Corporate Medical Policy: Narsoplimab-wuug (Yartemlea®) **"Notification"** **POLICY EFFECTIVE MAY 1, 2026**

Restricted Product(s):

- narsoplimab-wuug (Yartemlea®) intravenous infusion for administration by a healthcare professional

FDA Approved Use:

- For the treatment of adult and pediatric patients 2 years of age and older with hematopoietic stem cell transplant-associated thrombotic microangiopathy (TA-TMA)

Criteria for Medical Necessity:

The restricted product(s) may be considered medically necessary when the following criteria are met:

Initial Criteria for Approval:

1. The patient is 2 years of age or older; **AND**
2. The patient has a diagnosis of **hematopoietic stem cell transplant-associated thrombotic microangiopathy (TA-TMA) [medical record documentation required]**; **AND**
3. The patient is post-hematopoietic stem cell transplant (HSCT) **[medical record documentation required]**; **AND**
4. The diagnosis has been confirmed by at least ONE of the following:
    a. Histological evidence of microangiopathy on biopsy of affected organ (e.g., kidney, intestines) **[medical record documentation required]**; **OR**
    b. Presence of at least FOUR of the following diagnostic features **[medical record documentation required]**:
        i. Anemia (i.e., failure to achieve transfusion independence, hemoglobin decline from patient's baseline by at least 1 g/dL, or new onset of transfusion dependence); **OR**
        ii. Thrombocytopenia (i.e., higher than expected platelet transfusion needs, refractoriness to platelet transfusions, 50% reduction or greater in baseline platelet count after full platelet engraftment, or platelet count less than 150,000/µL); **OR**
        iii. Elevated lactate dehydrogenase (LDH); **OR**
        iv. Presence of schistocytes; **OR**
        v. Hypertension; **OR**
        vi. Elevated soluble complement 5b-9 (sC5b-9); **OR**
        vii. Renal dysfunction (e.g., proteinuria, defined as ≥ 1 mg/mg random urine to creatinine ratio [rUPCR]); **AND**
5. BOTH of the following:

a. Alternative diagnoses (e.g., autoimmune or alloimmune hemolytic anemia, thrombotic thrombocytopenic purpura, Shiga toxin-producing *Escherichia coli*-induced hemolytic uremic syndrome, etc.) have been ruled out **[medical record documentation required]**; **AND**
b. TA-TMA triggers (e.g., calcineurin inhibitor toxicity, GVHD, infections) have been evaluated and are being appropriately managed; **AND**

6. The prescriber is a specialist in the area of the patient's diagnosis (e.g., hematologist) or has consulted with a specialist in the area of the patient's diagnosis; **AND**
7. The requested quantity does NOT exceed the maximum units allowed for the duration of approval (see table below).

Duration of Approval: 12 weeks

Continuation Criteria for Approval:

1. The patient was approved through Blue Cross NC initial criteria for approval; **OR**
2. The patient would have met initial criteria for approval at the time they started therapy; **AND**
3. The patient has demonstrated a positive clinical response while using the requested agent, as indicated by BOTH of the following **[medical record documentation required]**:
   a. Improvement in thrombotic microangiopathy (TMA) laboratory markers (e.g., improvement in platelet counts, reduction in lactate dehydrogenase [LDH] and soluble complement 5b-9 [sC5b-9], resolution of schistocytes); **AND**
   b. Improvement in organ function (e.g., reduction in proteinuria, reduction in transfusion requirements, improvement in blood pressure control, resolution of gastrointestinal manifestations); **AND**
4. The patient has NOT experienced unacceptable toxicity or adverse events requiring discontinuation from the requested agent; **AND**
5. The prescriber is a specialist in the area of the patient's diagnosis (e.g., hematologist) or has consulted with a specialist in the area of the patient's diagnosis; **AND**
6. The requested quantity does NOT exceed the maximum units allowed for the duration of approval (see table below).

Duration of Approval: 12 weeks

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
narsoplimab-wuug (Yartemlea®) intravenous (IV) infusion	Hematopoietic stem cell transplant-associated thrombotic microangiopathy (TA-TMA) in patients 2 years and older	IV: • ≥ 50 kg: 370 mg IV once weekly • < 50 kg: 4 mg/kg IV once weekly Increase frequency to twice weekly if there is inadequate improvement in TA-TMA signs and symptoms	C9399** J3490** J3590**	8,880

***Maximum units allowed for duration of approval**
****Non-specific assigned HCPCS codes, must submit requested product NDC**

References: all information referenced is from FDA package insert unless otherwise noted below.

1. Dvorak CC, Higham C, Shimano KA. Transplant-Associated Thrombotic Microangiopathy in Pediatric Hematopoietic Cell Transplant Recipients: A Practical Approach to Diagnosis and Management. *Front Pediatr*. 2019;7. doi:10.3389/fped.2019.00133
2. Khaled SK, Claes K, Yeow Tee Goh, et al. 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.21.02389
3. Schoettler M, Carreras E, Cho B, et al. Harmonizing Definitions for Diagnostic Criteria and Prognostic Assessment of Transplantation-Associated Thrombotic Microangiopathy: A Report on Behalf of the European Society for Blood and Marrow Transplantation, American Society for Transplantation and Cellular Therapy, Asia-Pacific Blood and Marrow Transplantation Group, and Center for International Blood and Marrow Transplant Research. *Transplant Cell Ther.* 2023;29(3):151-163. doi:10.1016/j.jtct.2022.11.015
4. Schoettler ML, Gavriilaki E, Carreras E, et al. An ASTCT, CIBMTR, EBMT, and APBMT Consensus Statement Defining Response Criteria for Hematopoietic Cell Transplantation Associated Thrombotic Microangiopathy (TA-TMA) Directed Therapy. *Transplant Cell Ther.* 2025;31(9):610-623. doi:10.1016/j.jtct.2025.05.028

Policy Implementation/Update Information: Criteria and treatment protocols are reviewed annually by the Blue Cross NC P&T Committee, regardless of change. This policy is reviewed in Q2 annually.

May 2026: Criteria change: For initial criteria: Added requirement that the patient must be post-hematopoietic stem cell transplant for clarity. Removed requirement that diagnostic features must be from two or more time points within 14 days. Removed requirement that the patient must be classified as high-risk. Removed medical record documentation requirement from TA-TMA trigger evaluation. For continuation criteria: Added requirement that the patient has not experienced unacceptable toxicity with the requested agent. Duration of approval for both initial and continuation criteria was increased to 12 weeks, and the maximum units were updated to reflect the change. Other minor updates made throughout policy for clarity with no change to policy intent. **Policy notification given 3/1/2026 for effective date 5/1/2026.**
February 2026: Original medical policy criteria issued.