# Multiple Myeloma

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**INITIAL DIAGNOSTIC WORK-UP**

- History and physical
- CBC with differential, BUN, creatinine, electrolytes, LDH, calcium, albumin, beta-2 microglobulin, serum protein electrophoresis and immunofixation, serum free light chain assay (kappa and lambda), immunofixation, and quantitative immunoglobulins (IgG, IgM, IgA)
- 24 hour urine protein electrophoresis and immunofixation
- Skeletal survey
- PET/CT scan
- Unilateral bone marrow aspirate and biopsy
  - Bone marrow immunohistochemistry
  - Bone marrow flow cytometry
  - Cytogenetics
  - FISH (t(4;14), t(14:16), t(11:14), Del 13, Del 17p) Del 1p (CDKN2C), 1q21 (CKS1B)
- Dental evaluation
- Lifestyle risk assessment

**If indicated:**

- IgD and IgE
- Diagnostic imaging:
  - MRI (avoid gadolinium if creatinine clearance less than 30 mL/minute)
  - CT scan (consider avoiding intravenous contrast, if creatinine elevated)
  - Bone densitometry
  - Tissue biopsy to diagnose extraosseous plasmacytoma
  - Congo red staining of bone marrow and abdominal fat pad for amyloidosis (with or without Electron Microscopy [EM])
  - Serum viscosity
  - Gene expression profile (GEP)

**TREATMENT**

<table>
<thead>
<tr>
<th>Smoldering (asymptomatic) myeloma</th>
<th>Low/Intermediate risk</th>
<th>Observe at 2-3 month intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td>High risk</td>
<td></td>
<td>Observe or consider clinical trial</td>
</tr>
</tbody>
</table>

**FOLLOW-UP/SURVEILLANCE**

Prior to each cycle, obtain the following labs:

- CBC with differential, BUN, creatinine, calcium
- Quantitative immunoglobulins
- Serum protein electrophoresis
- Free light chains (FLC) as appropriate every month
- Urine protein electrophoresis
- If clinically indicated, consider:
  - Bone marrow aspirate and/or biopsy
  - Bone survey
  - MRI
  - PET/CT scan

If progression is observed, consider clinical trial

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1. Screening evaluation prior to initiation of bisphosphonates and/or SCT
2. See Physical Activity, Nutrition, and Tobacco Cessation algorithms; ongoing reassessment of lifestyle risks should be part of routine clinical practice
3. See Appendix A for Definitions

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**Note:** Consider Clinical Trials as treatment options for eligible patients.
Multiple Myeloma

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**Note:** Consider Clinical Trials as treatment options for eligible patients.

### RESPONSE

**Consolidation/maintenance therapy**

- Greater than or equal to very good partial response

**Consolidation/maintenance therapy**

- Consolidation/maintenance therapy or
- Second autologous SCT or
- Consider allogeneic SCT on clinical trial

**Consolidation/maintenance therapy** versus observation

**See follow-up and surveillance on Page 4**

### STEM CELL TRANSPLANT

**Is patient amenable to autologous SCT?**

- Yes
  - Autologous SCT
  - Greater than or equal to very good partial response
  - Less than very good partial response

- No
  - Offer autologous stem cell collection if patient is interested in delayed SCT
  - Continue induction therapy until plateau

### CONSOLIDATION/Maintenance

- Resume induction therapy until plateau
- Consolidaion/maintenance therapy versus observation

1 See Appendix D for Response Criteria
2 See Appendix E for Considerations For Undergoing SCT
3 See Appendix B for Treatment

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Multiple Myeloma

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**Note:** Consider Clinical Trials as treatment options for eligible patients.

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**RESPONSE**

**STEM CELL TRANSPLANT**

- Greater than or equal to very good partial response
  - Consolidation/maintenance therapy
    - Consolidation/maintenance therapy or
    - Second autologous SCT or
    - Consider allogeneic SCT on clinical trial

- Partial response
  - Salvage therapy (see Appendix B)

- Less than partial response
  - Less than partial response
    - Salvage therapy (see Appendix B)

- Less than partial response
  - Alternate salvage therapy (see Appendix B)
  - Autologous SCT

- Greater than or equal to partial response
  - Autologous SCT – Box A on Page 2 or
  - Continue salvage therapy (see Appendix B)

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**CONSOLIDATION/MAINTENANCE**

1. See Appendix D for Response Criteria
2. See Appendix B for Treatment
Multiple Myeloma

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**Note**: Consider Clinical Trials as treatment options for eligible patients.

