



**Instructions for Waldenström’s
Macroglobulinemia/Lymphoplasmacytic Lymphoma (MAC)
Post-HCT Data (Form 2119)**

This section of the CIBMTR Forms Instruction Manual is intended to be a resource for completing the Waldenström’s Macroglobulinemia and Lymphoplasmacytic Lymphoma Post-HCT Form.

E-mail comments regarding the content of the CIBMTR Forms Instruction Manual to: CIBMTRFormsManualComments@nmdp.org. Comments will be considered for future manual updates and revisions. For questions that require an immediate response, please contact your transplant center’s CIBMTR CRC.

TABLE OF CONTENTS

Key Fields	2
Disease Assessment at the Time of Best Response to HCT	2
Post-HCT Therapy	6
Laboratory Studies at the Time of Evaluation for this Reporting Period	10
Disease Status at the Time of Evaluation for this Reporting Period	12

**Waldenström’s Macroglobulinemia &
Lymphoplasmacytic Lymphoma Post-HCT Data**

Lymphoplasmacytic lymphoma (LPL) and subtype Waldenström’s macroglobulinemia (WM) are specific presentations of Non-Hodgkin lymphoma that are characterized by abnormal cellular populations containing small B-cells, plasma cells, and plasmacytoid lymphocytes. Additional hallmarks of Waldenström’s macroglobulinemia are bone marrow involvement (which may be present in lymphoplasmacytic lymphoma) and IgM paraprotein. Patients typically present with symptoms associated with anemia, such as weakness and fatigue. Workup often reveals normocytic, normochromatic anemia. Additional findings may include IgM paraprotein, clinical hyperviscosity syndrome, and neuropathy. LPL will generally involve the bone marrow and in some cases, the lymph nodes and other extranodal sites. A significant number of patients with WM will also have organomegaly and adenopathy. Advanced age, decreased performance

status, anemia, and elevated β_2 microglobulin have been associated with poorer outcomes, though there is no validated staging system to establish prognosis.

This form must be completed for all recipients randomized to the Comprehensive Report Form (CRF) track whose primary disease is reported on the Form 2400, question 357 as Non-Hodgkin lymphoma and question 583 as Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma. The Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma Post-HCT Data (Form 2119) must be completed in conjunction with each Post-HCT follow-up form (Forms 2100, 2200, 2300) completed. The form is designed to capture specific data occurring within the timeframe of each reporting period (i.e., between day 0 and day 100 for Form 2100, between day 100 and the six-month date of contact for Form 2200, between the date of contact for the six-month follow-up and the date of contact for the one-year follow-up for Form 2200, etc.).

Key Fields

Accuracy of the Key Fields is essential for ensuring that:

- Data are being reported for the correct recipient.
- Outcomes data accurately reflects appropriate transplant type and product for each transplant center.
- Data are being shared with the correct donor center, cord blood bank, cooperative registry, or other agency.

The Key Fields precede the form body and are automatically populated in the FormsNet3SM application based on information provided on the CRID Assignment Form 2804. If errors are noted in the key fields, correct Form 2804 and then review it for accuracy. After Form 2804 has been corrected, verify data has been updated on all completed forms. If the data has not been updated automatically, centers will need to reprocess the completed forms to correct the key field data. If errors are noted in key fields for second or subsequent transplants, contact your CRC to make any necessary corrections to the transplant or product type. Transplant and product type will not be automatically populated on product or donor specific forms (Forms 2004, 2005, and 2006) and will need to be manually reported.

Disease Assessment at the Time of Best Response to HCT

Question 1: Compared to the disease status prior to the preparative regimen, what was the best response to HCT since the date of last report? (Include response to any therapy given for post-HCT maintenance or

consolidation, but exclude any therapy given for relapsed, persistent, or progressive disease)

Any specified therapy administered post-HCT to prolong remission or for minimal residual disease is considered part of the HCT and should be included when assessing the recipient's response to transplant. Treatment given post-HCT for relapsed or persistent disease is not considered part of the HCT and should be excluded when assessing the response to HCT. If treatment was given post-HCT for relapsed or persistent disease, assess the patient's best response *prior* to the start of therapy. If therapy was only given for reasons other than relapsed or persistent disease, assess the patient's best response throughout the entire duration of the reporting period.

