HIGHMARK WHOLECARE

Updated: 04/2025
PARP Approved: 05/2025

Prior Authorization Criteria
Complement inhibitors

All requests for Complement inhibitors require a prior authorization and will be screened for medical necessity and appropriateness using the criteria listed below.

Complement inhibitors include Soliris (eculizumab), Ultomiris (ravulizumab-cwvz), Empaveli (pegcetacoplan), Fabhalta (iptacopan), Enjaymo (sutimlimab-jome), Tavneos (avacopan), Veopoz (pozelimab-bbfg), PiaSky (crovalimab-akkz), Voydeya (danicopan) and Zilbrysq (zilucoplan). New products with this classification will require the same documentation.

**** For requests for complement inhibitors for the treatment of myasthenia gravis, refer to the Myasthenia Gravis Medications Policy ****

Prior Authorization Criteria:

For all requests for Complement Inhibitors, all of the following criteria must be met in addition to the diagnosis specific criteria below:

- The requested dose and frequency is in accordance with FDA-approved labeling, nationally recognized compendia, and/or evidence-based practice guidelines
- Is age-appropriate according to FDA-approved package labeling, nationally recognized compendia, or peer-reviewed medical literature
- The member has received appropriate vaccinations as recommended in the FDA-approved package labeling unless contraindicated

Coverage may be provided with a diagnosis of **paroxysmal nocturnal hemoglobinuria (PNH)** and the following criteria are met:

- Medication is prescribed by, or in consultation with, a hematologist, oncologist, immunologist, or genetic specialist
- Member has a diagnosis of PNH confirmed by flow cytometry testing. Flow cytometry pathology report must be supplied and demonstrate at least 2 different GPI protein deficiencies within 2 different cell lines from granulocytes, monocytes, or erythrocytes
- Member has one of the following:
    - Member's hemoglobin is less than or equal to 7 g/dL
    - Member has symptoms of anemia and the hemoglobin is less than or equal to 9 g/dL **(Soliris only)** or 10.5g/dL **(Empaveli only)**
    - Member has symptoms of anemia and the hemoglobin is less than or equal to 10 g/dL **(Ultomiris and Fabhalta only)**
- Must have a Lactate dehydrogenase (LDH) level at least 1.5 times the upper limit of the normal range (laboratory results with reference range must be submitted)
- If requesting Soliris, must have documentation of inadequate response, contraindication or intolerance to Ultomiris.
- **Initial Duration of Approval:** 6 months
- **Reauthorization criteria**
    - Documentation of each of the following:
        - Documentation of a recent (within 3 months) LDH level that shows a reduction from baseline

        - Documentation that hemoglobin has not dropped by more than 2 g/dL from baseline.
            - If baseline hemoglobin was less than 9g/dL, then the most recent hemoglobin must remain above 7g/dL
- **Reauthorization Duration of Approval:** 12 months

Coverage may be provided with a diagnosis of **atypical hemolytic uremic syndrome (aHUS)** and the following criteria are met:

- Member weights at least 5 kilograms
- Medication is prescribed by, or in consultation with, a hematologist, oncologist, immunologist, genetic specialist, or nephrologist
- Must provide documentation of hemolysis such as an elevation in serum LDH and serum creatinine above the upper limits of normal or required dialysis.
- The diagnosis of aHUS is supported by the absence of Shiga toxin-producing *E.coli* infection
- Must provide documentation member does not have a disintegrin and metalloproteinase with thrombospondin type 1 motif member 13 (ADAMTS13) deficiency
- If requesting Soliris, must have documentation of inadequate response, contraindication or intolerance to Ultomiris.
- **Initial Duration of Approval:** 6 months
- **Reauthorization criteria**
    - Documentation from the provider that the member had a positive clinical response as evidenced by any of the following:
        - An increase in platelet count from baseline
        - Maintenance of normal platelet counts and LDH levels for at least four weeks
        - A 25% reduction in serum creatinine for a minimum of four weeks
        - The member has not experienced one of the following for at least 12 weeks after initiation of treatment:
            - A decrease in platelet count of >25% from baseline
            - Plasma exchange or plasma infusion
            - New dialysis requirement
- **Reauthorization Duration of Approval:** 12 months

Coverage may be provided with a diagnosis of **Neuromyelitis Optica Spectrum Disorder (NMOSD)** (Soliris (eculizumab) and Ultomiris (ravulizumab-cwvz) ONLY) and the following criteria are met:

- Medication is prescribed by, or in consultation with a neurologist
- Documentation of a positive test for AQP4-IgG antibodies
- The prescriber submits documentation of baseline number of relapse(s), which occurred over the last year.
- Documentation of an Expanded Disability Status Scale (EDSS) score of ≤ 7
- If using concurrent corticosteroids, dose is less than or equal to the equivalent of prednisone 20 mg per day
- Must have documentation of inadequate response, contraindication or intolerance to one (1) immunosuppressant (e.g., mycophenolate mofetil, azathioprine, methotrexate) or an inadequate response, contraindication or intolerance to rituximab or any of its biosimilars
- **Initial Duration of Approval:** 12 months

- **Reauthorization criteria**
    - Documentation the member has experienced a decrease from baseline in the number of NMOSD relapse(s).
- **Reauthorization Duration of Approval:** 12 months

Coverage may be provided with a diagnosis of **cold agglutinin disease (CAD)** and the following criteria are met:

- Documentation of the diagnosis of CAD confirmed by:
    - Evidence of hemolysis indicated by both of the following:
        - Lactate dehydrogenase (LDH) level above the upper limit of normal AND
        - Haptoglobin level below the lower limit of normal
- The member has a positive direct antiglobulin (Coombs) test for C3d only
- The member has a cold agglutinin titer of ≥ 64 at 4 degrees Celsius
- The member has a lack of overt malignant disease
- The member has a Hemoglobin level l ≤ 10.0 g/dL
- Documentation of a bilirubin level above normal reference range, including patients with Gilbert's syndrome
- Presence of one or more symptoms associated with CAD including:
    - Symptomatic anemia
    - Acrocyanosis
    - Raynaud's phenomenon
    - Hemoglobinuria
    - Disabling circulatory symptoms
    - Major adverse vascular event
- **Initial Duration of Approval: 6 months**
- **Reauthorization criteria**
    - Documentation of benefit from therapy including one of the following:
        - Increase in Hgb levels from baseline by ≥ 1.5g/dL or achieving Hgb level of ≥ 12 g/dL
        - Normalization of LDH and/or bilirubin levels
        - Decrease in transfusion burden
- **Reauthorization Duration of Approval: 12 months**

Coverage may be provided with a diagnosis of **Complement Hyperactivation, Angiopathic Thrombosis, and Protein-Losing Enteropathy (CHAPLE)** and the following criteria are met:

- Must be prescribed by or in consultation with a provider who specializes in the treatment of CHAPLE disease
- Member has a diagnosis of CD55-deficient protein-losing enteropathy (PLE), also known as CHAPLE disease confirmed by biallelic CD55 loss-of-function mutation detected by genetic testing
- Member has active disease defined as hypoalbuminemia (serum albumin concentration ≤3.2 g/dL) with one or more of the following in the last 6 months:
    - Abdominal pain
    - Vomiting
    - Diarrhea
    - Peripheral or facial edema
    - Infection with concomitant hypogammaglobinemia
    - New thromboembolic event

- Member will not receive the requested drug in combination with another complement inhibitor
- Member has adequate titers or will receive meningococcal vaccines at least two weeks prior to the first dose of Veopoz
- **Initial Duration of Approval: 6 months**
- **Reauthorization criteria**
    - No evidence of unacceptable toxicity or disease progression while on the requested medication
    - Demonstrates a positive response to therapy as defined by ALL of the following:
        - Improvement or stabilization in disease activity (e.g., improvement of clinical symptoms [abdominal pain, diarrhea, and/or edema], increase in or stabilization of IgG concentrations, increase in growth percentiles, reduction in hospitalizations)
        - Normalization of serum albumin levels
- **Reauthorization Duration of Approval: 12 months**

Coverage may be provided with a diagnosis of **Anti-Neutrophil Cytoplasmic autoantibody (ANCA)-Associated Vasculitis** and the following criteria are met:

- Member must have severe and active ANCA- associated vasculitis
- Disease is one of the following types:
    - Granulomatosis with polyangiitis (GPA)
    - Microscopic polyangiitis (MPA)
- Member is positive for proteinase 3 antibodies, myeloperoxidase antibodies, or anti-neutrophil cytoplasmic autoantibody (ANCA)
- Must be prescribed by or in consultation with a rheumatologist,
- nephrologist, or immunologist
- A baseline Birmingham Vasculitis Activity Score (BVAS) has been performed
- Must be used as adjunctive treatment in combination with standard therapy (e.g., prednisone, azathioprine, mycophenolate, methotrexate, rituximab, cyclophosphamide)
- **Initial Duration of Approval: 6 months**
- **Reauthorization criteria**
    - Member experienced a beneficial clinical response from baseline exhibited by improvement in estimated glomerular filtration rate, decrease in urinary albumin creatinine ratio, or improvement in the BVAS from baseline
    - Member has experienced an improvement in at least one symptom, such as joint pain, ulcers, myalgia, persistent cough, skin rash, abdominal pain, or improvement in function or activities of daily living
- **Reauthorization Duration of Approval: 12 months**