### FOLLOW-UP/SURVEILLANCE

If patient is in complete response,

- Consider obtaining bone marrow biopsy to confirm minimal residual disease (MRD) status

**Frontline therapy completed**

- Obtain the following labs at least every 3 months:
  - Quantitative immunoglobulins plus quantitation of M protein (serum protein electrophoresis, urine protein electrophoresis) at least every 3 months (consider free light chains (FLC) ratio as well)
  - CBC with differential, BUN, creatinine, calcium
  - Immunofixation (serum/urine) to confirm complete response or in select situations (relapse, monoclonal gammopathy of undetermined significance (MGUS) associated with complete response particularly after SCT, etc)
  - Skeletal survey annually or if symptomatic
  - If clinically indicated, consider:
    - Bone marrow biopsy
    - MRI
    - PET/CT scan

- Salvage therapy (see Appendix B)

**Progressive disease?**

- Yes
- No

- Continue consolidation/maintenance therapy (see Appendix B) until progressive disease

1 If patient is in complete response, consider obtaining bone marrow biopsy to confirm minimal residual disease (MRD) status
**Multiple Myeloma**

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**RELAPSE (PROGRESSIVE DISEASE) AFTER AUTOLOGOUS SCT**

1. Relapse (progressive disease) less than 1 year post autologous SCT
   - Salvage therapy with or without allogeneic SCT

2. Relapse (progressive disease) greater than or equal to 1 year post autologous SCT or any patient
   - Salvage therapy with or without autologous/allogeneic SCT

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1 See Appendix B for Treatment
Multiple Myeloma

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APPENDIX A: Definitions

<table>
<thead>
<tr>
<th>Smoldering (Asymptomatic) Myeloma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Both criteria must be met:</td>
</tr>
<tr>
<td>• Serum monoclonal protein (IgG or IgA) greater than or equal to 30 g/L or urinary monoclonal protein greater than or equal to 500 mg per 24 hour and/or clonal bone marrow plasma cells 10-60%</td>
</tr>
<tr>
<td>• Absence of myeloma defining events or amyloidosis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Active (Symptomatic) Myeloma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clonal bone marrow plasma cells greater than or equal to 10% or biopsy-proven bony or extramedullary plasmacytoma and any one or more of the following myeloma defining events:</td>
</tr>
<tr>
<td>• Evidence of end organ damage that can be attributed to the underlying plasma cell proliferative disorder, specifically:</td>
</tr>
<tr>
<td>○ Hypercalcemia: serum calcium greater than 0.25 mmol/L (greater than 1 mg/dL) higher than the upper limit of normal or greater than 2.75 mmol/L (greater than 11 mg/dL)</td>
</tr>
<tr>
<td>○ Renal insufficiency: CrCl less than 40 mL per minute or serum creatinine greater than 177 µmol/L (greater than 2 mg/dL)</td>
</tr>
<tr>
<td>○ Anemia: hemoglobin value of greater than 20 g/L below the lower limit of normal, or a hemoglobin value less than 100 g/L</td>
</tr>
<tr>
<td>○ Bone lesions: one or more osteolytic lesions on skeletal radiography, CT, or PET/CT</td>
</tr>
<tr>
<td>• Any one or more of the following biomarkers of malignancy:</td>
</tr>
<tr>
<td>○ Clonal bone marrow plasma cell percentage greater than or equal to 60%</td>
</tr>
<tr>
<td>○ Involved/uninvolved serum free light chain ratio greater than or equal to 100</td>
</tr>
<tr>
<td>○ Greater than 1 focal lesions on MRI studies</td>
</tr>
</tbody>
</table>

1 Clonality should be established by showing k/λ-light-chain restriction on flow cytometry, immunohistochemistry, or immunofluorescence. Bone marrow plasma cell percentage should preferably be estimated from a core biopsy specimen; in case of a disparity between the aspirate and core biopsy, the highest value should be used.

