Medical Policy

Utilization Management and Clinical Medical Policy

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Narsoplimab-wuug (Yartemlea)	MP-RX-FP-188-26	☒ MMM MA ☒ MMM MultiHealth	5/6/2026	5/6/2026
			Last Review Date: 5/6/2026	Frequently Revision: Annual

Service Category:

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Other: Part B Drugs

Service Description:

This document addresses the use of Yartemlea, a mannan-binding lectin-associated serine protease-2 (MASP-2) inhibitor approved by the U.S. Food and Drug Administration (FDA) for the treatment of adult and pediatric patients 2 years of age and older with hematopoietic stem cell transplant–associated thrombotic microangiopathy (TA-TMA). Yartemlea is a recombinant human monoclonal antibody administered as an intravenous infusion and is designed to inhibit activation of the lectin complement pathway, thereby reducing complement-mediated endothelial injury associated with TA-TMA.

Background Information:

Hematopoietic stem cell transplantation (HCT) is associated with multiple early and late complications that may significantly impact morbidity and mortality. One serious and potentially life-threatening complication is transplant-associated thrombotic microangiopathy (TA-TMA), a disorder characterized by endothelial injury leading to microvascular thrombosis, intravascular hemolysis, and organ dysfunction. TA-TMA most commonly develops within the first 100 days following transplantation, although later onset may occur. Clinical features include microangiopathic hemolytic anemia, thrombocytopenia, elevated lactate dehydrogenase (LDH), schistocytes on peripheral blood smear, hypertension, and acute or progressive kidney dysfunction. Multiorgan involvement, including pulmonary and neurologic complications, may be observed in severe cases. Reported incidence varies widely due to differing diagnostic criteria, with contemporary estimates generally ranging from approximately 2% to 39% among allogeneic HCT recipients. TA-TMA is associated with significant morbidity and mortality, with substantially reduced survival compared with transplant recipients without TA-TMA.

The pathogenesis of TA-TMA is multifactorial and involves endothelial injury triggered by conditioning regimens, calcineurin inhibitors, graft-versus-host disease (GVHD), infections, and complement activation. Increasing evidence supports a role for dysregulation of the complement system, including activation of the lectin pathway, in disease progression.

Yartemlea (narsoplimab-wuug) is a recombinant human monoclonal antibody that inhibits mannan-binding lectin-associated serine protease-2 (MASP-2), the effector enzyme of the lectin complement pathway, thereby blocking lectin pathway-mediated complement activation while preserving classical

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Narsoplimab-wuug (Yartemlea)	MP-RX-FP-188-26	☒ MMM MA ☒ MMM MultiHealth	5/6/2026 Last Review Date: 5/6/2026	5/6/2026 Frequently Revision: Annual

and alternative complement pathway function. Yartemlea is indicated for the treatment of adult and pediatric patients 2 years of age and older with hematopoietic stem cell transplant–associated thrombotic microangiopathy (TA-TMA).

The efficacy of Yartemlea was evaluated in a single-arm, open-label study (TA-TMA Study) enrolling 28 adult patients who developed TA-TMA following HCT and in an expanded access program (EAP), in which 19 adult and pediatric patients had evaluable patient-level response data from a larger treated cohort. In the TA-TMA Study, 24 patients received Yartemlea 4 mg/kg intravenously once weekly and 4 patients received 370 mg intravenously once weekly; the median duration of therapy was 8 weeks. TA-TMA response was defined as improvement in both laboratory markers (platelet count and LDH) and either improvement in organ function or independence from transfusions. In the TA-TMA Study, 17 of 28 patients (60.7%) achieved a TA-TMA response, and in the EAP cohort with evaluable data, 13 of 19 patients (68.4%) achieved a response. The 100-day survival from time of TA-TMA diagnosis was 73.4% in the TA-TMA Study and 73.7% in the EAP cohort.

Yartemlea is administered as an intravenous infusion over 30 minutes with weight-based dosing: patients weighing ≥50 kg receive 370 mg once weekly and those weighing <50 kg receive 4 mg/kg once weekly; dosing frequency may be increased to twice weekly if there is inadequate improvement in TA-TMA signs and symptoms. The product is diluted prior to administration and infused through a PVC or PVC-lined infusion line with a 0.2-micron polyethersulfone (PES) in-line filter and a polyurethane catheter; preparation differs for patients ≥10 kg (intravenous bag) versus <10 kg (syringe). The label also instructs not to co-administer other drugs through the same intravenous line.