If the recipient was in remission at the start of the preparative regimen, indicate "continued complete remission" and continue with question 2.

If the recipient was not in remission at the start of the preparative regimen, indicate their best response to transplant and continue with question 2. If the recipient did not have their disease evaluated by any method of assessment, including physical examination, report "not assessed" and continue with question 18.

Table 1. Disease status criteria for WM and LPL

DISEASE STATUS	DEFINITION
<p>Complete response (CR)</p> <p><i>Continue with question 2.</i></p>	<ul style="list-style-type: none"> • Disappearance of monoclonal protein on immunofixation (both serum and urine) • No histologic evidence of bone marrow involvement • Resolution of adenopathy and/or organomegaly on CT • Resolution of clinical signs or symptoms attributed to WM/LPL <p>Complete response requires confirmatory immunofixation.</p>
<p>Partial response (PR)</p> <p><i>Continue with question 2.</i></p>	<ul style="list-style-type: none"> • ≥ 50% reduction of serum monoclonal IgM spike on serum electrophoresis • ≥ 50% reduction of adenopathy and organomegaly on physical exam or CT • No new symptoms and no clinical signs of active disease

Table 1. Disease status criteria for WM and LPL (cont.)

DISEASE STATUS	DEFINITION
<p>Minor response/stable disease (MR/SD)</p> <p><i>Continue with question 2.</i></p>	<ul style="list-style-type: none"> • 25–49% reduction of serum monoclonal IgM spike on serum electrophoresis • No new symptoms and no clinical signs of active disease <p><u>Or</u></p> <ul style="list-style-type: none"> • < 25% reduction <u>and</u> < 25% increase of serum monoclonal IgM spike on serum electrophoresis • No progression of adenopathy, organomegaly, cytopenias, or clinically significant symptoms attributed to WM/LPL
<p>Progressive disease (PD)</p> <p><i>Continue with question 2.</i></p>	<ul style="list-style-type: none"> • ≥ 25% increase in serum monoclonal IgM spike from lowest nadir on serum electrophoresis • Progression of clinically significant findings or symptoms (for example, anemia, adenopathy, constitutional symptoms, amyloidosis, etc.) attributed to WM/LPL <p>Progression identified by increasing monoclonal protein on serum electrophoresis requires confirmatory test.</p>
<p>Not assessed</p> <p><i>Continue with question 18.</i></p>	<p>Patient's disease was not assessed by any method, including physical examination.</p>

Question 2: Was the date of best response previously reported?

If the patient achieved their best response to transplant in the current reporting period, indicate “no” and continue with question 3.

If the recipient achieved their best response to transplant during a previous reporting period, indicate “yes” and continue with question 18.

Question 3: Date assessed

Report the date of the assessment that established the best disease response to transplant. Enter the date the sample was collected for pathological and laboratory evaluation.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, [Guidelines for Completing Forms](#).

Questions 4-5: Absolute lymphocyte count

Indicate whether the lymphocyte count was “known” or “unknown” at the time of best response to transplant. If “known,” report the laboratory count and unit of measure documented on the laboratory report in question 5. If “unknown,” continue with question 6.

Questions 6-8: IgM

Indicate whether the IgM level was “known” or “unknown” at the time of best response to transplant. If “known,” report the laboratory value and unit of measure in question 7; report the laboratory upper limit of normal value and unit of measure in question 8. If “unknown,” continue with question 9.

Questions 9-10: Serum monoclonal protein (M-spike) (only from electrophoresis)

Indicate whether serum monoclonal protein quantification from electrophoresis was “known” or “unknown” at the time of best response to transplant. If “known,” report the laboratory value and unit of measure in question 10. If serum electrophoresis was done and did not show monoclonal protein, report “0.” If “unknown,” continue with question 11.

Questions 11-12: Urinary monoclonal protein (M-spike)

Indicate whether 24-hour urine monoclonal protein quantification from electrophoresis was “known” or “unknown” at the time of best response to transplant. If “known,” report the laboratory value and unit of measure in question 12. If urine electrophoresis was done and did not show monoclonal protein, report “0.” If “unknown,” continue with question 13.

