World Trade Center (WTC) Health Program Medical Coverage Determination
Monoclonal Gammopathy of Undetermined Significance
Publish Date: March 15, 2023

I. Coverage Overview

This Medical Coverage Determination (MCD) outlines the coverage of medically necessary treatment[1] services for Monoclonal Gammopathy of Undetermined Significance (MGUS) for WTC Health Program members.

MGUS is a condition in which abnormal levels of certain proteins are found in the blood. These abnormal levels of protein must be monitored by regular blood tests to check for any signs of cancer that could develop over time. The WTC Health Program may provide coverage of medically necessary MGUS services (i.e., initial diagnostic studies and, after diagnosis, further monitoring) when there are symptoms of a plasma cell neoplasm or clinical findings suggestive of MGUS. WTC Health Program providers may authorize a follow-up evaluation and ongoing monitoring of MGUS when the member meets all of the applicable requirements in this MCD. MGUS is NOT eligible for certification.

II. Clinical Summary

MGUS is a benign, pre-malignant[2] clonal plasma cell or lymphoplasmacytic proliferative disorder in which plasma cells produce abnormal levels of M proteins (monoclonal proteins). MGUS does not require treatment but is usually monitored for progression to a more advanced pre-malignant stage, a malignant plasma cell dyscrasia (e.g., multiple myeloma), or another lymphoproliferative disorder, with the intent of a timely diagnosis and prevention of serious complications from progression.[3,4] Approximately 1% of people with MGUS progress to develop multiple myeloma each year, as well as Waldenström's macroglobulinemia, light chain (AL) amyloidosis, smoldering multiple myeloma, solitary plasmacytoma, or another lymphoproliferative disorder.[5,6]

---

[1] The WTC Health Program defines medically necessary treatment as the provision of healthcare services to manage, ameliorate, or cure a WTC-related health condition or health condition medically associated with a WTC-related health condition. *See* 42 C.F.R. § 88.1 at https://www.cdc.gov/wtc/regulations2.html.

[2] MGUS is not reportable to the Surveillance, Epidemiology, and End Results (SEER) and the ICD10-CM system characterizes MGUS as benign (D47.2). Since the vast majority of medical literature and oncology authoritarian institutions – including NCCN and the ICD-O-3 system, have not definitively labeled MGUS as a malignant neoplasm, the Program is unable to certify MGUS as a WTC-related hematologic malignancy at this time.

[3] *See* Plasma Cell Neoplasms (Including Multiple Myeloma)Treatment: National Cancer Institute at https://www.cancer.gov/types/myeloma/hp/myeloma-treatment-pdq.

[4] Go, R. S., & Rajkumar, S. V. (2018). How I manage monoclonal gammopathy of undetermined significance. Blood, 131(2), 163–173. https://doi.org/10.1182/blood-2017-09-807560.

[5] *See* MGUS to Myeloma: Study Suggests Risk of Progression Can Change. National Institutes of Health National Cancer Institute (NIH NCI) at https://www.cancer.gov/news-events/cancer-currents-blog/2019/mgus-multiple-myeloma-progression-risk#:~:text=A%20new%20study%20suggests%20that,develop%20multiple%20myeloma%20each%20year.

[6] Kyle, R. A., Durie, B. G., Rajkumar, S., et al. International Myeloma Working Group (2010). Monoclonal gammopathy of undetermined significance (MGUS) and smoldering (asymptomatic) multiple myeloma: IMWG consensus perspectives risk factors for progression and guidelines for monitoring and management. Leukemia, 24(6), 1121–1127. https://doi.org/10.1038/leu.2010.60.

