PEGASUS). All patients received pegcetacoplan plus eculizumab during a 4 week run-in phase, then randomized in a 1:1 ratio to subcutaneous pegcetacoplan monotherapy (n = 41) or intravenous eculizumab (n = 39) for 16 weeks. This period was followed by a 32-week period in which all patients received open-label pegcetacoplan. The primary endpoint was the mean change in hemoglobin level from baseline to week 16. Secondary endpoints include proportion of patients that did not require transfusion during the randomized, controlled period, change from baseline to week 16 in absolute reticulocyte count, lactate dehydrogenase (LDH) level, and score on the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) scale. Clinical efficacy analysis found that pegcetacoplan was superior to eculizumab with respect to the change in hemoglobin level from baseline to week 16 with a mean difference between treatments of 3.84 g/dL (95% confidence interval [CI], 2.33 to 5.34; p < 0.001), with the increase of hemoglobin levels in patients receiving pegcetacoplan monotherapy seen as early as week 2 of the 16-week controlled trial period and maintained throughout the 16-week period. Additionally, 35 patients (85%) in the pegcetacoplan group were transfusion-free, whereas only 6 (15%) in the eculizumab group were transfusion-free (p < 0.001). FACIT-F scores increased with pegcetacoplan by 9.2 points and decreased with eculizumab by 2.7 points (adjusted mean difference of 11.9 points [95% CI, 5.49 to 18.25] at week 16). 73% of patients in the pegcetacoplan group had at least a 3-point

increase in FACIT-F scores at week 16, as compared with 0% in the eculizumab group (a 3-point change is considered clinically significant). Noninferiority of pegcetacoplan to eculizumab was shown for the change in absolute reticulocyte count. The researchers concluded that in patients with persistent anemia despite eculizumab therapy, pegcetacoplan was superior to eculizumab with respect to change in baseline hemoglobin levels and improvements in key clinical and hematologic variables, such as decrease in transfusions, and therefore treatment with pegcetacoplan may result in better control of PNH than treatment with eculizumab.³⁴

Generalized Myasthenia Gravis

Eculizumab is indicated for the treatment of generalized myasthenia gravis.¹

Howard et al completed a phase 3 randomized, double-blind, placebo-controlled, multi-center study (REGAIN) that assessed the efficacy and safety of eculizumab in patients 18 years of age and older, with a confirmed diagnosis of generalized myasthenia gravis.^{9,11} Patients were required to be classified by the Myasthenia Gravis Foundation of America as Class II to IV at screening, and a Myasthenia Gravis-Activities of Daily Living (MG-ADL) scale ≥ 6 at screening and randomization, and vaccination against *Neisseria meningitidis*. Patients were also to have failed at least two immunosuppressive agents, or failed at least one agent, and require chronic plasma exchange or IVIG for 12 months without symptom control. One hundred twenty-five patients were randomized to receive either placebo (n = 63), or eculizumab (n = 62): 900 mg IV weekly for 4 doses, followed by 1,200 mg IV every 2 weeks during weeks 4 through 26. Primary outcome measures included the change in total MG-ADL score and the change in MG-ADL total score from baseline at week 26 as compared to placebo. A clinical response in MG-ADL was defined as at least a 3-point improvement. The primary analysis showed no significant difference between eculizumab and placebo. In evaluating clinically meaningful response, a higher proportion of patients achieved a clinically meaningful response with eculizumab than with placebo (p < 0.05). No deaths or cases of meningococcal infection occurred during the study. The most common adverse events in both groups were headache and upper respiratory tract infection. Myasthenia gravis exacerbations were reported by six (10%) patients in the eculizumab group and 15 (24%) in the placebo group. Six (10%) patients in the eculizumab group and 12 (19%) in the placebo group required rescue therapy. The change in the MG-ADL score was not statistically significant between eculizumab and placebo, as measured by the worst-rank analysis. Eculizumab was well tolerated. The authors disclosed that the use of a worst-rank analytical approach proved to be an important limitation of this study since the secondary and sensitivity analyses results were inconsistent with the primary endpoint result. The authors state that further research into the role of complement is needed.

