<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>8:00–8:30 am</td>
<td>Multiple Myeloma Patient Testimonial and Workshop Assignments</td>
<td>Room 2002</td>
</tr>
<tr>
<td></td>
<td>Faculty Panel</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Identifying Indicators of Outcomes and Implementing Treatment Pathways</td>
<td></td>
</tr>
<tr>
<td></td>
<td>John M. Cruickshank, DO, MBA, CPE</td>
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</tr>
<tr>
<td></td>
<td>Carol Ann Huff, MD</td>
<td></td>
</tr>
<tr>
<td>9:25–10:20 am</td>
<td>Workshop 2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Applying Oncology Formulary and Benefit Design Innovations</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Jeffrey D. Dunn, PharmD, MBA</td>
<td></td>
</tr>
<tr>
<td></td>
<td>C. Daniel Mullins, PhD</td>
<td></td>
</tr>
<tr>
<td>10:20–11:15 am</td>
<td>Workshop 3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Supportive Care Requirements and Coordination of Patient-Centered Care</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Jack Aiello</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Kelly G. Bugos, RN, NP, MS</td>
<td></td>
</tr>
<tr>
<td>11:15 am–12:00 pm</td>
<td>Review of Workshop Key Take Aways and Multi-Stakeholder Question and Answer Session</td>
<td>Room 2002</td>
</tr>
<tr>
<td></td>
<td>Faculty Panel</td>
<td></td>
</tr>
</tbody>
</table>
Workshop Objectives

**Workshop 1:** Identifying Indicators of Outcomes and Implementing Treatment Pathways
- Enable decision making based on indicators of treatment outcomes for multiple myeloma
- Coordinate oncology care and health plan medical and pharmacy management services to improve outcomes for patients with multiple myeloma

**Workshop 2:** Applying Oncology Formulary and Benefit Design Innovations
- Enable the use of decision support tools to appropriately invest resources and reduce treatment variability with multiple myeloma therapies
- Construct a benefit design model for oral oncology drugs

**Workshop 3:** Supportive Care Requirements and Coordination of Patient-Centered Care
- Recommend methods to improve patient outcomes with supportive care for multiple myeloma within a health plan setting
- Implement accurate and appropriate counsel, as part of the treatment team, that will improve patient adherence to treatment recommendations
Workshop Assignments

1. Identify Current Gaps and Barriers vs. What is Achievable
2. What is the Desired Outcome?
3. Recommended Solutions
The Evolving Role of Managed Care and Oncology Pharmacy Management: Practical Recommendations for a Changing Environment
Workshop 1: Identifying Indicators of Outcomes and Implementing Treatment Pathways

Objectives

• Enable decision making based on indicators of treatment outcomes for multiple myeloma
• Coordinate oncology care and health plan medical and pharmacy management services to improve outcomes for patients with multiple myeloma
Identifying Indicators of Outcomes and Implementing Treatment Pathways

• Identify Current Gaps and Barriers vs. What is Achievable
  – Knowledge causes? Strategy causes? Performance causes?

• What is the Desired Outcome?
  – List the attributes that are needed

• Recommended Solutions
  – Identify practical next steps
Response Rates, Progression-Free Survival, Quality of Life: Defining the Managed Care Outcomes for Multiple Myeloma Treatments

Carol Ann Huff, MD
Associate Professor of Oncology and Medicine
Johns Hopkins University School of Medicine
The faculty reported the following financial relationships or relationships to products or devices they or their spouse/life partner have with commercial interests related to the content of this CME activity:

- Carol Ann Huff, MD
  - Consulting Fees: Celgene Corporation, Millennium Pharmaceuticals, Inc., Amgen Inc.
  - Contracted Research: Geron Corporation, Bristol-Myers Squibb
Epidemiology of Multiple Myeloma (MM)

- 21,700 new cases and 10,710 deaths from MM in the United States in 2011
- Slightly more common in men than in women
- Higher incidence in blacks vs whites (2:1)
- Median age at diagnosis is 69 years for men and 71 years for women

American Cancer Society. 
Overall Survival Has Improved in the Past Decade

Overall Survival in Multiple Myeloma Based on Year of Diagnosis

Initial Approach to Treatment of MM

**Nontransplantation candidate**
(based on age, performance score, and comorbidity)

- Induction treatment
- Maintenance

**Transplantation candidate**

- Induction treatment (nonalkylator-based induction x 4-6 cycles)
- Stem cell harvest
- Stem cell transplantation
- Maintenance
## Risk Stratification

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Standard Risk</th>
<th>High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FISH</strong></td>
<td>t(11;14)</td>
<td>Del (17p) t(4;14) t(14;16)</td>
</tr>
<tr>
<td><strong>Cytogenetics</strong></td>
<td>Hyperdiploidy</td>
<td>Hypodiploidy, del 13q</td>
</tr>
<tr>
<td><strong>B2-microglobulin</strong></td>
<td>&lt; 3.5 mg/dL</td>
<td>≥ 5.5 mg/dL</td>
</tr>
<tr>
<td><strong>Plasma Cell Labeling Index</strong></td>
<td>&lt;3%</td>
<td>≥3%</td>
</tr>
<tr>
<td><strong>Isotype</strong></td>
<td></td>
<td>IgA</td>
</tr>
<tr>
<td><strong>Gene expression profile</strong></td>
<td>Good risk</td>
<td>High risk</td>
</tr>
</tbody>
</table>

**FISH** = Fluorescence in situ hybridization.  
**Del (17p)** = Deletions of part of the short arm of chromosome 17

Therapeutic Options for Newly Diagnosed Multiple Myeloma: Transplant Ineligible
IFM 99-06: Superior Overall Survival with MPT vs MP or MEL100

Overall Survival

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Median Overall Survival (months)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MP (n = 196)</td>
<td>33.2±3.2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>MPT (n = 125)</td>
<td>51.6±4.5</td>
<td>.004</td>
</tr>
<tr>
<td>MEL100 (n = 126)</td>
<td>38.3±2.7</td>
<td></td>
</tr>
</tbody>
</table>

Patients 65 to 75 years of age

Median follow-up time = 51.5 months
Progression-free survival (MPT) = 27.5 months

IFM = Intergroupe Francophone du Myelome
MPT = melphalan/prednisone/thalidomide
MP = melphalan/prednisone
MEL100 = reduced-intensity stem cell transplantation using melphalan 100 mg/m².
VISTA: VMP vs MP in Untreated Myeloma: Long-term Follow-Up

Median follow-up: 36.7 mos; data cutoff March 2009, all patients completed VISTA study treatment

- OS benefit maintained; 35% reduced risk of death with VMP vs MP

VISTA= Velcade as Initial Standard Therapy in MM
VMP= bortezomib/melphalan/prednisone
MP= melphalan/prednisone
OS= overall survival

VMP: Efficacy in Patients With High-Risk FISH

FISH = Fluorescence in situ hybridization.
Del (17p) = Deletions of part of the short arm of chromosome 17