Absolute risks of MGUS progressing to malignancy in 20 years, based upon a risk stratification model described in the next section, ranges from 5% for low-risk MGUS to 21% for low-intermediate risk, 37% for high-intermediate risk MGUS, and 58% for high-risk MGUS.[7]

MGUS is usually diagnosed incidentally when evaluating signs and symptoms for a possible lymphoplasmacytic proliferative disorder. Criteria for general diagnosis of MGUS requires the presence of all the following three elements:

(1) serum monoclonal protein (M protein) at a concentration <3 g/dL;
(2) <10 percent monoclonal plasma cells in the bone marrow; and
(3) absence of end-organ damage (e.g., lytic bone lesions, anemia, hypercalcemia, renal insufficiency, and hyperviscosity) related to the proliferative process.[8]

Some of the conditions to which MGUS may progress (e.g., smoldering multiple myeloma, multiple myeloma, solitary plasmacytoma, and Waldenström macroglobulinemia) are eligible for certification as WTC-related cancer conditions.[9,10]

III. Covered MGUS Services

The WTC Health Program does not provide monoclonal gammopathy screening of asymptomatic members with no clinical findings suggestive of MGUS.[11] The Program will provide coverage of initial MGUS diagnostics in members with symptoms of a plasma cell neoplasm or clinical findings suggestive of MGUS during Program monitoring or screening evaluations without prior authorization.[12] A Prior Authorization Level 2 (PA2) is required for follow-up evaluation after the diagnosis of MGUS and for ongoing monitoring.

Coverage of MGUS services is permitted only when in accordance with Program guidelines.[13] The WTC Health Program may cover MGUS services beyond those referenced in this MCD on a case-by-case basis. Refer to the WTC Health Program Codebook for a full list of covered medical services, procedures, and diagnosis codes. MGUS services available for coverage under the WTC Health Program may include, but are not limited to:[14]

---

[7] Lipe, Brea, Kyle, R.A. American Society of Hematology. November 2016. Monoclonal Gammopathy of Undetermined Significance (MGUS): Diagnosis, Predictors of Progression, and Monitoring A Pocket Guide for the Clinician. https://www.hematology.org/-/media/Hematology/Files/Education/Clinicians/Guidelines-Quality/Documents/2016-MGUS-PocketGuide.pdf.

[8] Lipe, Brea, Kyle, R.A. American Society of Hematology. Monoclonal Gammopathy of Undetermined Significance (MGUS): Diagnosis, Predictors of Progression, and Monitoring A Pocket Guide for the Clinician. https://www.hematology.org/-/media/Hematology/Files/Education/Clinicians/Guidelines-Quality/Documents/2016-MGUS-PocketGuide.pdf.

[9] Rajkumar, S. V. (Sep 10, 2021). Clinical course and management of monoclonal gammopathy of undetermined significance. Retrieved November 5, 2021, from https://www.uptodate.com/contents/clinical-course-and-management-of-monoclonal-gammopathy-of-undetermined-significance?search=MGUS&source=search_result&selectedTitle=2~62&usage_type=default&display_rank=2

[10] *See* the WTC Health Program Administrative Manual [Chapter 3 Section 4.B] at https://www.cdc.gov/wtc/ppm.html#certification_conditions.

[11] Routine screening for MGUS is not recommended by the U.S. Preventive Services Task Force or professional clinical societies such as the International Myeloma Working Group or the American Society of Hematology.

[12] Example: elevated total protein in blood since the monitoring exam includes a blood test for total protein

[13] *See generally* WTC Health Program Administrative Manual for a full description of Program guidelines, policies, and procedures, at https://www.cdc.gov/wtc/ppm.html.

[14] Monitoring recommendations vary based on the MGUS risk level determined by a clinically acceptable risk stratification model and the recommendations of various clinical and research authorities such as the International Myeloma Working Group (IMWG) and the American Society of Hematology (ASH). The initial diagnosis and monitoring information noted here generally represents recommendations of the IMWG and ASH guidelines.