Neuromyelitis Optica Spectrum Disorder (NMOSD)

Eculizumab is indicated for the treatment of NMOSD.¹

Pittock et al conducted a randomized, double-blind, time-to-event trial (PREVENT) evaluating the safety and efficacy of eculizumab for the treatment of aquaporin-4-positive (AQP4-IgG) neuromyelitis optica spectrum disorder (NMOSD). The study enrolled 143 adults, of which 91% of patients were women. Patients were randomly assigned in a 2:1 ratio to receive either intravenous eculizumab (titrated up to 1,200mg every 2 weeks) or placebo. There was no active control. Patients were allowed to continue background immunosuppressant therapy. Patients were included if they had either 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 had occurred within the previous 12 months, and a score of 7 or less on the EDSS. The primary endpoint was the first adjudicated relapse. Secondary outcomes included the adjudicated annualized relapse rate, quality-of-life measures, and the score on the Expanded Disability Status Scale (EDSS). At baseline, the mean (\pm SD) annualized relapse rate during the previous 24 months was 1.99 ± 0.94 . The primary end point of adjudicated relapse occurred in 3 of 96 patients (3%) in the eculizumab group and in 20 of 47 (43%) in the placebo group (hazard ratio, 0.06; 95% confidence interval [CI], 0.02 to 0.20; p < 0.001). The median time until the first adjudicated relapse was not reached in the eculizumab group and was reached at 103 weeks in the placebo group. Most relapses were of myelitis. The adjudicated annualized relapse rate was 0.02 in the eculizumab group and 0.35 in the placebo group (rate ratio, 0.04; 95% CI, 0.01 to 0.15; p < 0.001). The mean change in the EDSS score was -0.18 in the eculizumab group and 0.12 in the placebo group (least-squares mean difference, -0.29; 95% CI, -0.59 to 0.01). Upper respiratory tract infections and headaches were more common in the eculizumab group. There was one death from pulmonary empyema in the eculizumab group.

Unproven/Not Medically Necessary

Eculizumab is not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).¹ While the few studies available demonstrate possible efficacy of eculizumab in treating Shiga toxin E. coli-related hemolytic uremic syndrome, further studies are warranted to demonstrate that it is both safe and effective for this indication.

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Soliris® (eculizumab) is a complement inhibitor indicated for:¹

- Treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis.
- Treatment of patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy.
- Treatment of adult patients with generalized Myasthenia Gravis (gMG) who are antiacetylcholine receptor (AChR) antibody positive.
- Treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive.

Limitations of Use¹: Soliris is not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).

The use of Soliris increases a patient's susceptibility to serious meningococcal infections (septicemia and/or meningitis). Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early:

- Vaccinate for meningococcal disease according to the most current Advisory Committee on Immunization Practices (ACIP) recommendations for patients with complement deficiencies.
- Revaccinate patients in accordance with ACIP recommendations, considering the duration of Soliris therapy.
- Immunize patients without a history of meningococcal vaccination at least 2 weeks prior to receiving the first dose of Soliris.
 - If urgent Soliris therapy is indicated in an unvaccinated patient, administer meningococcal vaccine(s) as soon as possible.
- Closely monitor patients for early signs and symptoms of meningococcal infection and evaluate patients immediately if an infection is suspected.

Soliris is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). Under the Soliris REMS program, prescribers must enroll in the program. Enrollment in the Soliris REMS program and additional information are available by telephone: 1-888-765-4747 or at <http://www.solirisrems.com/>.^{1,3,12,13}