**Time to Progression**

<table>
<thead>
<tr>
<th></th>
<th>Standard risk (n = 142): 23.1 mos (34 events)</th>
<th>High risk (n = 26): 19.8 mos (7 events)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR</td>
<td>1.297 (95% CI: 0.55-3.06; p = .55)</td>
<td></td>
</tr>
</tbody>
</table>

**Overall Survival**

<table>
<thead>
<tr>
<th></th>
<th>Standard risk (n = 142): median not reached (29 events)</th>
<th>High risk (n = 26): median not reached (6 events)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR</td>
<td>1.104 (95% CI: 0.444-2.743; p = .8311)</td>
<td></td>
</tr>
</tbody>
</table>

**High-risk t(4;14), t(14;16), del (17p) by FISH**

VMP = bortezomib/melphalan/prednisone

## Selected Phase III Trials: Newly Diagnosed MM

**CR or better**
- **PR or better:**
  - MP VISTA: 31%, 4%
  - MPT-Palumbo: 37%, 4%
  - MPT-Facon: 47%, 4%
  - VMP-VISTA: 41%, 30%
  - Ld-ECOG: 44%, 24%

**CR+VGPR**
- **Outcomes**
<table>
<thead>
<tr>
<th>MP VISTA</th>
<th>MPT-Palumbo</th>
<th>MPT-Facon</th>
<th>VMP-VISTA</th>
<th>Ld-ECOG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Age</td>
<td>71</td>
<td>72</td>
<td>68</td>
<td>71</td>
</tr>
<tr>
<td>TTP (Months)</td>
<td>27</td>
<td>~28</td>
<td>27</td>
<td>24</td>
</tr>
<tr>
<td>1-yr OS</td>
<td>87%</td>
<td>88%</td>
<td>~90%</td>
<td>96%</td>
</tr>
<tr>
<td>2-yr OS</td>
<td>70%</td>
<td>82%</td>
<td>~78%</td>
<td>83%</td>
</tr>
<tr>
<td>3-yr OS</td>
<td>54%</td>
<td>80%</td>
<td>69%</td>
<td>75%</td>
</tr>
</tbody>
</table>

CR=complete response; VGPR=very good partial response; PR=partial response; MP=melphalan/prednisone; VISTA= Velcade as Initial Standard Therapy in MM; MPT = melphalan/prednisone/thalidomide; VMP=bortezomib/melphalan/prednisone; Ld-ECOG=low dose dexamethasone – Eastern Cooperative Oncology Group; TTP=time to progression; NE= not evaluated; OS=overall survival

Therapeutic Options for Newly Diagnosed Multiple Myeloma: Transplant Eligible
### Selected Phase III Trials: Newly Diagnosed MM

#### Table: Summary of Phase III Trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>Median Age</th>
<th>TTP (Months)</th>
<th>1-yr OS</th>
<th>2-yr OS</th>
<th>3-yr OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>MP Vista</td>
<td>71</td>
<td>27</td>
<td>87%</td>
<td>70%</td>
<td>54%</td>
</tr>
<tr>
<td>MPT-Palumbo</td>
<td>72</td>
<td>~28</td>
<td>88%</td>
<td>82%</td>
<td>80%</td>
</tr>
<tr>
<td>MPT-Facon</td>
<td>68</td>
<td>27</td>
<td>~90%</td>
<td>~78%</td>
<td>69%</td>
</tr>
<tr>
<td>VMP-VISTA</td>
<td>71</td>
<td>24</td>
<td>96%</td>
<td>83%</td>
<td>75%</td>
</tr>
<tr>
<td>Ld-ECOG</td>
<td>54</td>
<td>NE</td>
<td>~85%</td>
<td>90%</td>
<td>~75%</td>
</tr>
<tr>
<td>Bortez/Dex IFM 05-01</td>
<td>NE</td>
<td>NE</td>
<td>96%</td>
<td>90%*</td>
<td>96%*</td>
</tr>
<tr>
<td>Thal/Dex MM003</td>
<td>64</td>
<td>22.8</td>
<td>~75%</td>
<td>90%</td>
<td>90%</td>
</tr>
<tr>
<td>Bortez/Thal/Dex GIMEMA</td>
<td>NE</td>
<td>NE</td>
<td>96%</td>
<td>90%*</td>
<td>96%*</td>
</tr>
</tbody>
</table>

*CR=complete response; VGP=very good partial response; PR=partial response; GIMEMA=Gruppo Italiano Malattie EMatologiche dell’Adulto; TTP=time to progression; NE=not evaluated; OS=overall survival

---

*Following stem cell transplant

---

E4A03: OS According to Treatment Beyond 4 Cycles

No Further Tx after 4 Cycles LD or Ld

- 55% 3-yr OS rate

ASCT after 4 Cycles LD or Ld

- 92% 3-yr OS rate

Primary Therapy beyond 4 Cycles

- 79% 3-yr OS rate

E4A03 = ECOG Phase III Newly Diagnosed MM Trial
OS = Overall survival
ASCT = autologous stem cell transplant
LD = high-dose dexamethasone
Ld = low-dose dexamethasone

Updated Analysis of Phase I/II Trial of RVD in Newly Diagnosed MM

- Maximum dose (up to 8 cycles)
  - Bortezomib 1.3 mg/m² (days 1, 4, 8, 11)
  - Lenalidomide 25 mg (days 1-14)
  - Dexamethasone 20 mg (days 1, 4, 8, 11)
    cycles 1-4 and 10 mg (days 1, 4, 8, 11)
    cycles 5-8

- Median PFS and OS not reached (follow-up 27 mo)
  - Estimated 24-mo PFS: 68% (95% CI: 55% to 78%)
  - Estimated 24-mo OS: 95% (95% CI: 86% to 98%)

- No unexpected toxicities observed
  - DVT/PE reported in 5% of patients

RVD=lenalidomide, bortezomib, dexamethasone
CR = Complete response
VGPR = Very good partial response
PR = Partial response
PFS = Progression-free survival

Maintenance Therapy
## Post ASCT Maintenance with Lenalidomide

<table>
<thead>
<tr>
<th>Study</th>
<th>Regimen</th>
<th>N</th>
<th>Response</th>
<th>PFS/EFS/TTP</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>McCarthy CALGB 100104</td>
<td>Len maint. post-ASCT Placebo</td>
<td>210</td>
<td></td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>(ASCO 2010; Abstract 8017)</td>
<td></td>
<td>208</td>
<td></td>
<td>25.5 mo Median TTP</td>
<td></td>
</tr>
<tr>
<td>Attal IFM-2005</td>
<td>Low-dose len maint. post-ASCT Placebo</td>
<td>307</td>
<td>77% 70%</td>
<td>68% 34%</td>
<td>HR = 0.46 p &lt; 10^{-7}</td>
</tr>
<tr>
<td>(ASCO 2010; Abstract 8018)</td>
<td></td>
<td>307</td>
<td>≥ VGPR</td>
<td>3-yr post-randomization PFS</td>
<td></td>
</tr>
</tbody>
</table>