A. Initial Diagnostic Studies — No PA required[15,16]

The following additional diagnostic studies may be covered in WTC Health Program members during their initial health evaluation, during routine medical monitoring, or during evaluation and management of another certified WTC-related health condition when symptoms of a plasma cell neoplasm or clinical findings suggestive of MGUS are detected:

- Complete blood count (CBC)
- Serum calcium and creatinine
- Serum protein electrophoresis (SPEP) and immunofixation
- Urine protein electrophoresis and immunofixation
- Serum free light chain (FLC) assay
- Quantitation of immunoglobulins
- Imaging-Skeletal Survey, whole body computed tomography (CT) scan (with or without positron emission tomography (PET)), or MRI
- Bone marrow aspiration and biopsy with cytogenetics and fluorescence in-situ-hybridization
- Lactate dehydrogenase
- B2 microglobulin
- C-reactive protein

B. Follow-up Evaluation Six Months After an Initial Diagnosis of MGUS and Ongoing Monitoring— PA2 required

The six-month evaluation is only available for responders and certified-eligible survivors. For screening-eligible survivors, these services are available during the initial health evaluation period only. Screening-eligible survivors are not eligible to receive additional monitoring once the initial health evaluation period ends, even if the member is diagnosed with MGUS. The six-month evaluation may include:

- CBC
- SPEP
- FLC assay
- Serum calcium
- Creatinine

C. Ongoing Monitoring for Certain Members Diagnosed with MGUS— PA2 required

Ongoing monitoring of members diagnosed with MGUS is only available for responders and certified-eligible survivors. For screening-eligible survivors, these services are available during the initial health evaluation period only. Screening-eligible survivors are not eligible to receive additional monitoring once the initial health evaluation period ends, even if the member is diagnosed with MGUS.

[15] Laubach, J. P. (Oct 2021). Diagnosis of monoclonal gammopathy of undetermined significance. Retrieved November 5, 2021 from https://www.uptodate.com/contents/diagnosis-of-monoclonal-gammopathy-of-undetermined-significance.
[16] Jens, H., et al. (2019). International myeloma working group consensus recommendations on imaging in monoclonal plasma cell disorders. The Lancet Oncology, 20(6), e302-e312, https://doi.org/10.1016/S1470-2045(19)30309-2.

MGUS monitoring involves risk stratification of persons diagnosed with MGUS (based on meeting the criteria outlined above) into four risk categories using a model that predicts the risk of progression of MGUS to multiple myeloma or related malignancy.[17] The risk stratification (Mayo Clinic model) is based on different combinations of the three abnormal risk factors below:[18,19]

- Serum M-protein level ≥1.5 g/dL
- Non-IgG MGUS (i.e., IgA, IgM, or IgD MGUS)
- Abnormal FLC ratio (i.e., a ratio of kappa to lambda FLCs <0.26 or >1.65)

The presence of three abnormal factors equates with high risk; two abnormal factors equates with high-intermediate risk; one abnormal factor equates with low-intermediate risk; and no abnormal factors (but still meeting the criteria for an MGUS diagnosis) equates with low risk. High, high-intermediate, and low-intermediate risk MGUS requires annual monitoring, while low-risk MGUS requires monitoring in less frequent intervals (e.g., every 2-3 years) or when symptoms of progression to lymphoplasmacytic malignancies develop.[20, 21]

Labs normally drawn at these ongoing monitoring visits are:

- CBC
- SPEP
- Serum calcium
- Creatinine
- FLC assay

IV. Coverage Guidelines – General Eligibility Requirements for Medically Necessary MGUS Services for Clinical Center of Excellence (CCE) and Nationwide Provider Network (NPN) Members

All MGUS services for the six-month evaluation and ongoing monitoring must meet the criteria below.

A. PA Level

1. Level 2 – Authorization by CCE/NPN Clinical Director

A PA2 is required for all MGUS services except the initial diagnostic studies. The CCE/NPN Clinical Director will determine whether the MGUS services are medically necessary to evaluate for potential WTC-related cancer conditions. The CCE/NPN