The prescribing information lists no contraindications. Key warnings and precautions include serious and life-threatening infections, which have occurred in patients treated with Yartemlea; patients should be monitored for signs and symptoms of infection and treated promptly, and those with active infections should be monitored closely for worsening infection. In the TA-TMA study, serious infections (independent of causality) were reported in 36% of patients, including sepsis, viral infections, pneumonia, bacteremia, fungal infection, gastroenteritis, respiratory tract infection, and urosepsis. In clinical trials, serious adverse reactions occurred in 61% of patients and fatal adverse reactions occurred in 7% (including neutropenic sepsis and septic shock). The most common adverse reactions (≥20%), regardless of causality, included viral infections, sepsis, hemorrhage, diarrhea, vomiting, nausea, neutropenia, pyrexia, fatigue, and hypokalemia.

Approved Indications

A. Yartemlea is indicated for the treatment of adult and pediatric patients 2 years of age and older with hematopoietic stem cell transplant–associated thrombotic microangiopathy (TA-TMA).

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Narsoplimab-wuug (Yartemlea)	MP-RX-FP-188-26	☒ MMM MA ☒ MMM MultiHealth	5/6/2026	5/6/2026
			Last Review Date: 5/6/2026	Frequently Revision: Annual

Other Uses

A. See background section above.

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Narsoplimab-wuug (Yartemlea)	MP-RX-FP-188-26	☒ MMM MA ☒ MMM MultiHealth	5/6/2026	5/6/2026
			Last Review Date: 5/6/2026	Frequently Revision: Annual

Medical Necessity Guidelines:

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Yartemlea® (narsoplimab-wuug)

A. Criteria For Initial Approval (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met all approval criteria.)*

i. The member is 2 years of age or older; **AND**

ii. The member has developed TA-TMA following hematopoietic stem cell transplantation; **AND**

iii. Documentation supports a confirmed diagnosis of TA-TMA based on the following clinical and laboratory findings:

A. Platelet count <150,000/µL; AND

B. Evidence of microangiopathic hemolysis, defined as the presence of schistocytes and serum lactate dehydrogenase (LDH) greater than the upper limit of normal (ULN) and/or haptoglobin less than the lower limit of normal (LLN); **AND**

C. Renal dysfunction attributable to TA-TMA.

B. Criteria For Continuation of Therapy

i. MMM considers continuation of Yartemlea medically necessary when all of the following criteria are met:

A. The member continues to meet the indication for hematopoietic stem cell transplant–associated thrombotic microangiopathy (TA-TMA); **AND**

B. There is documented evidence of clinical response to therapy, defined as improvement in laboratory markers of thrombotic microangiopathy, including improvement in platelet count and reduction in lactate dehydrogenase (LDH) toward or below the upper limit of normal, and/or improvement in organ function (e.g., stabilization or improvement in renal function) or reduced transfusion requirements; **AND**

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Narsoplimab-wuug (Yartemlea)	MP-RX-FP-188-26	☒ MMM MA ☒ MMM MultiHealth	5/6/2026	5/6/2026
			Last Review Date: 5/6/2026	Frequently Revision: Annual

C. There is no evidence of unacceptable toxicity, including uncontrolled serious infection or other severe adverse reactions attributable to therapy; **AND**

D. The requested duration of therapy is consistent with the prescribing information and clinical trial experience (typically 4 to 8 weeks), and extended therapy beyond this duration includes documented clinical justification demonstrating ongoing benefit.

C. Authorization Duration

i. Initial Approval Duration: Up to 8 weeks

ii. Reauthorization Approval Duration: Up to an additional 8 weeks, for a total treatment duration not to exceed 16 weeks, unless documentation demonstrates ongoing clinical benefit and medical necessity.