- IFM-2005: TTP (defined as rate of disease progression or death resulting from any cause) reduced by 58% vs placebo
- Toxicities more common with lenalidomide
- Findings of CALGB 100104 consistent with interim results of randomized IFM-2005-2

CALGB = The Cancer and Leukemia Group B  
IFM = Intergroupe Francophone du Myelome  
ASCT = autologous stem cell transplant  
PFS = progression-free survival  
EFS = event-free survival  
TTP = time to progression  
VGPR = very good partial response

MM-015 MPR Induction Followed by Lenalidomide Maintenance: PFS, OS

<table>
<thead>
<tr>
<th>Median PFS, mos</th>
<th>MPR-R (n = 152)</th>
<th>HR (vs MP)</th>
<th>MPR (n = 153)</th>
<th>HR (vs MP)</th>
<th>MP (n = 154)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>31</td>
<td>0.395</td>
<td>14</td>
<td>0.796</td>
<td>13</td>
</tr>
<tr>
<td>Age 65-75 yrs</td>
<td>NR</td>
<td>0.315</td>
<td>14.7</td>
<td>0.675</td>
<td>12.4</td>
</tr>
</tbody>
</table>

- No significant difference in OS among 3 treatment arms at median follow-up of 30 mos (ITT population)
- Reduced risk of disease progression
  - All patients, 60%; age 65-75 yrs, 69%
  - Landmark analysis: age 65-75 yrs, 65%; > 75 yrs, 70%

PFS = progression-free survival
OS = overall survival
MRP-R = melphalan/prednisone/lenalidomide followed by continuous lenalidomide
HR = hazard ratio
ITT = intent to treat
NR = not reached

Tools to Assess Efficacy / Means of Improving Safety
What Predicts Outcome?

- **Overall survival**
  - Time
  - Large patient numbers

- **Potential surrogate markers of benefit**
  - Depth of response
  - Time to progression
  - Quality of life
Does Response Predict Survival?

- Data conflicting
- Challenges in interpreting available data
  - Benchmarks differ (minimal response, VGPR, CR)
  - Definitions of response differ
  - Until recently, complete remission rare outside of transplantation
  - Time required to ascertain effect

VGPR=very good partial response
CR=complete response
Time to Progression, But Not Response, Predicts Survival

No difference in overall survival – regardless of response

Time to progression predicted overall survival – regardless of initial response

IFM 99-02/99-04 and TT2: VGPR/CR Improves Survival for High Risk Group

- VGPR or better led to improvement in event-free and overall survival
- Benefit seen only in patients with ISS stage II and III disease

CR is Important in High Risk Myeloma

- CR per se does not confer favorable outcome in majority (87%) of patients with MM


CR=complete response
TT2=total therapy 2
GEP=gene expression profiling
Emerging Principles of Treatment

- Suggestion that the depth of response may be a surrogate marker of long-term outcome
- Initial therapy should include lenalidomide and/or bortezomib
- Combination therapy often leads to higher response rates (3 or 4 drugs vs 2)
- Melphalan and prednisone should no longer be used alone
- Continuous therapy leads to longer remission duration
  - Unclear if continuous therapy confers survival benefit
Conclusions

• Treatment paradigms increasingly complex and often incorporate maintenance therapy

• Depth of response may be a surrogate marker for survival in high risk patients

• Although survival is improving, myeloma remains incurable
  – Not a question of if, but when, patients will receive most, if not all, available therapies
The Evolving Role of Managed Care and Oncology Pharmacy Management: Practical Recommendations for a Changing Environment

This activity is jointly sponsored by

Impact Education, LLC

Postgraduate Institute for Medicine

This activity is supported by an education grant from Celgene Corporation
Identifying Indicators of Outcomes and Implementing Treatment Pathways

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Chief Medical Officer
Lovelace Health Plan
Albuquerque, NM
Faculty Disclosure

- The *faculty* reported the following financial relationships or relationships to products or devices they or their spouse/life partner have with commercial interests related to the content of this CME activity:
  - John M. Cruickshank, DO, MBA, CPE has no financial interest/relationships relating to the topic of this activity
Outline

• Managing oncology care
• Treatment guidelines, clinical pathways, and evolution of endpoints
• Multiple myeloma drug formulary design
• Drug distribution via Specialty Pharmacy
Outline

• Managing oncology care
• Treatment guidelines, clinical pathways, and evolution of endpoints
• Multiple myeloma drug formulary design
• Drug distribution via Specialty Pharmacy
Oncology Drug Spending Continues to Increase

Cancer PMPY Rx Trend

<table>
<thead>
<tr>
<th>Year</th>
<th>Spending ($)</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010 (Actual)</td>
<td>$21.8</td>
<td></td>
</tr>
<tr>
<td>2011 (Forecast)</td>
<td>$27.3</td>
<td>↑25.3%</td>
</tr>
<tr>
<td>2012 (Forecast)</td>
<td>$33.9</td>
<td>↑24.0%</td>
</tr>
<tr>
<td>2013 (Forecast)</td>
<td>$41.5</td>
<td>↑23.0%</td>
</tr>
</tbody>
</table>

PMPY=per member per year

Cost of Multiple Myeloma Care is Disproportionately High

- Multiple myeloma (MM) represents a small percentage of all cancers, but its financial burden is disproportionately high
  - Per-patient cost of managing myeloma-related bone disease is 3x higher vs. cost of managing bone metastasis in lung cancer or breast cancer\(^1,2\)
  - Autologous stem cell transplantation adds ~$50,000\(^1,3\)
  - Drug costs can exceed $20,000 per patient\(^1\)
  - Disease-related complications also contribute to the economic burden\(^1\)

- Natural history of smoldering asymptomatic disease progressing to repeating cycle of active myeloma, treatment, relapse, and refractory parameters, requires a long-term, integrated treatment approach\(^4\)

Delivery of Multiple Myeloma Care Remains Fragmented

• Health plans, payers, providers, and pharmacy often aligned in silos with little integration or coordination of care
  – Misalignment of economic incentives between payer, providers, health plans, manufacturers, etc.

