

Multiple Myeloma Response Criteria

General Reporting Guidelines

- Use the multiple myeloma response criteria when determining the disease status for multiple myeloma and solitary plasmacytoma.
- At any response level, if some but not all criteria are met, the disease status should be downgraded to next lower level of response.
- The percentage of plasma cells in the bone marrow aspirate and / or biopsy may also be identified on a flow cytometry report. A flow cytometry report may **NOT** be used to confirm CR (e.g., < 5% plasma cells in the bone marrow).
- Immunofixation (IFE) and immunoelectrophoresis (IEP) are essentially measuring the same thing and either may be used to determine CR. Electrophoresis (SPEP and UPEP) are, however, different assessments.
- Review [Appendix G](#) for examples of how to determine disease status for Multiple Myeloma.



Urine Studies

In order to report a Stringent Complete Remission (sCR) or Complete Remission (CR), urine studies **MUST** be performed and agree with the international myeloma working group (IMWG) criteria provided above. As long as the negative serum electrophoresis and immunofixation studies have been confirmed, only one set of negative urine studies needs to be documented to report sCR or CR.

Stringent Complete Remission (sCR)

Follows criteria for CR as defined below, **plus all of the following**:

- Normal free light chain ratio,
- Absence of clonal cells in the bone marrow by immunohistochemistry or immunofluorescence (confirmation with repeat bone marrow biopsy not needed). (Presence and/or absence of clonal cells is based upon the κ/λ ratio. An abnormal κ/λ ratio by immunohistochemistry and/or immunofluorescence requires a minimum of 100 plasma cells for analysis. An abnormal ratio reflecting the presence of an abnormal clone is κ/λ of $> 4:1$ or $< 1:2$.)

sCR requires two consecutive assessments (by the same method) made at any time before the institution of any new therapy. If radiographic studies were performed, there must be no known evidence of new or progressive bone lesions. Radiographic studies are not required to satisfy sCR requirements.

Complete Remission (CR)

A treatment response where **all** of the following criteria are met:

- Negative immunofixation on serum and urine samples
- Disappearance of any soft tissue plasmacytomas
- < 5% plasma cells in the bone marrow (confirmation with repeat bone marrow biopsy not needed)

For recipients with **light chain only myeloma**, all of the following criteria must be met:

- Normal serum free light chain ratio
- Negative immunofixation on urine samples
- Disappearance of any soft tissue plasmacytomas
- < 5% plasma cells in the bone marrow (confirmation with repeat bone marrow biopsy not needed)

For recipients with **non-secretory myeloma**, all of the following criteria must be met:

- Disappearance of all soft tissue plasmacytomas
- < 5% plasma cells in the bone marrow (confirmation with repeat bone marrow biopsy not needed)

CR requires two consecutive assessments (by the same method) made at any time before the institution of any new therapy. If radiographic studies were performed, there must be no known evidence of new or progressive bone lesions. Radiographic studies are not required to satisfy CR requirements.

The method of the two consecutive assessments may be any of the biochemical tests (urine/serum testing) listed in the disease status criteria available in the manual. Though it is preferable the biochemical confirmatory testing include both the urine & serum, this disease status does not require two consecutive assessments by each method. As an example:

A recipient with IgG kappa myeloma receives therapy and has assessments performed on April 1, which appear to show resolution of disease. These include negative serum and urine immunofixations, a bone survey and PET/CT without evidence of active disease, and a negative bone marrow with 2% plasma cells. On May 1, the recipient has another negative serum immunofixation prior to proceeding with transplant on May 12. This recipient would be in complete remission at transplant, as they meet all specified CR criteria and have two consecutive negative serum immunofixation studies; additional imaging and bone marrow studies are not required.

Urine Studies: Never Done or Diagnosis Only

The disease response options below (Near Complete Remission, Very Good Partial Response, and Partial Response) may still be reported even if urine studies were never obtained or were only obtained at diagnosis. If urine studies were performed following the most recent line of therapy, the results must agree with the IMWG criteria for the disease status being reported. In any case, serum studies **MUST** be performed and agree with the international working group criteria for the disease status being reported (excluding non-secretory myeloma).

Near Complete Remission (nCR)

A treatment where **all** of the following criteria met:

- Serum and Urine M-protein detectable by immunoelectrophoresis¹ (immunofixation, IFE) but not on electrophoresis (SPEP and UPEP)
- < 5% plasma cells in bone marrow (confirmation with repeat bone marrow biopsy not needed).

nCR requires two consecutive assessments (by the same method) made at any time prior to the initiation of any new therapy, and no known evidence of new or progressive bone lesions if radiographic studies were performed; radiographic studies are not required to satisfy nCR requirements.

Very Good Partial Response (VGPR)

One or more of the following must be present:

- Serum and urine M-protein detectable by immunofixation but not on electrophoresis
- $\geq 90\%$ reduction in serum M-protein and urine M-protein level < 100 mg/24 hours.