Coverage may be provided with a diagnosis of **primary immunoglobulin A nephropathy (IgAN)** and the following criteria are met (Fabhalta only):

- The member has a diagnosis of IgAN confirmed by:
    - biopsy-proven IgAN
    - eGFR $\geq$ 20 mL/min/1.73 m^2
    - urine protein-to-creatinine ratio (UPCR) $\geq$1 g/g on a stable dose of maximally-tolerated renin-angiotensin system (RAS) inhibitor therapy with or without a stable dose of an SGLT2 inhibitor
- **Initial Duration of Approval:** 6 months

- **Reauthorization criteria**
    - Member experienced a beneficial clinical response from baseline exhibited by improvement or reduction in UPCR from baseline
- **Reauthorization Duration of Approval:** 12 months

Coverage may be provided with a diagnosis of **complement 3 glomerulopathy (C3G)** and the following criteria are met (**Fabhalta only**):

- The member has a diagnosis of native kidney C3G confirmed by:
    - biopsy proven native kidney C3G who had a urine protein-to-creatinine ratio (UPCR) ≥ 1 g/g and eGFR ≥ 30 mL/min/1.73 m^2
- Member must be on a maximally tolerated renin-angiotensin system (RAS) inhibitor
- The member must not have had a kidney transplant
- **Initial Duration of Approval:** 6 months
- **Reauthorization criteria**
    - Member experienced a beneficial clinical response from baseline exhibited by improvement or reduction in UPCR from baseline

  Reauthorization Duration of Approval: 12 months

Coverage may be provided for any non-FDA labeled indication if it is determined that the use is a medically accepted indication supported by nationally recognized pharmacy compendia or peer-reviewed medical literature for treatment of the diagnosis(es) for which it is prescribed. These requests will be reviewed on a case by case basis to determine medical necessity.

When criteria are not met, the request will be forwarded to a Medical Director for review. The physician reviewer must override criteria when, in their professional judgment, the requested medication is medically necessary.

Attachment 1. Expanded Disability Status Scale (EDSS)

Score	Description
1.0	No disability, minimal signs in one functional system (FS)
1.5	No disability, minimal signs in more than one FS
2.0	Minimal disability in one FS
2.5	Mild disability in one FS or minimal disability in two FS
3.0	Moderate disability in one FS, or mild disability in three or four FS. No impairment to walking
3.5	Moderate disability in one FS and more than minimal disability in several others. No impairment to walking
4.0	Significant disability but self-sufficient and up and about some 12 hours a day. Able to walk without aid or rest for 500m
4.5	Significant disability but up and about much of the day, able to work a full day, may otherwise have some limitation of full activity or require minimal assistance. Able to walk without aid or rest for 300m
5.0	Disability severe enough to impair full daily activities and ability to work a full day without special provisions. Able to walk without aid or rest for 200m
5.5	Disability severe enough to preclude full daily activities. Able to walk without aid or rest for 100m
6.0	Requires a walking aid –cane, crutch, etc.– to walk about 100m with or without resting
6.5	Requires two walking aids – pair of canes, crutches, etc. – to walk about 20m without resting

7.0	Unable to walk beyond approximately 5m even with aid. Essentially restricted to wheelchair; though wheels self in standard wheelchair and transfers alone. Up and about in wheelchair some 12 hours a day
7.5	Unable to take more than a few steps. Restricted to wheelchair and may need aid in transfering. Can wheel self but cannot carry on in standard wheelchair for a full day and may require a motorised wheelchair
8.0	Essentially restricted to bed or chair or pushed in wheelchair. May be out of bed itself much of the day. Retains many self-care functions. Generally has effective use of arms
8.5	Essentially restricted to bed much of day. Has some effective use of arms retains some self-care functions
9.0	Confined to bed. Can still communicate and eat
9.5	Confined to bed and totally dependent. Unable to communicate effectively or eat/swallow
10.0	Death

HIGHMARK WHOLECARE

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COMPLEMENT INHIBITORS
PRIOR AUTHORIZATION FORM- PAGE 1 of 4

Please complete and fax all requested information below including any progress notes, laboratory test results, or chart documentation as applicable to Highmark Wholecare Pharmacy Services. **FAX:** (888) 245-2049
If needed, you may call to speak to a Pharmacy Services Representative. **PHONE**: (800) 392-1147 Mon-Fri 8:30am to 5:00pm