• Many care decisions made with no regard for cost and outcomes knowledge
  – Lack of common data platforms to support decision making and patient monitoring

• Wide variation in treatment and treatment outcomes

• Inappropriate drug utilization
  – Non-evidence based and off label use

• Inconsistent drug benefit
  – Medical vs. pharmacy
  – Buy and bill vs. specialty pharmacy

The Zitter Group. Managed Care Oncology Index. Winter 2011.
Multiple Myeloma (Oncology) Benefit Design is Evolving

- MM is increasingly viewed as a chronic disease with long-term cost implications
- Payers and health plans now attempting to manage practice patterns, providers, patients, treatment options, and emerging therapies¹
- Goal is to identify a consistent therapeutic approach, reduce variation, decrease costs, engage providers, and increase quality¹,²

Key Features of Multiple Myeloma Management

- Use of treatment guidelines or pathway programs
  - Allows a balance of clinical, qualitative, and economic features that yield the most cost-effective treatment results
- Multiple myeloma drug formulary design
  - Tiering
    - Medical vs. pharmacy benefit
- Implementation of value-based care
- Drug distribution via Specialty Pharmacy
• Managing oncology care
• Treatment guidelines, clinical pathways, and evolution of endpoints
• Multiple myeloma drug formulary design
• Drug distribution via Specialty Pharmacy
Successful Outcomes Depends on the Collaboration of Providers and Payers

- One key to the successful management of a high-cost disease category is collaboration with the provider network on the development of a clinical pathway
  - Provides shared ownership of treatment outcomes
  - Acts as a vehicle to achieve buy-in from the general network
- Clinical pathways
  - Decrease treatment variability
  - Provide a process for evaluating new therapies and regimens
  - Enables development of a more comprehensive program such as a patient-centered medical home or the accountable care organizations

NCCN Treatment Guidelines Provide Evidence-based Direction to MM Care

• National Comprehensive Cancer Network (NCCN) guidelines outlines standards for the diagnosis, prognosis, treatment, and appropriate follow-up of patients with myeloma
  – Provides comprehensive guidance across the natural history of the disease
  – Identifies primary treatment modalities
  – Includes supporting references, background information, and discussion of ongoing controversies
  – Integrates clinical data and expert judgment to incorporate real-world clinical experience

• Uses an evidence-based approach when evidence is available
  – Evidence-based expert consensus when high-level evidence is lacking

Payers are increasingly insisting that agents and regimens demonstrate improvement in outcomes before their cost will be fully reimbursed.

Overall Survival (OS) has historically been the gold standard endpoint for a new oncology drug approval.

Recently, approval has been based on surrogate endpoints, including objective response rate (ORR), progression-free survival (PFS), disease-free survival (DFS), and time to progression (TTP).

However, surrogate endpoints do not always translate into a survival benefit as long-term data mature.

Use of different endpoints makes the comparison of comparing therapies difficult.

Biomarkers and Surrogate Endpoints

- Confidence in surrogate endpoints may increase as biomarkers are identified that indicate the patients who will respond to a treatment
  - Pairing biomarkers with drugs also has the potential to reduce the risk of adverse events

- As biomarker technology improves, health plans will have the ability to target patients for treatment with specific therapies, predict outcomes, and thus reduce costs
• Managing oncology care
• Treatment guidelines, clinical pathways, and evolution of endpoints
• **Multiple myeloma drug formulary design**
• Drug distribution via Specialty Pharmacy
<table>
<thead>
<tr>
<th>Drug</th>
<th>LOB</th>
<th>Average Member Share per Claim</th>
<th>Max 4th Tier Co-Insurance</th>
<th>Average 3rd Tier Copay</th>
<th>Average 2nd Tier Copay</th>
</tr>
</thead>
<tbody>
<tr>
<td>Revlimid</td>
<td>LSP</td>
<td>33% coinsurance</td>
<td>$350</td>
<td>$70</td>
<td>$36</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Commercial</td>
<td>20% coinsurance</td>
<td>$250</td>
<td>$60</td>
<td>$30</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Medicaid</td>
<td>$0</td>
<td>Exception, no 4th tier</td>
<td>Exception; no 3rd tier</td>
<td>No copay for Salud; $3 copay for SCI</td>
</tr>
<tr>
<td>Thalomid</td>
<td>LSP</td>
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<tr>
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<td>Medical benefit (no copay)</td>
<td>NA</td>
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</table>
Payers, But Not Necessarily Patients, Prefer Oral Agents

- Intravenous (IV) and injected treatments have historically been the primary methods of drug administration in MM
  - Oral therapy is now becoming more prevalent
- Currently, IV treatments are covered under the medical benefit and oral therapies by the pharmacy plan
- Payers tend to prefer oral agents over IV/infused agents
  - Easier to manage access than infused agents
- Patients often prefer an IV/infused therapy because of the cost share associated with oral drugs
  - When an oral treatment is more effective, patients are sometimes forced to make their treatment choice based on cost, rather than efficacy

The Zitter Group. Managed Care Oncology Index. Winter 2011.
Outline

- Managing oncology care
- Treatment guidelines, clinical pathways, and evolution of endpoints
- Multiple myeloma drug formulary design
- Drug distribution via Specialty Pharmacy
Use of Specialty Pharmacy Services and Multiple Myeloma

• Specialty pharmacy shifts distribution to specialty pharmacy vendors and sends payment through the pharmaceutical benefit

• Features of specialty pharmacy
  – Increases payer control over drug utilization and ultimately, costs
  – Ancillary services often include patient education and compliance monitoring

• Potential issues include
  – Increased fragmentation of care between the specialty pharmacy and the oncology care team
  – Logistic procedures may be different for each drug or class of drugs
  – Need for informatics systems that facilitate information flow between specialty pharmacy and the healthcare team, especially since oncology patients have frequently evolving medication regimens

Successful management of MM requires

- Implementation of a broad treatment strategy rather than reliance on one model or tool
- A strategy that supports, rather than hinders, successful payer/physician collaboration
- Evidence-based medical decision making guided by recognized treatment guidelines
- Check points along the full continuum of care to both control costs and enhance quality
- Technology platforms that facilitate communication and the rapid exchange of data
Identifying Indicators of Outcomes and Implementing Treatment Pathways

• Identify Current Gaps and Barriers vs. What is Achievable
  – Knowledge causes? Strategy causes? Performance causes?

• What is the Desired Outcome?
  – List the attributes that are needed

• Recommended Solutions
  – Identify practical next steps
Workshop 1 Recommendations

John M. Cruickshank, DO, MBA, CPE
Chief Medical Officer
Lovelace Health Plan
Workshop 1 Recommendations

Identifying Indicators of Outcomes and Implementing Treatment Pathways

• Current Gaps and Barriers
  – Care outcomes that can differ or are impacted by office infused treatments vs. specialty pharmacy distribution
  – Multiple pathways used by oncology groups across broad geographies
  – Being up to date on most current data because of all the complex and frequently changing guidelines
  – Balancing internal vs. external sources of pharmacoeconomic analyses
  – How to know when treatments are not as effective as end of life nears
Workshop 1 Recommendations

Identifying Indicators of Outcomes and Implementing Treatment Pathways

• Desired Outcome
  – Technology platforms that monitor treatment utilization
  – Ability to have a particular treatment in a position of superiority
  – Shared ownership of outcomes among key stakeholders
  – Episodes of care with bundled payment methods
Workshop 1 Recommendations

Identifying Indicators of Outcomes and Implementing Treatment Pathways

• Practical Next Steps
  – Reduce the number of multiple pathways being used down to a manageable level
  – Implement NCCN guidelines on a consistent basis
  – Use peer-reviewed data to close gaps in between updates to guidelines as needed for payer approval
  – Align pharmacy benefit design with NCCN guidelines to reduce barriers to access for appropriate therapies
The Evolving Role of Managed Care and Oncology Pharmacy Management: Practical Recommendations for a Changing Environment
Workshop 2: Applying Oncology Formulary and Benefit Design Innovations

Objectives

• Enable the use of decision support tools to appropriately invest resources and reduce treatment variability with multiple myeloma therapies

• Construct a benefit design model for oral oncology drugs
Applying Oncology Formulary and Benefit Design Innovations

- Identify Current Gaps and Barriers vs. What is Achievable
  - Knowledge causes? Strategy causes? Performance causes?