References

1. Soliris® [prescribing information]; Boston, MA: Alexion Pharmaceuticals, Inc.; November 2020.
2. Hillmen P, Muus P, Röth A, et al; Long-term safety and efficacy of sustained eculizumab treatment in patients with paroxysmal nocturnal haemoglobinuria; Br J Haematol; 2013 Apr 25.
3. Soliris REMS. Available at: <http://www.solirisrems.com/>. Accessed July 16, 2023.
4. Lapeyraque AL, Malina M, Fremeaux-Bacchi V, et al; Eculizumab in severe Shiga-toxin-associated HUS. N Engl J Med; 2011 Jun 30; 364 (26): 2561-3.
5. Kielstein JT, Beutel G, Fleig S, et al; Best supportive care and therapeutic plasma exchange with or without eculizumab in Shiga-toxin-producing E. coli O104:H4 induced haemolytic-uraemic syndrome: an analysis of the German STEC-HUS registry; Nephrol Dial Transplant; 2012 Oct; 27 (10): 3807-15.
6. Delmas Y1, Vendrely B, Clouzeau B, et al; Outbreak of Escherichia coli O104:H4 haemolytic uraemic syndrome in France: outcome with eculizumab; Nephrol Dial Transplant; 2014 Mar; 29 (3): 565-72.
7. Howard JF Jr, Barohn RJ, Cutter GR, et al. A randomized, double-blind, placebo-controlled phase II study of eculizumab in patients with refractory generalized myasthenia gravis. Muscle Nerve. 2013 Jul;48(1):76-84.

8. Alexion Pharmaceuticals. Safety and Efficacy Study of Eculizumab in Patients With Refractory Generalized Myasthenia Gravis. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2017 May 19]. Available from: <https://clinicaltrials.gov/ct2/show/NCT00727194>. NCT00727194 NLM Identifier: NCT00727194.
9. Alexion Pharmaceuticals. Safety and Efficacy of Eculizumab in Refractory Generalized Myasthenia Gravis (REGAIN Study). In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2017 May 19]. Available from: <https://clinicaltrials.gov/ct2/show/NCT01997229>. NCT01997229 NLM Identifier: NCT01997229.
10. Alexion Pharmaceuticals. ECU-MG-302: An Extension Trial of ECU-MG-301 to Evaluate Safety and Efficacy of Eculizumab in Refractory Generalized Myasthenia Gravis. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2017 May 19]. Available from: <https://clinicaltrials.gov/ct2/show/NCT02301624>. NCT02301624 NLM Identifier: NCT02301624.
11. Howard JF Jr, Utsugisawa K, Benatar M, et al. Safety and efficacy of eculizumab in anti-acetylcholine receptor antibody-positive refractory generalized myasthenia gravis (REGAIN): a phase 3, randomized, double-blind, placebo-controlled, multicentre study. *Lancet Neurol*. 2017 Dec;16(12):976-986.
12. Ultomiris™ [prescribing information]. Boston, MA: Alexion Pharmaceuticals, Inc.; July 2022.
13. Ultomiris REMS. Available at: <http://www.ultomirisrems.com/>. Accessed July 16, 2023.
14. Lee JW, Sicre de Fontbrune F, Wong Lee L, et al. Ravulizumab (ALXN1210) vs eculizumab in adult patients with PNH naive to complement inhibitors: the 301 study. *Blood*. 2018 Dec 3.
15. Kulasekararaj AG, Hill A, Rottinghaus ST, et al. Ravulizumab (ALXN1210) vs eculizumab in C5-inhibitor-experienced adult patients with PNH: the 302 study. *Blood*. 2018 Dec 3.
16. Parker C, Omine M, Richards S, et al. Diagnosis and management of paroxysmal nocturnal hemoglobinuria. *Blood*. 2005 Dec 1; 106(12): 3699–3709.
17. Devalet B, Mullier F, Chatelain B, et al. Pathophysiology, diagnosis, and treatment of paroxysmal nocturnal hemoglobinuria: a review. *Eur J Haematol*. 2015 Sep;95(3):190-8.
18. Sutherland DR, Keeney M, Illingworth A. Practical guidelines for the high-sensitivity detection and monitoring of paroxysmal nocturnal hemoglobinuria clones by flow cytometry. *Cytometry B Clin Cytom*. 2012 Jul;82(4):195-208.
19. Röth A, Maciejewski J, Nishimura JI, et al. Screening and diagnostic clinical algorithm for paroxysmal nocturnal hemoglobinuria: Expert consensus. *Eur J Haematol*. 2018 Jul;101(1):3-11.
20. Campistol JM, Arias M, Ariceta G, et al. An update for atypical haemolytic uraemic syndrome: diagnosis and treatment. A consensus document. *Nefrologia* 2013;33:27–45.
21. Franchini M. Atypical hemolytic uremic syndrome: from diagnosis to treatment. *Clin Chem Lab Med*. 2015 Oct;53(11):1679-88.
22. Trebst C, Jarius S, Berthele A, et al. Update on the diagnosis and treatment of neuromyelitis optica: Recommendations of the Neuromyelitis Optica Study Group (NEMOS). *J Neurol*. 2014 Jan;261(1):1-16. doi: 10.1007/s00415-013-7169-7. Epub 2013 Nov 23.
23. Scott TF, Frohman EM, DeSeze J, et al. Evidence-based guideline: Clinical evaluation and treatment of transverse myelitis: Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology* 2011 Dec 13;77(24):2128-34.
24. Sellner JI, Boggild M, Clanet M, et al. EFNS guidelines on diagnosis and management of neuromyelitis optica. *Eur J Neurol*. 2010 Aug;17(8):1019-32.
25. Wingerchuk DM, Banwell B, Bennett JL, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. *Neurology*. 2015 Jul 14;85(2):177-89.
26. Pittock SJ, Berthele A, Fujihara K, et al. Eculizumab in Aquaporin-4-Positive Neuromyelitis Optica Spectrum Disorder. *N Engl J Med*. 2019 May 3.
27. Kim SH, Huh SY, Lee SJ, et al. A 5-year follow-up of rituximab treatment in patients with neuromyelitis optica spectrum disorder. *JAMA Neurol*. 2013 Sep 1;70(9):1110-7.
28. Mealy MA, Wingerchuk DM, Palace J, et al. Comparison of Relapse and Treatment Failure Rates Among Patients With Neuromyelitis Optica: Multicenter Study of Treatment Efficacy. *JAMA Neurol*. 2014 Mar;71(3):324-30.