D. Conditions Not Covered

Any use of Yartemlea is considered experimental, investigational, or unproven, including, but not limited to, the following (this list may not be all inclusive):

i. Requests for Yartemlea when the above Medical Necessity criteria are not met.

ii. Use of Yartemlea for indications other than hematopoietic stem cell transplant–associated thrombotic microangiopathy (TA-TMA).

iii. Use of Yartemlea for thrombotic microangiopathy not associated with hematopoietic stem cell transplantation, including but not limited to immune thrombotic thrombocytopenic purpura (TTP) and atypical hemolytic uremic syndrome (aHUS).

iv. Concurrent use of Yartemlea with other complement pathway inhibitors (e.g., eculizumab, ravulizumab, pegcetacoplan, crovalimab) unless medical necessity is clearly documented and reviewed on a case-by-case basis.

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Narsoplimab-wuug (Yartemlea)	MP-RX-FP-188-26	☒ MMM MA ☒ MMM MultiHealth	5/6/2026	5/6/2026
			Last Review Date: 5/6/2026	Frequently Revision: Annual

Limits or Restrictions:

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Approved Indication	Recommended Dosing/Limits

Hematopoietic Stem Cell Transplant–Associated Thrombotic Microangiopathy (TA-TMA)	• The recommended dosage of Yartemlea is administered as an intravenous (IV) infusion over 30 minutes.
	  ○ For patients weighing 50 kg or greater: 370 mg administered intravenously once weekly.
	  ○ For patients weighing less than 50 kg: 4 mg/kg administered intravenously once weekly.
	• Quantity Limit: Not to exceed 2,960 mg (16 mL or 8 vials) per 28 days (equivalent to up to 370 mg twice weekly)

Exceptions	
None	

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Narsoplimab-wuug (Yartemlea)	MP-RX-FP-188-26	☒ MMM MA ☒ MMM MultiHealth	5/6/2026	5/6/2026
			Last Review Date: 5/6/2026	Frequently Revision: Annual

Codes Information:

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. 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.

ICD-10 Diagnostic Codes:

Codes	Description
M31.11	Hematopoietic stem cell transplantation-associated thrombotic microangiopathy [HSCT-TMA]

HCPCS Codes:

Codes	Description
J3590	Unclassified drugs (when billed for Yartemlea and no product-specific HCPCS code has been assigned)

CPT Codes:

Codes	Description
96365	Intravenous infusion, for therapy, prophylaxis, or diagnosis; initial, up to 1 hour

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Narsoplimab-wuug (Yartemlea)	MP-RX-FP-188-26	☒ MMM MA ☒ MMM MultiHealth	5/6/2026	5/6/2026
			Last Review Date: 5/6/2026	Frequently Revision: Annual

Reference Information:

1. Hingorani S, Abudayyeh A, Jhaveri KD. Kidney disease following hematopoietic cell transplantation. In: UpToDate. Palevsky PM, Negrin RS, eds. Lam AQ, deputy ed. Waltham, MA: UpToDate Inc. Literature review current through January 2026. Topic last updated January 30, 2026. Accessed February 19, 2026.
2. Khaled SK, Claes K, Goh YT, Kwong YL, Leung N, Mendrek W, Nakamura R, Sathar J, Ng E, Nangia N, Whitaker S, Rambaldi A; OMS721-TMA-001 Study Group Members. Narsoplimab, a mannan-binding lectin-associated serine protease-2 inhibitor, for the treatment of adult hematopoietic stem-cell transplantation–associated thrombotic microangiopathy. *J Clin Oncol.* 2022;40(22):2447-2457. doi:10.1200/JCO.21.02359.
3. Pandrowala A, Ganatra P, Krishnan VP, Sharma AN, Chavan S, Bodhanwala M, Agarwal B, Hiwarkar P. Narsoplimab for severe transplant-associated thrombotic microangiopathy. *Thromb J.* 2023;21(1):26. doi:10.1186/s12959-023-00463-2.
4. Yartemlea [prescribing information]. Seattle, WA: Omeros Corporation; 2026.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Narsoplimab-wuug (Yartemlea)	**MP-RX-FP-188-26**	☒ **MMM MA** ☒ **MMM MultiHealth**	**5/6/2026**	**5/6/2026**
			Last Review Date: **5/6/2026**	**Frequently Revision:** **Annual**

Policy History:

Type of Review	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Policy Inception	New policy creation.	3/9/2026	5/6/2026
Choose an item.			