- What is the Desired Outcome?
  - List the attributes that are needed

- Recommended Solutions
  - Identify practical next steps
Applying Formulary and Benefit Design Innovations

C. Daniel Mullins, PhD
Professor
Pharmaceutical Health Services Research Department
University of Maryland School of Pharmacy
The **faculty** reported the following financial relationships or relationships to products or devices they or their spouse/life partner have with commercial interests related to the content of this CME activity:

- C. Daniel Mullins, PhD
  - **Consultant Fees**: Amgen, Inc., Bayer Corporation, Bristol-Myers Squibb, GlaxoSmithKline, Mitsubishi, Novartis Pharmaceuticals Corporation, Pfizer, Inc
  - **Fees for Non-CME/CE Services**: Pfizer, Inc
  - **Contracted Research**: Amgen, Inc., Bayer Corporation, Pfizer, Inc
Global Learning Objectives

• Review the current evidence-based data to enable decision making based on indicators of treatment outcomes for multiple myeloma
• Demonstrate the use of CER as a decision support tool to appropriately invest resources and reduce treatment variability with multiple myeloma therapies
• Recommend methods to improve patient outcomes with supportive care for multiple myeloma within a health plan setting
• Evaluate innovative oncology pharmacy benefit models and specialty management services
• Provide accurate and appropriate counsel as part of the managed care treatment team
Outline

• Oncology Comparative Effectiveness Research (CER) as a Decision Support Tool
  – Evidence gaps and uncertainty
  – CER as a tool to fill evidence gaps

• Reimbursement that is Patient-Centered: It’s an Investment in Patients’ Health
  – Translation for patients and their care providers
  – From CER to PCOR

• Improving Patient Outcomes through Patient-Centered Outcomes Research (PCOR)
Outline

• Oncology Comparative Effectiveness Research (CER) as a Decision Support Tool
  – Evidence gaps and uncertainty
  – CER as a tool to fill evidence gaps

• Reimbursement that is Patient-Centered: It’s an Investment in Patients’ Health
  – Translation for patients and their care providers
  – From CER to PCOR

• Improving Patient Outcomes through Patient-Centered Outcomes Research (PCOR)
• National Cancer Care Network (NCCN) estimates $\frac{1}{2}$ to $\frac{3}{4}$ of all cancer drugs used off-label\(^1\)

• Survey of oncologists identified at least 87 distinct oral anticancer therapies used outside labeled indications\(^2\)

• Some argue that useful evidence is simply not being generated so compendia cannot synthesize evidence

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Oncology CER Evidence Gaps
Oncology CER as a Decision Support Tool

- CER evidence requirements
  - Outcomes, NOT surrogates
  - Clinically meaningful
  - Patient-centered outcomes
  - Cost
    - (I don’t care what they say, CER includes costs)

- Translated for patients
- Translated for physicians
- Translated for payers
Oncology CER as a Decision Support Tool

- Guideline concordant care
  - Reduces variability in outcomes
  - Reduces variability in costs
  - Invests in patients’ health & improves health outcomes
  - Reduces wasteful spending by reducing toxicities
Indirect Treatment Comparisons (ITC)

- One study compares Tx A vs. Tx B
- One study compares Tx C vs. Tx B

- Indirect treatment comparison
  - Uses study designs from individual studies
  - Estimates relative value of Tx B vs. Tx C
  - An indirect CER measure
Indirect Treatment Comparisons

- From simple to more complex
  - Naïve indirect comparison
  - Network meta-analysis
  - Mixed treatment comparisons

- Indirect treatment comparison
  - Uses more complete set of data
  - Heterogeneity across trial reduces validity of ITC
Outline

• Oncology Comparative Effectiveness Research (CER) as a Decision Support Tool
  – Evidence gaps and uncertainty
  – CER as a tool to fill evidence gaps

• Reimbursement that is patient-centered: it’s an investment in patients’ health
  – Translation for patients and their care providers
  – From CER to PCOR

• Improving Patient Outcomes through Patient-Centered Outcomes Research (PCOR)
Research Results from a Patient’s Perspective
Research Results from a Payer’s Perspective
Oncology CER to Oncology PCOR

• Patient and payer engagement in study design
  – Comparators
  – Outcomes
  – Understanding of benefits and risks

• Translation of results
  – Applicable
  – Meaningful
Patient-Centered Reimbursement

- Patients have a vital need to access most promising cancer care, but unclear what is most promising
- Oncologists have few treatment options supported by strong evidence
- Payers must make coverage and reimbursement decisions with little reliable evidence
  - Conflicting pressure from multiple sides
- Pharmaceutical industry’s most effective drug therapies are not utilized optimally in the market
Outline

• Oncology Comparative Effectiveness Research (CER) as a Decision Support Tool
  – Evidence gaps and uncertainty
  – CER as a tool to fill evidence gaps

• Reimbursement that is Patient-Centered: It’s an Investment in Patients’ Health
  – Translation for patients and their care providers
  – From CER to PCOR

• Improving Patient Outcomes through Patient-Centered Outcomes Research (PCOR)
Improving Patient Outcomes Through PCOR

- Meaningful outcomes
  - Informed patients
  - Motivated patients

- Applicable evidence
  - Patient-centered decision making
  - Evidence-based decision support tools
PCOR for Multiple Myeloma

- **Treatment effectiveness**
  - Limited to a few trials
  - Need for PROs
  - Use of indirect treatment comparisons

- Need “real world” evidence for newer therapies

- Treatment costs range from minimal to very expensive
Estimating Costs for Multiple Myeloma

- Treatment regimens constantly changing
- Combination therapies are common
- Treatment algorithms affect duration of use, indirectly affecting costs
PCOR for Multiple Myeloma Treatments

- Subgroup of responders
  - Prospective identification of subgroups
- Value varies by treatment population
  - Technologies perhaps not cost-effective for everyone
  - Very cost-effective for the responsive patient
The Evolving Role of Managed Care and Oncology Pharmacy Management:
Practical Recommendations for a Changing Environment
Applying Formulary and Benefit Design Innovations

Jeffrey D. Dunn, PharmD, MBA
Formulary and Contract Manager
SelectHealth, Inc.
• The faculty reported the following financial relationships or relationships to products or devices they or their spouse/life partner have with commercial interests related to the content of this CME activity:
  – Jeffrey D. Dunn, PharmD, MBA
    • Consulting Fees: ChemGenex Pharmaceuticals Ltd., Novartis Pharmaceuticals Corporation, Genentech, Inc., Dendreon Corporation
Objective

• Constructing a benefit design model for oral oncology drugs
Outline

• Current issues and trends in oncology pharmacy management
• Benefit design considerations for oncology pharmacy
• Summary
Outline

