

## IMWG Criteria for the Diagnosis of Myeloma and Guidelines for the Diagnostic Work-Up of Myeloma

Criteria for a diagnosis of myeloma followed by the examinations, tests, and imaging studies that are recommended by the Working Group for the diagnosis of myeloma and related organ dysfunction.

These recommendations are excerpted from Palumbo A *et al.* International Myeloma Working Group guidelines for the management of multiple myeloma patients ineligible for standard high-dose chemotherapy with autologous stem cell transplantation, *Leukemia* (2009), 1-15.

[http://myeloma.org/pdfs/IMWG\\_guidelines\\_ineligible.pdf](http://myeloma.org/pdfs/IMWG_guidelines_ineligible.pdf)

Below are the criteria for a diagnosis of myeloma followed by the examinations, tests, and imaging studies that are recommended by the Working Group for the diagnosis of myeloma and related organ dysfunction. Please see also the International Myeloma Working Group (IMWG) consensus statement and guidelines regarding the current role of imaging techniques in the diagnosis and monitoring of multiple myeloma. (Dimopoulos MA *et al.* *Leukemia* (2009), 1-12).

[http://myeloma.org/pdfs/IMWG\\_consensus\\_imaging.pdf](http://myeloma.org/pdfs/IMWG_consensus_imaging.pdf)

Diagnosis	Diagnostic Criteria: All Three Required
Symptomatic multiple myeloma <sup>a</sup>	<ul style="list-style-type: none"> <li>• Monoclonal plasma cells in the bone marrow X10% and/or presence of a biopsy-proven plasmacytoma</li> <li>• Monoclonal protein present in the serum and/or urine<sup>b</sup></li> <li>• Myeloma-related organ dysfunction (X1)<sup>c</sup></li> </ul> <p style="text-align: right;">[C] Calcium elevation in the blood (serum calcium &gt;10.5 mg/l or upper limit of normal)</p>

	<p>[R] Renal insufficiency (serum creatinine &gt;2mg per 100 ml)</p> <p>[A] Anemia (hemoglobin &lt;10 g per 100 ml or 2 g &lt;normal)</p> <p>[B] Lytic bone lesions or osteoporosis<sup>d</sup></p>
<p>Monoclonal gammopathy of undetermined significance (MGUS)</p>	<ul style="list-style-type: none"> <li>• Serum monoclonal protein low<sup>e</sup></li> <li>• Monoclonal bone marrow plasma cells &lt;10%</li> <li>• No evidence of end-organ damage attributable to the clonal plasma cell disorder:</li> </ul> <p style="padding-left: 40px;">Normal serum calcium, hemoglobin level and serum creatinine</p> <p style="padding-left: 40px;">No bone lesions on full skeletal X-ray survey and/or other imaging if performed</p> <p style="padding-left: 40px;">No clinical or laboratory features of amyloidosis or light chain deposition disease</p>
<p>Smoldering or indolent myeloma<sup>f</sup></p>	<ul style="list-style-type: none"> <li>• Monoclonal protein present in the serum 3 g per 100 ml or higher or</li> <li>• Monoclonal plasma cells 10% or greater present in the bone marrow and/or a tissue biopsy</li> <li>• No evidence of end-organ damage attributable to the clonal plasma cell disorder:</li> </ul> <p style="padding-left: 40px;">Normal serum calcium, hemoglobin level and serum creatinine</p> <p style="padding-left: 40px;">No bone lesions on full skeletal X-ray</p>

	<p>survey and/or other imaging if performed</p> <p>No clinical or laboratory features of amyloidosis or light chain deposition disease</p>
Solitary plasmacytoma of bone	<ul style="list-style-type: none"> <li>• Biopsy-proven plasmacytoma of bone in a single site only.</li> <li>• X-rays and magnetic resonance imaging and/or FDG PET imaging (if performed) must be negative outside the primary site.</li> <li>• The primary lesion may be associated with a low serum and/or urine M-component</li> <li>• The bone marrow contains no monoclonal plasma cells</li> <li>• No other myeloma-related organ dysfunction</li> </ul>

Adapted with permission from Kyle and Rajkumar, Criteria for diagnosis, staging, risk stratification and response assessment of multiple myeloma. *Leukemia* 2009; 23: 3–9.  
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2627786/pdf/nihms80531.pdf>

<sup>a</sup>These criteria identify Stage IB and Stages II and III A/B myeloma by Durie/Salmon stage. Stage IA becomes smoldering or indolent myeloma.

<sup>b</sup>If no monoclonal protein is detected (non-secretory disease), then  $\geq$  30% monoclonal bone marrow plasma cells and/or a biopsy-proven plasmacytoma required.

<sup>c</sup>A variety of other types of end-organ dysfunctions can occasionally occur and lead to a need for therapy. Such dysfunction is sufficient to support classification as myeloma if proven to be myeloma related.

<sup>d</sup>If a solitary (biopsy-proven) plasmacytoma or osteoporosis alone (without fractures) is the sole defining criteria, then  $\geq$  30% plasma cells are required in the bone marrow.

<sup>e</sup>Low is defined as serum M protein <3.0 g per 100 ml.

<sup>f</sup>These criteria identify Stage IA myeloma by Durie/Salmon stage.

## **RECOMMENDED EXAM, TESTS, AND IMAGING STUDIES FOR THE DIAGNOSIS OF MYELOMA**

1. History and Physical Examination
2. Routine Testing
  - Complete blood count with differential and peripheral blood smear review
  - Chemistry panel including calcium and creatinine
  - Serum protein electrophoresis, immunofixation
  - Nephelometric quantitation of immunoglobulins
  - Routine urinalysis, 24 h urine collection for proteinuria, electrophoresis and immunofixation
  - Quantification of both urine M-component level and albuminuria
3. Bone Marrow Testing: Obtain an aspirate plus trephine biopsy with testing for cytogenetics, fluorescent in situ hybridization (FISH) and immunophenotyping.
4. Imaging
  - Bone survey including spine, pelvis, skull, humeri and femurs.
  - Magnetic resonance imaging of the axial skeleton is very informative if available/feasible, but is not mandatory.
  - Whole-body fluorodeoxyglucose/positron emission tomography imaging is also not mandatory, but can be used to confirm MGUS (positron emission tomography negative) or exclude unsuspected and/or extramedullary myeloma (positron emission tomography positive), infection, and/or an associated second malignancy. Positron emission tomography imaging was recently approved by CMS/Medicare (United States) for use in myeloma.