If the serum and urine M-protein are not measurable (i.e., do not meet the following criteria at time of diagnosis):

- Serum M-protein ≥ 1 g/dL
- Urine M-protein ≥ 200 mg/24 hours;

then a $\geq 90\%$ decrease in the difference between involved and uninvolved free light chain levels is required in place of the M-protein criteria (provided the serum free light chain assay shows involved level > 10 mg/dL and the serum free light chain is abnormal).

VGPR requires two consecutive assessments (by the same method) made at any time before the institution of any new therapy. If radiographic studies were performed, there must be no known evidence of new or progressive bone lesions. Radiographic studies are not required to satisfy VGPR requirements.

Partial Response (PR)

Both of the following must be present:

- $\geq 50\%$ reduction in serum M-protein
- Reduction in 24-hour urinary M-protein by $\geq 90\%$ or to < 200 mg/24 hours.

If the serum and urine M-protein are not measurable (i.e., do not meet the following criteria at time of diagnosis):

- Serum M-protein ≥ 1 g/dL
- Urine M-protein ≥ 200 mg/24 hours;

then a $\geq 50\%$ decrease in the difference between involved and uninvolved free light chain levels is required in place of the M-protein criteria (provided the serum free light chain assay shows involved level > 10 mg/dL and the serum free light chain is abnormal).

If serum and urine M-protein and serum-free light assay are not measurable, a $\geq 50\%$ reduction in bone marrow plasma cells is required in place of M-protein, provided the baseline bone marrow plasma cell percentage was $\geq 30\%$.

In addition to the above-listed criteria, if soft tissue plasmacytomas were present at baseline, a $\geq 50\%$ reduction in their size is also required.

PR requires two consecutive assessments (by the same method) made at any time before the institution of any new therapy. If radiographic studies were performed, there must be no known evidence of new or progressive bone lesions. Radiographic studies are not required to satisfy PR requirements.

Stable Disease (SD)

Does not meet the criteria for CR, VGPR, PR, or PD.

SD requires two consecutive assessments (by the same method) made at any time before the institution of any new therapy. If radiographic studies were performed, there must be no known evidence of new or progressive bone lesions. Radiographic studies are not required to satisfy SD requirements.

Progressive Disease (PD)

Requires **one or more** of the following:

Increase of $\geq 25\%$ from the lowest response value achieved in:

- Serum M-component with an absolute increase ≥ 0.5 g/dL (for progressive disease, serum M-component increases of ≥ 1 g/dL are sufficient if the starting M-component is ≥ 5 g/dL); *and/or*
- Urine M-component with an absolute increase ≥ 200 mg/24 hours; *and/or*
- For recipients without measurable serum and urine M-protein levels, the difference between involved and uninvolved free light chain levels with an absolute increase > 10 mg/dL; *and/or*

Bone marrow plasma cell percentage with absolute percentage $\geq 10\%$; *and/or*

Definite development of new bone lesions or soft tissue plasmacytomas, or definite increase in the size of any existing bone lesions or soft tissue plasmacytomas ($\geq 50\%$ increase from nadir in size of >1 lesion, or a $\geq 50\%$ increase in the longest diameter of a previous lesion >1 cm in short axis); *and/or*

Development of hypercalcemia (corrected serum calcium > 11.5 mg/dL or 2.65 mmol) that can be attributed solely to the plasma cell proliferative disorder.

PD requires two consecutive assessments (by the same method) made at any time before classification as disease progression, and/or the start of any new therapy.

Relapse from CR

Requires one or more of the following:

- Reappearance of serum or urine M-protein by immunofixation or electrophoresis; *and/or*
- Development of $\geq 5\%$ plasma cells in the bone marrow; *and/or*
- Appearance of any other sign of progression (e.g., new plasmacytoma, lytic bone lesion, hypercalcemia).

Relapse requires two consecutive assessments (by the same method) made at any time before classification as relapse, and/or the start of any new therapy.

Manual Updates:

Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for this form, please [click here](#) or reference the retired manual section on the [Retired Forms Manuals](#) webpage.

Date	Manual Section	Add/ Remove/ Modify	Description
10/25/19	Multiple Myeloma Response Criteria	Modify	<p>Removed the previously modified (struck out text has been deleted and red text has been added) response criteria for Relapse from CR:</p> <p>Relapse from CR <i>Requires one or more of the following:</i></p> <ul style="list-style-type: none"> • <i>Reappearance of serum or urine M-protein by immunofixation or electrophoresis; and/or</i> • <i>Development of $\geq 5\%$ plasma cells in the bone marrow; and/or</i> • <i>Appearance of any other sign of progression (e.g., new plasmacytoma, lytic bone lesion, hypercalcemia).</i> <p>Positive immunofixation alone in a patient previously classified as achieving a complete response should not be considered a relapse.</p>
4/19/19	Multiple Myeloma Response Criteria	Modify	<p>Modified (struck out text has been deleted and red text has been added) the response criteria for Relapse from CR:</p> <p>Relapse from CR <i>Requires one or more of the following:</i></p> <ul style="list-style-type: none"> • Reappearance of serum or urine M-protein by immunofixation or electrophoresis; and/or • <i>Development of $\geq 5\%$ plasma cells in the bone marrow; and/or</i> • <i>Appearance of any other sign of progression (e.g., new plasmacytoma, lytic bone lesion, hypercalcemia).</i> <p>Positive immunofixation alone in a patient previously classified as achieving a complete response should not be considered a relapse.</p>
12/3/18	Multiple Myeloma Response Criteria	Modify	<p>Separated the blue note box regarding urine studies to better reflect requirements needed for sCR and CR versus requirements needed for nCR, VGPR, and PR.</p>
11/20/18	Multiple Myeloma Response Criteria	Add	<p>Added the following (in red) to the Near Complete Remission (nCR) response criteria: $< 5\%$ plasma cells in bone marrow (confirmation with repeat bone marrow biopsy not needed).</p>
3/19/18	Multiple Myeloma Response Criteria	Add	<p>Added in Progressive Disease (PD) response criteria (red) with regards to plasmacytomas: <i>Definite development of new bone lesions or soft tissue plasmacytomas, or definite increase in the size of any existing bone lesions or soft tissue plasmacytomas ($\geq 50\%$ increase from nadir in size of >1 lesion, or a $\geq 50\%$ increase in the longest diameter of a previous lesion >1 cm in short axis).</i></p>