• Current issues and trends in oncology pharmacy management
• Benefit design considerations for oncology pharmacy
• Summary
Status of Oncology Treatments Has Changed: Cancer is Now on the Table

Price and value of therapies rarely questioned

Vigorous debate about the overall value* of treatments

Pre-specialty oncology drug era

Specialty oncology drug era

Payers now actively apply payment reforms and quality measurement to cancer services

*clinical, pharmacoeconomic, humanistic, societal, etc.
Plans Need to Find a Balance Between Cost Shifting to Patients and Compliance to Therapy

- Member decision factors
  - Cost share
  - Compliance
  - Efficacy/tolerability

- Benefit design factors
  - Medical vs. pharmacy
  - Copay vs. coinsurance
  - Specialty tiers
Drug and Disease Cost Issues and Trends

- **Drug costs**
  - Drug acquisition
    - Pipeline burgeoning with novel biologic agents
    - Patients are living longer with cancer and there is a shift towards more expensive oral, chronic, daily therapies

- **Administrative burden**
  - Elusiveness of data to determine total costs due to lack of transparency driven by medical/pharmacy benefit designs
    - Patient education/health management programs
    - Management of safety monitoring

- **Total costs need to be evaluated**
  - Direct and indirect
Current Issues in Clinical Management

- Complexity of treatment regimens
  - Levels of evidence
  - Bioethics
    - Curable, improved survival, palliation, occasional response
  - Variable endpoints and outcomes
- Off-label use of drugs
- Lack of consensus among guidelines and pathways with multiple compendia
  - More than just the National Comprehensive Cancer Network (NCCN) or other consensus pathways?
- Patient education and supportive care, particularly end of life counseling
Current Issues in Provider Relations

• Fee schedules and reimbursement
• Location/place of therapy
• Route of administration - incentives
• Support for mandated clinical pathways
• Politics and other network issues
  – Managing oncology networks must be done carefully so that oncologists are not dissatisfied which can affect the plan’s attractiveness to potential clients
Outline

• Current issues and trends in oncology pharmacy management
• Benefit design considerations for oncology pharmacy
• Summary
Current Trends and Issues in Benefit Design

• Medical vs. pharmacy
  – Migration of coverage from medical to pharmacy benefit
  – Expect more drugs covered by the medical benefit to be reviewed by plan pharmacy and therapeutics (P&T) committees

• Plan sponsors have been hesitate to implement changes for oncology
  – Growing interest driven by cost
  – Emerging delivery channels/channel complexity
  – Copay vs. coinsurance
  – Specialty tiers
  – Biosimilars
    • First follow-on biologics or biosimilars may be available mid-decade or earlier
Cancer Treatments are Third Largest Specialty Category Under Pharmacy Benefit

With several novel biologic oncology drugs in the pipeline, cancer may soon have the highest PMPY in the specialty category.

PMPY = per member per year
In 2010, Cancer Treatments Made Up 17% of Specialty Spend Under the Pharmacy Benefit

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<th>Rank</th>
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<th>PMPY spend</th>
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Benefit Design Issues for Oncology Pharmacy

• No single standard in the marketplace
• Most plans use traditional cost-management methods applied to other chronic diseases (e.g., asthma, hypertension)
  – Adaptation of existing tiered formulary methodology
  – Demand management through cost-sharing and other barrier to access
• Most current designs have no consideration on patients total out-of-pocket burden
• Is oncology a “value-based” disease state?

Considerations for Oncology Pharmacy Management Strategies

• Incentive programs
  – Member
  – Physician: differential reimbursement, pay for performance

• Specialty Pharmacy integration

• Coordination/collaboration
  – Data management/widespread use of information technology

• Case management
  – Needs to be more active and educated

• Patient support programs
  – Mandatory?
  – Use of support programs provided by the drug manufacturer?
Benefit Design Changes: Now and in the Future

• Injectable/medical formulary
  – Issues:
    • Timing of adjudication
    • Data captured
    • Data reported – not NCPDP
    • Benefit structure – tiering, etc, ability to scale
  – Needs:
    • Better data
      – Real time adjudication
      – NDCs or more timely and specific codes
  – Examples
    • Oncology, DME
Benefits Need Defined Criteria Detailing When and How Oncology Drugs Will be Used

- Stratify guidelines (eg, NCCN) by costs and survivability rates to define preferred protocols
- Develop a standardized Plan of Care with reimbursement aligned with each preferred protocol
  - Position cognitive services and clinical outcomes as the primary basis for payment
- Encourage use of preferred protocols and products via a tiered oncology benefit paradigm
- Reduce large variations in the late stages of care, particularly during last-effort salvage therapy
  - Offer incentives to providers to discuss treatment options and costs with the patient and family

Charles BM. Oncology 2011: today’s payer strategies and tomorrow’s market innovations. Specialty Pharmacy Times. Published Online: December 5, 2011.
Impact of Patient Cost Sharing on Total Costs

- Oncology drug use largely insensitive to cost sharing
  - High variation in the willingness of patient to pay for care
  - Once treatment is begun, out-of-pocket cost changes have little effect on ongoing treatment\(^1\)
    - Pay often find alternative ways to access medications, e.g., Patient Assistance Programs

- Coinsurance has little effect on total plan sponsor costs unless there is no cap on patient out-of-pocket costs\(^2\)

- Patient adherence declines once out-of-pocket costs reach $1,000\(^2\)
  - However, there is little documentation of poor outcomes due to high out-of-pocket costs

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2. Willey VJ. *Health Aff.* 2008;27:824-834.
Value-Based Benefit Design

• Value-based design is an engagement tool for the consumer, plan sponsor, and provider

• Value-based design uses data to invest in incentives that
  – Change behaviors to improve health, productivity, quality, and financial trends

Value-Based Oncology Pharmacy Management Approach

• Focus is on long-term outcome of improved functional health
• Total cost picture to include indirect costs
• Subsidizes effective services through lowered out-of-pocket exposure
• Varied financial subsidy based on specific disease/clinical scenarios
• Potential for good fit with future trends
  - Outcomes-based contracting
  - Implementation with comparative effectiveness research results (CER)

• Payment/delivery paradigm emphasis is on rewarding value instead of volume
  – Value-based purchasing, shared savings, gain-sharing, bundled payments, capitation, etc.