2 If bone marrow has less than 10% clonal plasma cells, more than one bone lesion is required to distinguish from solitary plasmacytoma with minimal marrow involvement.

3 These values are based on the serum Freelite assay (The Binding Site Group, Birmingham, UK). The involved free light chain must be greater than or equal to 100 mg/L.

4 Each focal lesion must be 5 mm or more in size.
### APPENDIX B: Treatment

#### Induction Therapy for Stem Cell Transplant Candidates:

<table>
<thead>
<tr>
<th>Preferred treatments:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Carfilzomib/lenalidomide/dexamethasone</td>
<td>Bortezomib/lenalidomide/dexamethasone</td>
</tr>
<tr>
<td>Carfilzomib/cyclophosphamide/dexamethasone</td>
<td>Bortezomib/cyclophosphamide/dexamethasone</td>
</tr>
<tr>
<td>Bortezomib</td>
<td>Lenalidomide</td>
</tr>
</tbody>
</table>

#### Others:
- Carfilzomib/dexamethasone
- Bortezomib/dexamethasone
- Lenalidomide/dexamethasone

#### Special considerations:
- If neuropathy, consider lenalidomide/dexamethasone containing therapy or carfilzomib containing regimen
- If renal impairment:
  - Dose reduce lenalidomide according to guidelines
  - Use carfilzomib with caution; close renal monitoring is warranted
- Check 2D echocardiogram or equivalent prior to use of carfilzomib to ensure adequate baseline ejection fraction (EF)
- If diabetic, consider low-dose dexamethasone-based combination therapy and consultation to Endocrinology - Diabetes for diabetes management

#### Primary Treatment for Non-Stem Cell Transplant Candidates:
- Consider treatments indicated for stem cell transplant candidates plus ixazomib/lenalidomide/dexamethasone

#### Consolidation/Maintenance Therapy:
- Lenalidomide
- Ixazomib
- Bortezomib

#### Salvage Therapy:
- Elotuzumab/bortezomib/dexamethasone
- Elotuzumab/lenalidomide/dexamethasone
- Ixazomib/dexamethasone
- Ixazomib/lenalidomide/dexamethasone
- Ixazomib/pomalidomide/<dexamethasone
- Lenalidomide/dexamethasone
- Panobinostat/bortezomib/dexamethasone
- Panobinostat/carfilzomib
- Panobinostat/lenalidomide/dexamethasone
- Pomalidomide/<bortezomib/dexamethasone
- Pomalidomide/<carfilzomib/dexamethasone
- Pomalidomide/cyclophosphamide/dexamethasone
- Pomalidomide/dexamethasone
- Pomalidomide/elotuzumab/dexamethasone

#### Consider in aggressive disease:
- Dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide (DT-PACE) with or without bortezomib (VTD-PACE)
- Modified hyperfractionated cyclophosphamide/bortezomib/doxorubicin/dexamethasone
- Proteasome inhibitor and immunomodulator combination for high risk disease

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1 Two prior therapies should include proteasome inhibitor and lenalidomide agent and have disease progression on or within 60 days of last therapy

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Approved by The Executive Committee of Medical Staff 09/25/2018
APPENDIX C: Adjunctive Treatment