PROVIDER INFORMATION

Requesting Provider:	NPI:
Provider Specialty:	Office Contact:
Provider Specialty:	Office NPI:
Office Address:	Office Phone:
	Office Fax:

MEMBER INFORMATION

Member Name:	DOB:	
Member ID:	Member weight:	Height:

REQUESTED DRUG INFORMATION

Medication:	Strength:	
Directions:	Quantity:	Refills:
Is the member currently receiving requested medication? ☐ Yes ☐ No	Date Medication Initiated:	

Billing Information

This medication will be billed: ☐ at a pharmacy **OR** ☐ medically, JCODE:_____
Place of Service: ☐ Hospital ☐ Provider's office ☐ Member's home ☐ Other

Place of Service Information

Name:	NPI:
Address:	Phone:

REFERENCE VALUES

Lab	Initial (Pre-Treatment) Value	Reference Range	Date	Post-Therapy Value (Reauthorization only)	Reference Range	Date
Hemoglobin (Hgb)						
Lactate dehydrogenase (LDH)						
Platelet count						
Serum Creatinine						
Bilirubin						
GPI Protein Deficiencies						
UPCR						

Diagnosis: _____

For Paroxysmal Nocturnal Hemoglobinuria (PNH) only:
Does the member's flow cytometry pathology report demonstrate at least 2 different GPI protein deficiencies within 2 different cell lines from granulocytes, monocytes, or erythrocytes? Please include a copy ☐ Yes ☐ No
Does the patient have symptoms of anemia? ☐ Yes ☐ No

For Atypical Hemolytic Uremic Syndrome only:
Has the absence of Shiga toxin-producing *E.coli* been confirmed? ☐ Yes ☐ No
Does the member have an ADAMTS13 deficiency? ☐ Yes ☐ No Is the member currently on dialysis? ☐ Yes ☐ No
with at least 1 immunosuppressive therapy while on chronic plasmapheresis or plasma exchange (PE)? ☐ Yes ☐ No

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COMPLEMENT INHIBITORS
PRIOR AUTHORIZATION FORM (CONTINUED) – PAGE 2 OF 4

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MEMBER INFORMATION

Member Name:	DOB:	
Member ID:	Member weight:	Height:

MEDICAL HISTORY (Complete for ALL requests)

For Neuromyelitis Optica Spectrum Disorder (NMOSD):
Is documentation of a positive test for AQP4-IgG antibodies provided? ☐ Yes ☐ No
What is the member's Expanded Disability Status Scale (EDSS) score? _____
How many relapses has the member had over the last year? _____
If using corticosteroids, is the dose less than or equal to the equivalent of prednisone 20 mg per day? ☐ Yes ☐ No
Is there documentation of inadequate response, contraindication or intolerance to an immunosuppressant, rituximab or any of its biosimilars? ☐ Yes ☐ No

For cold agglutinin disease (CAD):
Has the diagnosis been confirmed by both an LDH level above the upper limits of normal and haptoglobin level below the lower limit of normal? ☐ Yes, include documentation ☐ No
Does the member have a positive direct antiglobulin (Coombs) test for C3d? ☐ Yes, include documentation ☐ No
What is the members cold agglutinin titer? _____
Does the member have a bilirubin level above normal reference range? ☐ Yes, include documentation ☐ No
Does the member have the presence of one or more symptoms associated with CAD? ☐ Yes, include documentation ☐ No

For CHAPLE disease:
Does the member have a diagnosis of CD55-deficient protein-losing enteropathy (PLE), also known as CHAPLE disease confirmed by biallelic CD55 loss-of-function mutation detected by genetic testing? ☐ Yes, include documentation ☐ No
Does the member have active disease defined as hypoalbuminemia (serum albumin concentration ≤3.2 g/dL) with one or more symptoms associated with CHAPLE disease in the last 6 months? ☐ Yes, include documentation ☐ No
Will the member be using the requested medication in combination with another complement inhibitor? ☐ Yes ☐ No
Has the member received the meningococcal vaccine or has adequeate titers (Veopoz only)? ☐ Yes ☐ No

For Anti-Neutrophil Cytoplasmic autoantibody (ANCA) - Associated Vasculitis:
Does the member have severe and active ANCA- associated vasculitis? ☐ Yes ☐ No
Does the member have GPA or MPA type? ☐ Yes ☐ No
Is the member positive for proteinase 3 antibodie, myeloperoxidase antibodies, or anti-neutrophil cytoplasmic autoantibody (ANCA)? ☐ Yes ☐ No
Has a baseline BVAS been peformed? ☐ Yes ☐ No
Will the requested medication ben used as adjunctive treatment in combination with standard therapy? ☐ Yes ☐ No