• Incentives such as the CMS 5-Start Rating System are being implemented to coordinate care among/across providers
  – Beginning in January 2012, plans with ≥ 4 stars receive bonuses along with higher rebates and plans with ≤ 3 stars will be flagged as “low-quality” on the Medicare website

• New structures are promoting actual and virtual integration
  – Accountable Care Organizations (ACO), medical homes, home-based chronic care management, community health teams, health care innovation zones
Features of an ACO

Can provide or manage a continuum of care as a real or virtually integrated delivery system

Are of a sufficient size to support comprehensive performance measurement

Capable of prospectively planning budgets and resource needs

ACO Implications and Opportunities for Cancer Care

Challenges

• Complex nature of cancer care
  • Variety of specialists (in separate silos)
  • Surgeries
  • Imaging
  • Medications

Opportunities

• Reduce variation in quality and cost in “3 big-ticket areas”:
  1. treatment decision-making and therapeutic intervention
  2. identification and management of side effects
  3. delivery of end-of-life palliative care

• Opportunity with cancer centers to tie service payments to benchmarks for quality, outcomes, and patient safety

• Potential savings will be driven by the design of incentive structures
  • The more oncologists are allowed to provide cost-effective care, the more likely they will be to participate
Outline

- Current issues and trends in oncology pharmacy management
- Benefit design considerations for oncology pharmacy
- Summary
Summary

• Historically, little effort expended to manage oncology pharmacy utilization
  – However, recent scientific and therapeutic advances has allowed many cancers to be managed like a chronic condition

• Cancer drugs currently the 3rd largest specialty category under the pharmacy budget

• Payers are challenged to devise a pharmacy benefit that strikes a balance between increasing patient OOP expenses and the risk of non-compliance

• Affordable Care Act is driving benefit design innovations
Applying Oncology Formulary and Benefit Design Innovations

• Identify Current Gaps and Barriers vs. What is Achievable
  – Knowledge causes? Strategy causes? Performance causes?

• What is the Desired Outcome?
  – List the attributes that are needed

• Recommended Solutions
  – Identify practical next steps
Workshop 2 Recommendations

C. Daniel Mullins, PhD
Professor
Pharmaceutical Health Services Research Department
University of Maryland School of Pharmacy
Workshop 2 Recommendations

Applying Oncology Formulary and Benefit Design Innovations

- Current Gaps and Barriers
  - Elusiveness of data
  - Emotional and political disease state
  - Bad benefit design
  - High cost of drugs and cost sharing
  - Employer resistance
  - Oncologist resistance
  - Family/caregiver dynamic and impact on decision making
  - Lack of treatment guidelines
  - Administrative burden
  - IT issues, data coding, processing and analysis
  - Public relations concerns
  - How to address federal mandates
Workshop 2 Recommendations

Applying Oncology Formulary and Benefit Design Innovations

• Desired Outcome
  – Evidence-base
  – Include oncologists in discussions
  – Migration from Medical to Pharmacy
  – Copay vs. coinsurance
  – Specialty tiers
  – Incentive programs directly with providers and potentially members
  – More effective indirect treatment comparisons (ITC)
  – Continued discussions of overall value of treatments
  – Patient-centered reimbursements
  – Value-based benefit design
  – Specific guidelines
  – Cancer pathways
Workshop 2 Recommendations

Applying Oncology Formulary and Benefit Design Innovations

• Practical Next Steps
  – Improve communication and collaboration with oncologists now
  – Tiered oncology benefit model
  – Invest in technology to improve access to data and collaboration
  – Specialty pharmacy integration
  – Patient-centered medical home
  – Case management
  – Patient support groups included in benefit designs
  – Education and disease management programs, using proven models in other disease states
  – Require NDCs or more timely and specific codes
The Evolving Role of Managed Care and Oncology Pharmacy Management: Practical Recommendations for a Changing Environment
Supportive Care Requirements and Coordination of Patient-Centered Care

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Faculty Disclosure

- The **faculty** reported the following financial relationships or relationships to products or devices they or their spouse/life partner have with commercial interests related to the content of this CME activity:
  - Kelly G. Bugos, RN, MS, NP has no financial interest/relationships relating to the topic of this activity
  - Jack Aiello has no financial interest/relationships relating to the topic of this activity
Workshop 3: Supportive Care Requirements and Coordination of Patient-Centered Care

Objectives

• Recommend methods to improve patient outcomes with supportive care for multiple myeloma within a health plan setting

• Implement accurate and appropriate counsel, as part of the treatment team, that will improve patient adherence to treatment recommendations
Supportive Care Requirements and Coordination of Patient-Centered Care

• Identify Current Gaps and Barriers vs. What is Achievable
  – Knowledge causes? Strategy causes? Performance causes?

• What is the Desired Outcome?
  – List the attributes that are needed

• Recommended Solutions
  – Identify practical next steps
Jack’s Story
Supportive Care for Multiple Myeloma

- Bone health and disease
- Hypercalcemia
- Renal Dysfunction
- Pain
- Peripheral Neuropathy
- Infection
- Anemia
- Thrombosis
- Hyperviscosity

Multiple Myeloma-Related Bone Disease

- Most common presenting symptom is bone pain secondary to
  - Compression fractures: spine
  - Pathologic fractures: long bones
  - Osteolytic lesions: punch out
  - Osteoporosis
  - Spinal cord compression
Multiple Myeloma-Related Bone Disease Treatment: Bisphosphonates

- **Action**
  - Inhibit osteoclast activity

- **Result**
  - Gain in bone mass
  - Decreased pain
  - Less bone-related complications and less hypercalcemia

Multiple Myeloma-Related Bone Disease Treatment: Bisphosphonates (cont’d)

• All patients receiving primary myeloma therapy should be given bisphosphonates (category 1)

• Zoledronic acid = pamidronate
  – Reducing skeletal events in randomized trials

• MRC IX trial: Zoledronic Acid >> clodronic acid
  – Reduced skeletal events
  – Reduced mortality by 16%
  – Extended median OS by 5.5 months

• Monitor for renal dysfunction

Osteonecrosis of the Jaw and Bisphosphonate Therapy

Osteonecrosis of the Jaw

Image courtesy of Pamela Hallquist Viale. Reprinted with permission.
Additional Treatments for Multiple Myeloma-Related Bone Disease

- Kyphoplasty
- Vertebroplasty
- Radiation therapy
- Orthopedic intervention
- Physical therapy, exercise
- Good body mechanics, pillows
Hypercalcemia

• Consequence of disease
• Immediate treatment
  – Hydration/furosemide
  – Bisphosphonates- zoledronic acid preferred

Renal Dysfunction

• Precautions
  – Maintain hydration
  – IV contrast
  – NSAIDs

Types of Pain Associated with Multiple Myeloma

Neuropathic vs Musculoskeletal (nociceptive) Pain

- Stabbing
- Burning
- Electric-shock-like
- Tenderness
- Achiness
- Stiffness

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Treatment of Multiple Myeloma-Related Pain

- Analgesics
  - Opioids
    - Side effects: sedation (decreases with time), nausea, constipation, pruritus (antihistamine, lubrication), depression
  - Nonsteroidal anti-inflammatory drugs
    - Caution: renal insufficiency, GI and cardiac complications

- Synergistic agents
  - Amytriptyline, sleep agents, anti-depressants

- Low dose radiation therapy (10-30 Gy)
  - Uncontrolled pain
Neuropathic Pain and Multiple Myeloma

• Most common cause is chemotherapy
• Other causes include routine alcohol use, diabetes, thyroid disorder and cardiovascular disease
• Types of neuropathic pain
  – Sensory
    • Numbness, tingling, decreased sensation or hypersensitivity
  – Motor
    • Difficulties with large muscle actions such as walking
    • Difficulties with fine motor action such as buttoning a shirt, lifting a coin off the table, etc.
Treatment of Neuropathic Pain