### Bone Disease:
- Prior to starting bisphosphonate/denosumab:
  - Comprehensive dental exam plus appropriate dentistry prior to treatment
  - Treatment and resolution of active oral infections prior to treatment
  - Check 25-hydroxyvitamin D and corrected serum calcium levels and supplement as needed
- **Monoclonal Antibodies (denosumab)** – Preferred
  - For prevention of skeletal-related events:
    - Denosumab 120 mg SQ every 4 weeks
  - Monitoring during therapy:
    - Check serum creatinine, calcium, phosphorus and magnesium during the first weeks of therapy initiation
    - CrCl less than 30 mL/minute: use is not recommended¹
- **Bisphosphonates (pamidronate and zoledronic acid)**
  - Zoledronic acid 4 mg every 3 months (preferred) and pamidronate 90 mg once monthly for 2 years, then re-evaluate. If skeletal related event (SRE) occurs, reinstitute treatment.
  - All patients treated with bisphosphonate should receive a greater than or equal to 2 hour infusion of pamidronate and greater than or equal to 15 minute infusion of zoledronic acid.
  - Renal impairment dose adjustments:
    - Zoledronic acid
      - CrCl 50 - 60 mL/minute: reduce dose to 3.5 mg
      - CrCl 40 - 49 mL/minute: reduce dose to 3.3 mg
      - CrCl 30 - 39 mL/minute: reduce dose to 3 mg
      - CrCl less than 30 mL/minute: use is not recommended
    - Pamidronate - consider dose reduction to 30 mg – 60 mg if creatinine greater than 3 mg/dL or creatinine clearance less than 30 mL/minute

### Bone Disease – continued
- Monitoring during therapy:
  - Check creatinine prior to each infusion (hold bisphosphonate if creatinine has risen greater than or equal to 0.5 mg/dL change or twice the baseline value if original creatinine was less than 1.4 mg/dL)
  - Every 3-6 months check for albuminuria; if greater than 500 mg/24 hours hold treatment until return to baseline. If reintitimating, infuse zoledronic acid over 30 minutes and pamidronate over 4 hours.
- Discontinue bisphosphonates if osteonecrosis of the jaw develops
- **Infection:**
  - Intravenous immunoglobulin therapy should be considered in the setting of recurrent life-threatening infection, hypogammaglobulinemia, and/or if greater than or equal to 3 infections/year
  - Consider pneumococcal vaccinations (PCV13 and PPSV23) per CDC guidelines
  - Consider annual influenza vaccine
  - Consider high-dose influenza vaccine for patients greater than or equal to 65 years old and patients who have previously undergone a SCT
  - Herpes zoster prophylaxis is indicated for patients treated with proteasome inhibitors, daratumumab, and/or high dose dexamethasone
  - Consider use in patients receiving elotuzumab
  - Consider avoiding concomitant quinolone therapy for patients on bortezomib-containing regimens
  - Anti fungal, antibacterial, and anti-zoster prophylaxis is indicated for patients receiving hyperfractionated cyclophosphamide-based therapy
  - See Appendix F for post-transplant infection prophylaxis and vaccination schedule

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1 Patients with CrCl less than 30 mL/minute were excluded in myeloma studies

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CDC = Centers for Disease Control and Prevention
PCV13 = pneumococcal conjugate vaccine
PPSV23 = pneumococcal polysaccharide vaccine

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APPENDIX C: Adjunctive Treatment - continued

<table>
<thead>
<tr>
<th>Renal Dysfunction:</th>
<th>Radiation Therapy:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maintain hydration to avoid renal failure</td>
<td>Low-dose radiation therapy (20-30 Gy) can be used as palliative treatment for uncontrolled pain, impending or overt pathologic fracture, and/or impending or overt cord compression</td>
</tr>
<tr>
<td>Avoid use of nonsteroidal anti-inflammatory drugs (NSAID)</td>
<td>Limited involved sites should be used to decrease the impact of radiation on stem-cell harvest and potential future treatments</td>
</tr>
<tr>
<td>Avoid gadolinium if creatinine clearance less than 30 mL/minute</td>
<td>Orthopedic or Neurosurgical:</td>
</tr>
<tr>
<td>Avoid iodine IV contrast</td>
<td>Consider vertebroplasty or kyphoplasty for symptomatic vertebral compression fractures</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Coagulation/thrombosis:</th>
<th>Consultation with orthopedic surgery should be sought as appropriate for impending or overt long bone fractures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients receiving thalidomide, lenalidomide, or pomalidomide and dexamethasone and/or anthracyclines should be given appropriate thromboprophylaxis according to the International Myeloma Working Group Guideline</td>
<td>Consultation with neurosurgery should be sought in the setting of impending or overt spinal cord compression or vertebral column instability</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hypercalcemia:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Prompt treatment with steroid containing chemotherapy</td>
<td></td>
</tr>
<tr>
<td>Hydration, furosemide, and/or calcitonin</td>
<td></td>
</tr>
<tr>
<td>Bisphosphonates</td>
<td></td>
</tr>
<tr>
<td>o Dose adjustments for renal impairment not required</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Symptomatic Hyperviscosity:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasmapheresis should be used as adjunctive therapy</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>GI Prophylaxis:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients receiving steroids should receive prophylaxis with a proton pump inhibitor or H₂-receptor antagonist</td>
<td></td>
</tr>
</tbody>
</table>
APPENDIX D: Response Criteria for Multiple Myeloma