Questions 13-14: Bone marrow aspirate (examined for histologic involvement)

Indicate whether the extent of histologic involvement in the bone marrow aspirate was “known” or “unknown” at the time of best response to transplant. If bone marrow aspirate was not examined, report “not applicable.” If “known,” report the extent of aspirate histologic involvement in question 14. If “unknown” or “not applicable,” continue with question 15.

Questions 15-16: Bone marrow biopsy (examined for histologic involvement)

Indicate whether the extent of histologic involvement in the bone marrow biopsy was “known” or “unknown” at the time of best response to transplant. If bone marrow biopsy was not examined, report “not applicable.” If “known,” report the extent of biopsy histologic involvement in question 16. If “unknown” or “not applicable,” continue with question 17.

Question 17: Specify the type of histological involvement in marrow

WM and LPL are often characterized by histologic involvement of the bone marrow. However, there are variations in the type of involvement:¹

- *Lymphoplasmacytoid*: This variant is primarily defined by small lymphocytes with some plasmacytoid lymphocytes and rare mature plasma cells. Lymphoplasmacytoid cells (plasmacytoid lymphocytes) are mononuclear cells with dark, irregular nuclei. They are slightly larger than a small lymphocyte. Additionally, mitotic and large cells are rare.
- *Lymphoplasmacytic*: In this variant, the involved cells are a mix of small lymphocytes, plasmacytoid lymphocytes, and mature plasma cells. Mitotic and large cells are rare.
- *Polymorphous*: This variant can resemble either lymphoplasmacytoid or lymphoplasmacytic variants, but mitotic and large cells are more common. Large cells are still less common than in large cell lymphomas.

Specify the type of histologic involvement as indicated by the pathology report or transplant physician. Report “unknown” if the bone marrow was not examined, there was no bone marrow involvement, or if the type of histologic involvement cannot be specified.

¹Ioachim HL, Medeiros LJ. (2009) *Lymph Node Pathology, 4th edition*. Philadelphia, PA: Lippincott Williams & Wilkins.

Post-HCT Therapy

Complete a “Line of Therapy” section for each line of therapy administered during the current reporting period. If multiple lines of therapy were administered, copy and complete questions 19-56 for each line of therapy.

Question 18: Was therapy given since the date of the last report for reasons other than relapse or progressive disease? (Include any maintenance and consolidation therapy)

Indicate if the recipient received treatment for WM/LPL during the current reporting period for any reason other than relapsed or persistent disease, e.g., maintenance or consolidation therapy. If the patient received therapy for reasons other than relapsed or persistent disease, check “yes” and continue with question 19. If the patient did not receive therapy, or only received therapy for relapsed or persistent disease, check “no” and continue with question 57.

Question 19: Systemic therapy

Systemic therapy refers to a delivery mechanism where a therapeutic agent is delivered orally or intravenously, enters the bloodstream, and is distributed throughout the body.

Indicate "yes" if the patient received systemic therapy and continue with question 20. If the patient did not receive systemic therapy, indicate "no" and continue with question 48.

Questions 20-21: Date therapy started

Indicate "known" if the therapy start date is documented, and specify the start date in question 21. If the date is unknown, indicate this and continue with question 22.

Questions 22-23: Number of cycles

Indicate if the number of cycles is "known" or "unknown." If the number of cycles is known, continue with question 23 and specify the number of cycles of chemotherapy administered. If the patient received a single administration or one line of chemotherapy, indicate a single cycle. If the patient received long-term maintenance therapy consisting of a single agent, indicate "known" for question 82; leave question 83 blank and override the error as "not applicable."

If the number of cycles is unknown, continue with question 24.

Questions 24-47: Specify systemic therapy agents

Systemic therapy agents and treatment regimens vary based on disease, prognosis, and protocol. Drugs may be administered in an inpatient or outpatient setting, and treatment may consist of one or multiple drugs. Additionally, drugs may be administered on a single day, over consecutive days, or continuously.