[17] Once a diagnosis of MGUS is confirmed, the qualitative and quantitative characteristics of these MGUS abnormalities have been shown to be prognostic factors for the progression of MGUS. See also footnotes 17 and 18.
[18] Rajkumar, S. V. (Sep 10, 2021). Clinical course and management of monoclonal gammopathy of undetermined significance. Retrieved November 5, 2021, from https://www.uptodate.com/contents/clinical-course-and-management-of-monoclonal-gammopathy-of-undetermined-significance?search=MGUS&source=search_result&selectedTitle=2~62&usage_type=default&display_rank=2
[19] Rajkumar, S. V., Kyle, R. A., et al. (2005). Serum free light chain ratio is an independent risk factor for progression in monoclonal gammopathy of undetermined significance. Blood, 106(3), 812–817. https://doi.org/10.1182/blood-2005-03-1038
[20] Go, R. S., & Rajkumar, S. V. (2018). How I manage monoclonal gammopathy of undetermined significance. Blood, 131(2), 163–173. https://doi.org/10.1182/blood-2017-09-807560.
[21] Kyle, R. A., Durie, B. G., Rajkumar, et al. International Myeloma Working Group (2010). Monoclonal gammopathy of undetermined significance (MGUS) and smoldering (asymptomatic) multiple myeloma: IMWG consensus perspectives risk factors for progression and guidelines for monitoring and management. Leukemia, 24(6), 1121–1127. https://doi.org/10.1038/leu.2010.60

Clinical Director will also ensure that the member meets the PA criteria listed below in Section IV.D.1. and confirm that the criteria are appropriately documented in the member's medical record.

For detailed PA procedures, see instructions found in the WTC Health Program's Administrative Manual.[22]

B. PA2 Criteria

The initial PA2 for the MGUS six-month evaluation and ongoing monitoring will only cover a 3-year authorization period.

1. Initial Authorization Criteria for MGUS Six-Month Evaluation and Ongoing Monitoring

The CCE/NPN Clinical Director may authorize MGUS services if **ALL** the criteria below (**a.** through **d.**) are met and clearly documented in the member's medical record:

a. The member is a WTC responder or certified-eligible survivor. These services are available for screening-eligible survivors during the initial health evaluation period only. Screening-eligible survivors are not eligible for the follow-up evaluation or ongoing monitoring outside of the initial health evaluation period even if the member is diagnosed with MGUS.

b. The services are provided while the member is under the care of a WTC Health Program-affiliated provider.

c. MGUS services are determined to be medically necessary because follow-up evaluation and/or ongoing monitoring is required to evaluate for potential WTC-related cancer conditions.

d. The WTC Health Program-affiliated provider must furnish a plan of care to the CCE/NPN Clinical Director.

2. Subsequent Authorizations

The PA2 for MGUS services signed and authorized by the CCE/NPN Clinical Director will only cover a 3-year authorization period. The authorization period starts the day the member begins receiving MGUS services at the six-month evaluation and is valid for 3 years from that date. Subsequent authorizations may cover additional monitoring of MGUS beyond the initial authorization period.

A new PA2 is required for each subsequent 3-year authorization period. The WTC Health Program-affiliated provider must furnish a plan of care to the CCE/NPN Clinical Director prior to the end of the current authorization period, and before the start of each new authorization period. The CCE/NPN Clinical Director must sign and authorize a new PA2 based on the criteria above. For each 3-year authorization period, documentation of the member's clinical status as well as documentation of the member's compliance with monitoring must be available within the member's file.

[22] WTC Health Program Administrative Manual, Chapter 4, Section 3.4, at https://www.cdc.gov/wtc/ppm.html#medical_prior.

V. Exclusions

A. Monoclonal gammopathy screening of asymptomatic members with no clinical findings suggestive of MGUS
B. Certification of MGUS as a WTC-related health condition
C. Certification of any nonmalignant conditions resulting from or associated with an MGUS diagnosis or the monitoring of MGUS

VI. Prior Authorization Request Submission Requirements

The PA2 for MGUS services must be signed and authorized by the CCE/NPN Clinical Director and maintained in the member's medical record. The CCE/NPN Clinical Director will maintain documentation that demonstrates MCD criteria has been met in the member's medical record, as well as documentation related to the PA2.

All documentation for completed MGUS service authorizations are subject to audit by the WTC Health Program.

VII. Billing/Coding Guidelines

All applicable codes are listed in the WTC Health Program Codebook, located on the Centralized Accessible Real-time Enterprise (CARE) portal.

For consideration of codes that are not currently included in the WTC Health Program Codebook, please submit a WTC-5 Medical Code Request form to the Third Party Administrator (TPA) contractor via the standard WTCMedCode@csra.com mailbox process.