For Primary immunoglobulin A nephropathy (IgAN):
Does the member have IgAN confirmed by biopsy? ☐ Yes ☐ No
Does the member have eGFR ≥ 20 mL/min/1.73 m2? ☐ Yes ☐ No
Does the member have a urine protein-to-creatinine ratio (UPCR) ≥ 1g/g on a stable dose of maximally-tolerated renin-angiotensin system (RAS) inhibitor therapy with or without a stable dose of an SGLT2 inhibitor? ☐ Yes ☐ No

For Complement 3 Glomerulopathy (C3G):
Member has a diagnosis of native kidney c3G confirmed by a biopsy? ☐ Yes ☐ No
What is the member's UPCR? _____
Is the member on a maximally tolerated renin-angiotensis system (RAS) inhibitor? ☐ Yes ☐ No
Has the member had a kidney transplant? ☐ Yes ☐ No

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COMPLEMENT INHIBITORS
PRIOR AUTHORIZATION FORM (CONTINUED) – PAGE 3 OF 4

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MEMBER INFORMATION

Member Name:	DOB:	
Member ID:	Member weight:	Height:

CURRENT or PREVIOUS THERAPY

Medication Name	Strength/ Frequency	Dates of Therapy	Status (Discontinued & Why / Current)

REAUTHORIZATION

Has the member experienced a significant improvement with treatment? ☐ Yes, include documentation ☐ No

For Paroxysmal Nocturnal Hemoglobinuria (PNH):
Is there documentation of recent LDH and hemoglobin levels? ☐ Yes- please document above. ☐ No

For Atypical Hemolytic Uremic Syndrome:
Has the patient been able to maintain a normal platelet or LDH level for at least four weeks? ☐ Yes ☐ No
Has the patient experienced a 25% serum creatinine reduction for at least four weeks? ☐ Yes ☐ No
In the past 12 weeks, has the patient had any of the following?
A decrease in platelet count of >25% from baseline ☐ Yes ☐ No
Increased need for plasma exchange or plasma infusion ☐ Yes ☐ No
New dialysis requirement ☐ Yes ☐ No

For NMOSD:
Has the member experienced a decrease from baseline in the number of NMODS relapses? ☐ Yes – please list above ☐ No

For cold agglutinin disease (CAD):
Is there documentation the member has received benefit from the request therapy including one of the following? ☐ Yes, include documentation ☐ No

- Increase in Hgb levels from baseline by ≥ 1.5g/dL or achieving Hgb level of ≥ 12 g/dL
- Normalization of LDH and/or bilirubin levels
- Decrease in transfusion burden

For CHAPLE disease:
Is there any evidence of unacceptable toxicity or disease progression while on the requested medication? ☐ Yes ☐ No
Does the member demonstrate a positive response to therapy as defined by ALL of the following? ☐ Yes ☐ No

- Improvement or stabilization in disease activity (e.g., improvement of clinical symptoms [abdominal pain, diarrhea, and/or edema], increase in or stabilization of IgG concentrations, increase in growth percentiles, reduction in hospitalizations)
- Normalization of serum albumin levels

For Anti-Neutrophil Cytoplasmic autoantibody (ANCA) - Associated Vasculitis:
Has the member experienced a beneficial clinical response from baseline exhibited by improvement in estimated glomerular filtration rate, decrease in urinary albumin creatinine ratio, or improvement in the BVAS from baseline? ☐ Yes ☐ No
Has the member experienced an improvement in at least one symptom, such as joint pain, ulcers, myalgia, persistent cough, skin rash, abdominal pain, or improvement in function or activities of daily living? ☐ Yes ☐ No

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COMPLEMENT INHIBITORS
PRIOR AUTHORIZATION FORM (CONTINUED) – PAGE 4 OF 4

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MEMBER INFORMATION

Member Name:	DOB:	
Member ID:	Member weight:	Height:

REAUTHORIZATION (continued)

For Primary immunoglobulin A nephropathy (IgAN):
Has the member experienced a beneficial clinical response from baseline exhibited by improvement or reduction in UPCR?
☐ Yes ☐ No

For Complement 3 Glomerulopathy (C3G):
Has the member experienced a beneficial clinical response from baseline by showing an improvement or reduction in UPCR from baseline? ☐ Yes ☐ No_____

SUPPORTING INFORMATION or CLINICAL RATIONALE

Prescribing Provider Signature	Date