Indicate "yes" or "no" for each therapeutic agent listed. Do not leave any response blank. If the recipient received an agent that is not listed, check "yes" for "other systemic therapy" and specify the treatment in question 47.

Question 48: Radiation therapy

Radiation therapy uses high-energy, ionizing radiation to kill malignant cells. Much like non-targeted systemic therapy, radiation therapy does not specifically target malignant cells and does have significant side effects. For that reason, high-dose radiation often targets a limited field.

Indicate if the recipient received radiation treatment for WM or LPL during the current reporting period. If "yes," continue with question 49. If "no," continue with question 53.

Question 49: Date therapy started

Specify the first date of radiation administration. If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, [Guidelines for Completing Forms](#).

Questions 50-52: Specify radiation site(s)

Specify radiation site(s). If question 48 is answered "yes," at least one site of radiation therapy must be specified in questions 50-52.

Question 53: Best response to line of therapy

Indicate the patient's best response to this line of therapy.

Table 2. Best response criteria for WM and LPL

DISEASE STATUS	DEFINITION
Complete response (CR)	<ul style="list-style-type: none"> • Disappearance of monoclonal protein on immunofixation (both serum and urine) • No histologic evidence of bone marrow involvement • Resolution of adenopathy and/or organomegaly on CT • Resolution of clinical signs or symptoms attributed to WM/LPL <p>Complete response requires confirmatory immunofixation.</p>
Partial response (PR)	<ul style="list-style-type: none"> • ≥ 50% reduction of serum monoclonal IgM spike on serum electrophoresis • ≥ 50% reduction of adenopathy and organomegaly on physical exam or CT • No new symptoms and no clinical signs of active disease
Minor response/stable disease (MR/SD)	<ul style="list-style-type: none"> • 25–49% reduction of serum monoclonal IgM spike on serum electrophoresis • No new symptoms and no clinical signs of active disease <p><u>Or</u></p> <ul style="list-style-type: none"> • < 25% reduction <u>and</u> < 25% increase of serum monoclonal IgM spike on serum electrophoresis • No progression of adenopathy, organomegaly, cytopenias, or clinically significant symptoms attributed to WM/LPL

Table 2. Best response criteria for WM and LPL (cont.)

DISEASE STATUS	DEFINITION
Progressive disease (PD)	<ul style="list-style-type: none"> • $\geq 25\%$ increase in serum monoclonal IgM spike from lowest nadir on serum electrophoresis • Progression of clinically significant findings or symptoms (for example, anemia, adenopathy, constitutional symptoms, amyloidosis, etc.) attributed to WM/LPL <p>Progression identified by increasing monoclonal protein on serum electrophoresis requires confirmatory test.</p>
Not assessed	Patient's disease was not assessed by any method, including physical examination.

Question 54: Date assessed

Enter the date the best response to the line of therapy was established. Report the date of the pathological (e.g., bone marrow biopsy), radiological (e.g., CT), or biochemical (e.g., SPEP) evaluation. Enter the date the sample was collected for examination for pathological and/or laboratory evaluation, or enter the date the imaging took place for radiologic assessment. If no pathological, radiographic, or laboratory assessment was performed to establish the best response to the line of therapy, report the office visit in which the physician clinically assessed the recipient's response.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, [Guidelines for Completing Forms](#).

Question 55: Did disease relapse/progress following this line of therapy?

Relapse is the recurrence of disease after CR. WM or LPL relapse is demonstrated by reappearance of disease characteristics, including IgM paraprotein, lymphadenopathy and/or organomegaly, and bone marrow histologic involvement.

WM or LPL progression criteria are specified in Table 2 above. Indicate if relapse or progression occurred following the line of therapy being reported. If question 53 is answered "progressive disease," question 55 must be "yes."

Question 56: Date of relapse/progression

Enter the date of the assessment that identified relapse or progression following the line of therapy and *continue with question 59*. Enter the date the sample was collected for pathological and laboratory evaluation or enter the date the imaging

took place. If the physician determined evidence of relapse during an office visit, report the date of assessment.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, [Guidelines for Completing Forms](#).

Question 57: Has disease relapsed or progressed since the date of last report?