<table>
<thead>
<tr>
<th>Standard IMWG Criteria</th>
<th>Response Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stringent complete response</td>
<td>Complete response as defined below plus normal FLC ratio and absence of clonal cells in bone marrow biopsy by immunohistochemistry (k/λ ratio less than or equal to 4:1 or greater than or equal to 1:2 for k and λ patients, respectively, after counting greater than or equal to 100 plasma cells)</td>
</tr>
<tr>
<td>Complete response</td>
<td>Negative immunofixation on the serum and urine and disappearance of any soft tissue plasmacytomas and less than 5% plasma cells in bone marrow aspirates</td>
</tr>
<tr>
<td>Very good partial response</td>
<td>Serum and urine M-protein detectable by immunofixation but not on electrophoresis or greater than or equal to 90% reduction in serum M-protein plus urine M-protein level less than 100 mg per 24 hours</td>
</tr>
</tbody>
</table>
| Partial response                   | Greater than or equal to 50% reduction of serum M-protein plus reduction in 24 hour urinary M-protein by greater than or equal to 90% or to less than 200 mg per 24 hours  
If the serum and urine M-protein are unmeasurable, a greater than or equal to 50% decrease in the difference between involved and uninvolved FLC levels is required in place of the M-protein criteria  
If serum and urine M-protein are unmeasurable, and serum-free light assay is also unmeasurable, greater than or equal to 50% reduction in plasma cells is required in place of M-protein, provided baseline bone marrow plasma-cell percentage was greater than or equal to 30%. In addition to these criteria, if present at baseline, a greater than or equal to 50% reduction in the size (SPD) of soft tissue plasmacytomas is also required. |
| Minimal response                   | Greater than or equal to 25% but less than or equal to 49% reduction of serum M-protein and reduction in 24 hour urine M-protein by 50-89%. In addition to the above listed criteria, if present at baseline, a greater than or equal to 50% reduction in the size (SPD) of soft tissue plasmacytomas is also required. |
| Stable disease                     | Not recommended for use as an indicator of response; stability of disease is best described by providing the time-to-progression estimates. Not meeting criteria for complete response, very good partial response, partial response, minimal response, or progressive disease. |

IMWG = International Myeloma Working Group  
SPD = sum of the product of the maximal perpendicular diameters of measured lesions
## APPENDIX D: Response Criteria for Multiple Myeloma - continued

<table>
<thead>
<tr>
<th>Standard IMWG Criteria</th>
<th>Response Criteria</th>
</tr>
</thead>
</table>
| **Progressive disease** | Any one or more of the following criteria:  
  - Increase of 25% from lowest confirmed response value in one or more of the following criteria:  
    - Serum M-protein (absolute increase must be greater than or equal to 0.5 g/dL)  
    - Serum M-protein increase greater than or equal to 1 g/dL, if the lowest M component was greater than or equal to 5 g/dL  
    - Urine M-protein (absolute increase must be greater than or equal to 200 mg/24 hour)  
    - In patients without measurable serum and urine M-protein levels, the difference between involved and uninvolved FLC levels (absolute increase must be greater than 10 mg/dL)  
    - Appearance of a new lesion(s), greater than or equal to 50% increase from nadir in SPD of greater than 1 lesion, or greater than or equal to 50% decrease in the longest diameter of a previous lesion greater than 1 cm in short axis  
    - Greater than or equal to 50% increase in circulating plasma cells (minimum of 200 cells per µL) if this is the only measure of disease |