29. Sato D, Callegaro D, Lana-Peixoto MA, Fujihara K. Treatment of neuromyelitis optica: an evidence based review. *Arq Neuropsiquiatr* 2012;70(1):59-66.
30. Ciron J, Audoin B, Bourre B, et al. Recommendations for the use of Rituximab in neuromyelitis optica spectrum disorders. *Rev Neurol (Paris)*. 2018 Apr;174(4):255-264.
31. Wingerchuk DM, Banwell B, Bennett JL, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. *Neurology*. 2015 Jul 14;85(2):177-89.
32. Nikoo Z, Badihian S, Shaygannejad V, et al. Comparison of the efficacy of azathioprine and rituximab in neuromyelitis optica spectrum disorder: a randomized clinical trial. *J Neurol*. 2017 Sep;264(9):2003-2009.
33. Gao F, Chai B, Gu C, et al. Effectiveness of rituximab in neuromyelitis optica: a meta-analysis. *BMC Neurol*. 2019 Mar 6;19(1):36.

Guideline History/Revision Information

Date	Summary of Changes
04/01/2024	<p>Supporting Information</p> <ul style="list-style-type: none"> • Updated <i>FDA</i> section to reflect the most current information • Archived previous policy version MMG142.R

Instructions for Use

This Medical Management Guideline provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this guideline, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Management Guideline is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the InterQual[®] criteria, to assist us in administering health benefits. UnitedHealthcare West Medical Management Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

Member benefit coverage and limitations may vary based on the member's benefit plan Health Plan coverage provided by or through UnitedHealthcare of California, UnitedHealthcare Benefits Plan of California, UnitedHealthcare of Oklahoma, Inc., UnitedHealthcare of Oregon, Inc., UnitedHealthcare Benefits of Texas, Inc., or UnitedHealthcare of Washington, Inc.