Relapse is the recurrence of disease after CR. WM or LPL relapse is demonstrated by reappearance of disease characteristics, including IgM paraprotein, lymphadenopathy and/or organomegaly, and bone marrow histologic involvement.

WM or LPL progression criteria are specified in Table 2 above. Indicate if relapse or progression occurred at any time during the reporting period.

Question 58: Date of relapse/progression

Enter the date of the assessment that identified relapse or progression during the reporting period. Enter the date the sample was collected for pathological and laboratory evaluation or enter the date the imaging took place. If the physician determined evidence of relapse during an office visit, report the date of assessment.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, [Guidelines for Completing Forms](#).

Laboratory Studies at the Time of Evaluation for this Reporting Period

These questions are intended to determine the status of the recipient at the last evaluation for this reporting period. Testing may have been performed multiple times during the reporting period; report the most recent laboratory values. Reported values should be within a reasonable time frame of the date of contact, or approximately one month prior to the date of contact. If the recipient received any treatment or therapy for relapse, progression, or persistent disease, leave this section of the form blank and continue with the signature section.

Questions 59-60: Absolute lymphocyte count

Indicate whether the lymphocyte count was “known” or “unknown” at the time of evaluation for the reporting period. If “known,” report the laboratory count and unit of measure documented on the laboratory report in question 60. If “unknown,” continue with question 61.

Questions 61-63: IgM

Indicate whether the IgM level was “known” or “unknown” at the time of evaluation for the reporting period. If “known,” report the laboratory value and unit of measure in question 62; report the laboratory upper limit of normal value and unit of measure in question 63. If “unknown,” continue with question 64.

Questions 64-65: Serum monoclonal protein (M-spike) (only from electrophoresis)

Indicate whether serum monoclonal protein quantification from electrophoresis was “known” or “unknown” at the time of evaluation for the reporting period. If “known,” report the laboratory value and unit of measure in question 65. If serum electrophoresis was done and did not show monoclonal protein, report “0.” If “unknown,” continue with question 66.

Questions 66-67: Urinary monoclonal protein (M-spike)

Indicate whether 24-hour urine monoclonal protein quantification from electrophoresis was “known” or “unknown” at the time of evaluation for the reporting period. If “known,” report the laboratory value and unit of measure in question 67. If urine electrophoresis was done and did not show monoclonal protein, report “0.” If “unknown,” continue with question 68.

Questions 68-69: Bone marrow aspirate (examined for histologic involvement)

Indicate whether the extent of histologic involvement in the bone marrow aspirate was “known” or “unknown” at the time of evaluation for the reporting period. If bone marrow aspirate was not examined, report “not applicable.” If “known,” report the extent of aspirate histologic involvement in question 69. If “unknown” or “not applicable,” continue with question 70.

Questions 70-71: Bone marrow biopsy (examined for histologic involvement)

Indicate whether the extent of histologic involvement in the bone marrow biopsy was “known” or “unknown” at the time of evaluation for the reporting period. If bone marrow biopsy was not examined, report “not applicable.” If “known,” report the extent of biopsy histologic involvement in question 71. If “unknown” or “not applicable,” continue with question 72.

Question 72: Specify the type of histological involvement in marrow

WM and LPL are often characterized by histologic involvement of the bone marrow. However, there are variations in type of involvement:¹

- *Lymphoplasmacytoid*: This variant is primarily defined by small lymphocytes with some plasmacytoid lymphocytes and rare mature plasma cells. Lymphoplasmacytoid cells (plasmacytoid lymphocytes) are

mononuclear cells with dark, irregular nuclei. They are slightly larger than a small lymphocyte. Additionally, mitotic and large cells are rare.

- *Lymphoplasmacytic*: In this variant, the involved cells are a mix of small lymphocytes, plasmacytoid lymphocytes, and mature plasma cells. Mitotic and large cells are rare.
- *Polymorphous*: This variant can resemble either lymphoplasmacytoid or lymphoplasmacytic variants, but mitotic and large cells are more common. Large cells are still less common than in large cell lymphomas.