| **Clinical relapse** | Clinical relapse requires one or more of the following criteria:  
  - Direct indicators of increasing disease and/or end organ dysfunction (CRAB features) related to the underlying clonal plasma-cell proliferative disorder. It is not used in calculation of time to progression-free survival but is listed as something that can be reported optionally or for use in clinical practices:  
    - Development of new soft tissue plasmacytomas or bone lesions (osteoporotic fractures do not constitute progression)  
    - Define increase in the size of existing plasmacytomas or bone lesions. A definite increase is defined as a 50% (and greater than or equal to 1 cm) increase as measured serially by the SPD of the measurable lesion  
    - Hyperviscosity related to serum paraprotein |

| **Relapse from complete response**  
(to be used only if the end point is disease-free survival) | Any one or more of the following criteria:  
  - Reappearance of serum or urine M-protein by immunofixation or electrophoresis  
  - Development of greater than or equal to 5% plasma cells in the bone marrow  
  - Appearance of any other sign of progression (i.e., new plasmacytoma, lytic bone lesions, or hypercalcaemia see above) |

| **Relapse from MRD negative**  
(to be used only if the end point is disease-free survival) | Any one or more of the following criteria:  
  - Loss of MRD negative state (evidence of clonal plasma cells on NGF or NGS or positive imaging study for recurrence of myeloma)  
  - Reappearance of serum or urine M-protein by immunofixation or electrophoresis  
  - Development of greater than or equal to 5% clonal plasma cells in the bone marrow  
  - Appearance of any other sign of progression (i.e., new plasmacytoma, lytic bone lesion, or hypercalcaemia) |

CRAB features = calcium elevation, renal failure, anaemia, lytic bone lesions

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# APPENDIX D: Response Criteria for Multiple Myeloma - continued

<table>
<thead>
<tr>
<th>IMWG MRD Criteria</th>
<th>Response Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sustained MRD-negative</td>
<td>• MRD negativity in the marrow (NGF or NGS or both) and by imaging as defined below, confirmed minimum of 1 year apart. Subsequent evaluations can be used to further specify the duration of negativity (e.g., MRD-negative at 5 years).</td>
</tr>
<tr>
<td>Flow MRD-negative</td>
<td>• Absence of phenotypically aberrant clonal plasma cells by NGF on bone marrow aspirate using the EuroFlow standard operation procedure for MRD detection in multiple myeloma (or validated equivalent method) with a minimum sensitivity of 1 in $10^5$ nucleated cells or higher</td>
</tr>
<tr>
<td>Sequencing MRD-negative</td>
<td>• Absence of clonal plasma cells by NGS on bone marrow aspirate in which presence of a clone is defined as less than two identical sequencing reads obtained after DNA sequencing of bone marrow aspirates using the LymphoSIGHT platform (or validated equivalent method) with a minimum sensitivity of 1 in 10 nucleated cells or higher</td>
</tr>
<tr>
<td>Imaging plus MRD-negative</td>
<td>• MRD negativity as defined by NGF or NGS plus disappearance of every area of increased tracer uptake found at baseline or a preceding PET/CT or decrease to less mediastinal blood pool SUV or decrease to less than that of surrounding normal tissue</td>
</tr>
</tbody>
</table>

MRD = minimal residual disease  
NGF = next-generation flow  
NGS = next-generation sequencing  
SUV = maximum standardized uptake value
APPENDIX E: Considerations For Undergoing Autologous SCT