10/ 14/ 17	Multiple Myeloma Response Criteria	Add	<p>Added the bullet points below to General Reporting Guidelines. Note, the second bullet point above was previously available in this section as a footnote.</p> <ul style="list-style-type: none"> • <i>Use the multiple myeloma response criteria when determining the disease status for multiple myeloma and solitary plasmacytoma.</i> • <i>Immunofixation (IFE) and immunoelectrophoresis (IEP) are essentially measuring the same thing and either may be used to determine CR. Electrophoresis (SPEP and UPEP) are, however, different assessments.</i>
5/1/ 17	Multiple Myeloma Response Criteria	Modify	<p>Corrected an error in the criteria for Near Complete Remission. <i>A treatment where all of the following criteria met:</i></p> <ul style="list-style-type: none"> • <i>Serum and Urine M-protein detectable by immunoelectrophoresis¹ (immunofixation, IFE) but not on electrophoresis (SPEP and UPEP)</i> • \leq < 5% plasma cells in bone marrow.
1/ 23/ 17	Multiple Myeloma Response Criteria	Add	<p>Added General Reporting Guidelines. This information was previously available in Pre-TED and Multiple Myeloma Response Criteria sections of the Forms Instructions Manual.</p>
8/ 26/ 16	Multiple Myeloma Response Criteria	Modify	<p>Updated PR criteria: If the serum and urine M-protein are not measurable (i.e., do not meet the following criteria <i>at time of diagnosis</i>):</p>
6/ 27/ 16	Multiple Myeloma Response Criteria	Modify	<p>Changed text in information box regarding Urine Studies: In order to report a Stringent Complete Remission (sCR) or Complete Remission (CR), urine studies MUST be performed and agree with the international myeloma working group (IMWG) criteria provided above. <i>As long as the negative serum electrophoresis and immunofixation studies have been confirmed, only one set of negative urine studies needs to be documented to report sCR or CR.</i> Urine electrophoresis and immunofixation studies may not be performed in all cases. The disease response options below (Near Complete Remission, Very Good Partial Response, and Partial Response) may still be reported even if urine studies were never obtained or were only obtained at diagnosis. If urine studies were performed following the most recent line of therapy, the results must agree with the international working group IMWG criteria for the disease status being reported. In any case, serum studies MUST be performed and agree with the international working group criteria for the disease status being reported (<i>excluding non-secretory myeloma</i>).</p>
6/ 24/ 16	Multiple Myeloma Response Criteria	Add	<p>Added information box: Urine Studies In order to report a Stringent Complete Remission or Complete Remission, urine studies MUST be performed and agree with the international working group criteria provided above. Urine electrophoresis and immunofixation studies may not be performed in all cases. The disease response options below (Near Complete Remission, Very Good Partial Response, and Partial Response) may still be reported even if urine studies were never obtained or were only obtained at diagnosis. If urine studies were performed following the most recent line of</p>

			therapy, the results must agree with the international working group criteria for the disease status being reported. In any case, serum studies MUST be performed and agree with the international working group criteria for the disease status being reported.
6/ 24/ 16	Multiple Myeloma Response Criteria	Add	Added link to Appendix W below disease status criteria.
1/ 19/ 16	Multiple Myeloma Response Criteria	Add	Added the following text to CR: The method of the two consecutive assessments may be any of the biochemical tests (urine/serum testing) listed in the disease status criteria available in the manual. Though it is preferable the biochemical confirmatory testing include both the urine & serum, this disease status does not require two consecutive assessments by each method. As an example: [see in text]
9/ 27/ 15	Multiple Myeloma Response Criteria	Add	Added a footnote: Immunofixation (IFE) and immunoelectrophoresis (IEP) are essentially measuring the same thing and either may be used to determine CR. Electrophoresis (SPEP and UPEP) are, however, different assessments.
5/ 29/ 15	Multiple Myeloma Response Criteria	Add	Added the following text to VGPR : ... then a $\geq 90\%$ decrease in the difference between involved and uninvolved free light chain levels is required in place of the M-protein criteria .

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