Specify the type of histologic involvement as indicated by the pathology report or transplant physician. Report “unknown” if the bone marrow was not examined, there was no bone marrow involvement, or if the type of histologic involvement cannot be specified.

¹Ioachim HL, Medeiros LJ. (2009) *Lymph Node Pathology, 4th edition*. Philadelphia, PA: Lippincott Williams & Wilkins.

Question 73: Was there any clinical or radiological (e.g., CT, PET, PET/CT) evidence of organ involvement at the time of evaluation for this reporting period?

Indicate whether the recipient had clinical or radiological evidence of organ involvement at the time of evaluation for the reporting period. This includes clinical manifestations of WM/LPL such as palpable lymphadenopathy or hyperviscosity syndrome, and radiological evidence such as organomegaly or lymphadenopathy. Do not include biochemical markers as clinical involvement, as they are captured in other data fields in this form section.

Questions 74-77: Specify site(s)

Indicate “yes” or “no” for each site specified in questions 74-76. Do not leave any response blank. If “yes” is indicated for “other site,” specify the site in question 77. Include clinical manifestations (such as hyperviscosity syndrome or cold agglutinin disease) under “other site.” If the patient had clinical or radiological evidence of disease indicated in question 73, at least one of questions 74-76 must be answered “yes.”

Disease Status at the Time of Evaluation for this Reporting Period

Question 78: What is the current disease status?

Indicate the disease status of WM or LPL at last evaluation during the reporting period.

Table 3. Disease status criteria for WM and LPL

DISEASE STATUS	DEFINITION
<p>Complete response (CR)</p> <p><i>Continue with question 79.</i></p>	<ul style="list-style-type: none"> • Disappearance of monoclonal protein on immunofixation (both serum and urine) • No histologic evidence of bone marrow involvement • Resolution of adenopathy and/or organomegaly on CT • Resolution of clinical signs or symptoms attributed to WM/LPL <p>Complete response requires confirmatory immunofixation.</p>
<p>Partial response (PR)</p> <p><i>Continue with question 79.</i></p>	<ul style="list-style-type: none"> • ≥ 50% reduction of serum monoclonal IgM spike on serum electrophoresis • ≥ 50% reduction of adenopathy and organomegaly on physical exam or CT • No new symptoms and no clinical signs of active disease
<p>Minor response/stable disease (MR/SD)</p> <p><i>Continue with question 79.</i></p>	<ul style="list-style-type: none"> • 25–49% reduction of serum monoclonal IgM spike on serum electrophoresis • No new symptoms and no clinical signs of active disease <p><u>Or</u></p> <ul style="list-style-type: none"> • < 25% reduction <u>and</u> < 25% increase of serum monoclonal IgM spike on serum electrophoresis • No progression of adenopathy, organomegaly, cytopenias, or clinically significant symptoms attributed to WM/LPL
<p>Progressive disease (PD)</p> <p><i>Continue with question 79.</i></p>	<ul style="list-style-type: none"> • ≥ 25% increase in serum monoclonal IgM spike from lowest nadir on serum electrophoresis • Progression of clinically significant findings or symptoms (for example, anemia, adenopathy, constitutional symptoms, amyloidosis, etc.) attributed to WM/LPL <p>Progression identified by increasing monoclonal protein on serum electrophoresis requires confirmatory test.</p>

Table 3. Disease status criteria for WM and LPL (cont.)

DISEASE STATUS	DEFINITION
Not assessed <i>Continue with signature section.</i>	Patient's disease was not assessed by any method, including physical examination.

Question 79: Date assessed

Enter the date of the most recent assessment establishing disease status within the reporting period. The date reported should be that of the most disease-specific assessment within a reasonable timeframe of the date of contact (approximately 30 days). Clinical and hematologic assessments include pathological evaluation (e.g., bone marrow biopsy), radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), and laboratory assessment (e.g., SPEP), in addition to clinician evaluation and physical examination. Enter the date the sample was collected for pathological and laboratory evaluation; enter the date the imaging took place for radiographic assessment, or the date of physical examination.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, [Guidelines for Completing Forms](#).

Signature

The FormsNet3SM application will automatically populate the signature data fields, including name and email address of person completing the form and date upon submission of the form.