<table>
<thead>
<tr>
<th>Clinical Eligibility Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>● No uncontrolled cardio/pulmonary conditions</td>
</tr>
<tr>
<td>● Adequate peripheral venous access or adequate option for central venous access for autologous apheresis donors</td>
</tr>
<tr>
<td>● Negative pregnancy test for women of child-bearing potential</td>
</tr>
<tr>
<td>● No known allergy to cytokines if cytokines are to be used</td>
</tr>
<tr>
<td>● Patients with sickle cell anemia and other hemoglobinopathies are candidates for autologous stem cell transplant as long as their clinical condition permits the collection of sufficient stem cells</td>
</tr>
<tr>
<td>Labs:</td>
</tr>
<tr>
<td>○ WBC - recommend greater than 3 K/microliter (minimum greater than 2 K/microliter)</td>
</tr>
<tr>
<td>○ Platelets - recommend greater than 75 K/microliter (minimum greater than 50 K/microliter)</td>
</tr>
<tr>
<td>● Negative pregnancy test for women of child-bearing potential</td>
</tr>
<tr>
<td>● No known allergy to cytokines if cytokines are to be used</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical Suitability Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>● Durie Salmon stage (should be II or III to qualify)</td>
</tr>
<tr>
<td>● Partial response to prior therapy (defined as a 50% decrease either in measurable serum and/or paraprotein or in bone marrow infiltration sustained for at least one month)</td>
</tr>
<tr>
<td>● Adequate cardiac, renal, pulmonary, and hepatic function</td>
</tr>
</tbody>
</table>
### APPENDIX F: Post-SCT Infection Prophylaxis and Vaccination Schedule (Adults)

#### Antibacterial Prophylaxis

- **Levofloxacin** 500 mg IV/PO once daily, starting Day -1 or if patient neutropenic at start of chemotherapy/admission (ANC less than or equal to 1 K/microliter)
  - Continue until ANC is greater than 1 K/microliter after engraftment or until patient becomes febrile
  - Adjust dose for CrCl less than 50 mL/minute
- **Alternative options** (i.e., allergy or intolerance to fluoroquinolones)
  - Cefepoxide 200 mg PO twice daily, starting Day -1 or if patient neutropenic at start of chemotherapy/admission (ANC less than or equal to 1 K/microliter)

#### Antifungal Prophylaxis

- **Fluconazole** 400 mg PO/IV daily from Day -1 until engraftment
- **Alternative options** (i.e., allergy or intolerance to azoles)
  - Caspofungin 50 mg IV once daily
  - Prior history of mold infection:
    - Voriconazole 200 mg PO twice daily
    - Posaconazole 300 mg PO once daily

#### PCP Prophylaxis

Start by engraftment (Day +30 and ANC greater than 1.5 K/microliter) and continue for at least 6 months after transplant
- **First line option:** sulfamethoxazole/trimethoprim (Bactrim)
  - Consider initiation of folic acid 1 mg PO once daily when patients started on Bactrim prophylaxis
    - Bactrim DS (800/160 mg) 1 tablet PO daily on Monday, Wednesday, and Friday
    - Bactrim SS (400/80 mg) 1 tablet PO daily
    - Bactram DS (800/160 mg) 1 tablet PO daily (reserve for patients with history of toxoplasmosis, history of toxoplasmosis IgG positive, or PCP)
- **Second line options** (if sulfa intolerant):
  - Consider sulfamethoxazole/trimethoprim desensitization in patients with mild rash or unknown reaction to sulfa
    - Inhaled pentamidine 300 mg every 21-28 days via Respigrad II nebulizer
    - Pentamidine 4 mg/kg IV over 90 minutes every 21 days
    - Atovaquone 1500 mg PO once daily
    - Dapsone 100 mg PO once daily
      - Test for G6PD deficiency prior to initiation of therapy
      - Avoid if history of life threatening reaction to sulfamethoxazole/trimethoprim

#### Antiviral Prophylaxis

- **Herpes simplex virus (HSV)**
  - Valacyclovir 500 mg PO daily starting Day -1 and continue for 6-12 months after transplant
  - Alternative option: acyclovir 400 mg PO twice daily
  - If patient unable to take medications by mouth:
    - Acyclovir 250 mg/m² or 5 mg/kg IV every 12 hours
    - Patients with severe mucositis: acyclovir 250 mg/m² or 5 mg/kg IV every 8 hours
  - Adjust for renal impairment
- **Varicella zoster virus (VZV)**
  - Patients with a history of shingles or VZV seropositive
    - Valacyclovir 500 mg PO twice daily, starting Day -1 for 1 year
    - Alternative option: acyclovir 800 mg PO twice daily
    - If patient unable to take medications by mouth: acyclovir 250 mg/m² or 5 mg/kg IV every 8 hours

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**Continue on next page**
### APPENDIX F: Post-SCT Infection Prophylaxis and Vaccination Schedule (Adults) - continued

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Dose/Route</th>
<th>Time Post Transplant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>6 months</td>
</tr>
<tr>
<td>Pneumococcal conjugate (PCV, Prevnar 13®)</td>
<td>0.5 mL IM</td>
<td>X</td>
</tr>
<tr>
<td>Pneumococcal polysaccharide (PPSV23, Pneumovax®)</td>
<td>0.5 mL SC or IM</td>
<td>X</td>
</tr>
<tr>
<td>Haemophilus influenzae (Hib)</td>
<td>0.5 mL IM</td>
<td>X</td>
</tr>
<tr>
<td>Diphtheria, tetanus, acellular pertussis (DTaP)</td>
<td>0.5 mL IM</td>
<td>X</td>
</tr>
<tr>
<td>Inactive polio (IPV)²</td>
<td>0.5 mL SC or IM</td>
<td>X</td>
</tr>
<tr>
<td>Hepatitis B (HepB)</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Seasonal influenza³ (September to January/February)</td>
<td>0.25 mL IM</td>
<td>X</td>
</tr>
</tbody>
</table>

1 May substitute Tdap if DTaP unavailable
2 DTaP and IPV may be given via the combination Kinrix® at the same intervals per chart above
3 Continue yearly for life

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### APPENDIX F: Post-SCT Infection Prophylaxis and Vaccination Schedule (Adults) - continued

#### Optional Vaccines

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Dose/Route</th>
<th>Time Post Transplant</th>
<th>Greater than or equal to 24 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measles, mumps, and rubella (MMR – live vaccine)</td>
<td>0.5 mL SC</td>
<td>Contraindicated in patients less than 24 months post-SCT, on immunosuppression, and/or active GVHD</td>
<td>X</td>
</tr>
<tr>
<td>Varicella virus vaccine² (Varivax® – live vaccine)</td>
<td>0.5 mL SC</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Human papilloma virus³ (HPV, Gardasil 9®)</td>
<td>0.5 mL IM</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Meningococcal conjugate vaccine (MCV4, Menactra®)</td>
<td>0.5 mL IM</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Meningococcal type B vaccine (Bexsero®)</td>
<td>0.5 mL IM</td>
<td>X³</td>
<td></td>
</tr>
</tbody>
</table>
| Hepatitis A (Havrix®)                           | • Less than or equal to 18 years: 0.5 mL IM  
• Greater than or equal to 19 years: 1 mL IM | X                                                         | X                                 |

¹ For live attenuated vaccines, patients must be greater than 2 years post SCT, greater than 1 year off immunosuppression, and greater than 8 months since IVIG
² At the present, there is insufficient data to recommend the new recombinant varicella zoster vaccine (Shingrix®). Use is unlikely to be harmful and more evaluation is currently underway.
³ For male and female patients age 9 to 26 years
⁴ Two doses 4 weeks apart

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Multiple Myeloma

The following is not meant to be a comprehensive list of available effective treatments for myeloma. Myeloma treatments are changing rapidly and new treatments and added information regarding previous treatment treatments are available frequently. As a result, updates should be taken into consideration and for similar reasons, regimens reported only by abstract have been included on this reference list.


**SUGGESTED READINGS**

Continued on next page
Multiple Myeloma


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Multiple Myeloma

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SUGGESTED READINGS - continued


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SUGGESTED READINGS - continued


SUGGESTED READINGS - continued


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SUGGESTED READINGS - continued


Multiple Myeloma

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SUGGESTED READINGS - continued


Continued on next page
SUGGESTED READINGS - continued


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Multiple Myeloma

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DEVELOPMENT CREDITS

This practice algorithm is based on majority expert opinion of the Myeloma Center Faculty at the University of Texas MD Anderson Cancer Center. It was developed using a multidisciplinary approach that included input from the following:

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