• Medications
  – Systemic
    • Anticonvulsants: Gabapentin (Neurontin®), Carbamazepine (Tegretol®)
    • Tricyclic Antidepressants (nortriptyline, amitriptyline)
    • Pregabalin (Lyrica®)
  – Topical
    • Capsaicin (Zostrix)
    • Compounded creams
Vitamins/Supplements Commonly Used for Peripheral Neuropathy

**Vitamin/Supplement**
- Multi-B complex (B1, B6, folic acid)
- Vitamin E
- Vitamin D
- Fish Oils (Omega-3, EPA, DHA)
- Magnesium
- Potassium
- Quinine (Tonic Water)
- Acetyl-L-carnitine
- Alpha Lipoic Acid
- L-Glutamine

**Dosing Regimen**
- B6 50-100 mg/d
- Folic acid 1 mg/d
- 400 IU/d
- 400-800 IU/d
- 1-2 caps (2 grams/d)
- 250 mg bid
- Rx depends on serum level, nutritional sources
  - 1 glass bid
  - 500 mg bid (2 grams/d/ max)
  - 300-1000 mg/d
  - 1 gm tid (max)

Other Interventions for Neuropathic Pain

- Treatment
- Acupuncture
- TENS
- Exercise
- Foot Massage
- Hydrotherapy
- OT/PT
Deconditioning

• **Cause**
  – Steroid myopathy
  – Inactivity

• **Treatment and Prevention**
  – Aerobic exercise
  – Strengthening of proximal muscles
  – Stretching
Causes of Infection in Multiple Myeloma

- High incidence due to immunosuppression from defective production of immunoglobulins
- Further compromised by treatment with systemic chemotherapy
  - Steroids
  - Bortezomib

<table>
<thead>
<tr>
<th>Immunoglobulin</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgG</td>
<td>Coats micro-organisms, allowing for uptake by other immune cells</td>
</tr>
<tr>
<td>IgA</td>
<td>Protects body entrances—tears, saliva, respiratory and gastrointestinal secretions</td>
</tr>
<tr>
<td>IgM</td>
<td>Kills bacteria in blood stream</td>
</tr>
<tr>
<td>IgE</td>
<td>Hypersensitivity and allergy response</td>
</tr>
<tr>
<td>IgD</td>
<td>B lymphocyte regulation and production</td>
</tr>
</tbody>
</table>
Infection: Prophylactic Treatment

Prophylaxis

• Give PCP, herpes, and antifungal prophylaxis if on high-dose dexamethasone

• Give Herpes zoster prophylaxis for patients treated with bortezomib

• Consider bacterial prophylaxis

• Intravenous immunoglobulin therapy should be considered in the setting of recurrent life-threatening infection

• Consider pneumovax and influenza vaccine

• Handwashing

Infection: Prophylactic Treatment During Neutropenia

Prophylaxis during neutropenia

• Bacterial
  – Consider fluoroquinolones

• Fungal
  – Consider fluconazole
    • Neutropenia and mucositis periods

• Viral
  – HSV and VZV
    • Acyclovir, famciclovir, valacyclovir, etc.

HSV = herpes simplex virus
VZV = varicella zoster virus

## Recommended Adult Immunization Schedule: United States, 2012

<table>
<thead>
<tr>
<th>VACCINE GROUP</th>
<th>AGE</th>
<th>19-26 years</th>
<th>27-49 years</th>
<th>50-59 years</th>
<th>60-64 years</th>
<th>≥65 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetanus, diphtheria, pertussis (Td/Tdap)*</td>
<td>Substitute one-time dose of Tdap for Td booster; then boost with Td every 10 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Td booster every 10 years</td>
</tr>
<tr>
<td>Human papillomavirus*</td>
<td>3 doses (females)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Varicella*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2 doses</td>
</tr>
<tr>
<td>Zoster</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1 dose</td>
</tr>
<tr>
<td>Measles, mumps, rubella*</td>
<td>1 or 2 doses</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1 dose</td>
</tr>
<tr>
<td>Influenza*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1 dose annually</td>
</tr>
<tr>
<td>Pneumococcal (polysaccharide)</td>
<td>1 or 2 doses</td>
<td></td>
<td></td>
<td></td>
<td>1 dose</td>
<td></td>
</tr>
<tr>
<td>Hepatitis A*</td>
<td></td>
<td>2 doses</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis B*</td>
<td></td>
<td>3 doses</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meningococcal*</td>
<td></td>
<td>1 or more doses</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

For all persons in this category who meet the age requirements and who lack evidence of immunity (e.g., lack documentation of vaccination or have no evidence of prior infection)

Recommended if some other risk factor is present (e.g., based on medical, occupational, lifestyle, or other indications)

No recommendation

Flu vaccine every year, all ages. For immunocompromised patients, use inactivated form.


*Covered by the Vaccine Injury Compensation Program.
Anemia

MM
- Defined as
  - Hb <10 gm/dL
- Treat disease

NCCN CA and Chemo Guidelines
- If anemia not due to iron deficiency, treatment is RBC or EPO
- **EPO** (dose as per package insert)
  - Risks include
    - VTE
    - Decrease Survival
    - Increase time to tumor progression
  - Benefits include
    - Transfusion avoidance
    - Gradual improvement in fatigue
- **RBCs**
  - Risks include
    - Transfusion reaction
    - CHF
    - Virus transmission
  - Benefits include
    - Rapid improvement of Hb and fatigue

Venous Thromboembolism (VTE) Prevention

Incidence
- Hypercoaguable state
- Immobility from pain, bone disease
- IMiDs

What is the role for prophylaxis?
## VTE Risk Factors

<table>
<thead>
<tr>
<th>MM</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>M Spike &gt; 1.6 gm/dL</td>
<td>Prior h/o VTE</td>
</tr>
<tr>
<td>Progressive Disease</td>
<td>Advancing age</td>
</tr>
<tr>
<td>Treatment with lenalidomide/dexamethasone</td>
<td>Poor Mobility</td>
</tr>
<tr>
<td>Hyperviscosity</td>
<td>Obesity BMI &gt; 35</td>
</tr>
<tr>
<td>Central Venous Catheter use</td>
<td>Smoking</td>
</tr>
<tr>
<td>Major surgery</td>
<td></td>
</tr>
</tbody>
</table>

Thromboprophylaxis by Risk Stratification

- High risk outpatients (>2 risk factors), inpatients
  - Including thalidomide/lenalidomide with dexamethasone (> 480 mg/month)
    - Warfarin (INR 2-3)
    - LMWH (ie, enoxaparin 40 mg/d sq)

- Low risk outpatients (1 risk factor)
  - Aspirin 81-325 mg/d po

Hyperviscosity

- Diagnosed by serum viscosity
- Treat disease
- If symptomatic
  - Plasmapheresis

Nurse Practitioner and Pharmacist Interactions

- System limitations to handle prescriptions by NP/PA
  - 846,000,000 prescriptions/year
  - 14.1 prescriptions filled/pharmacist/hour
- Common reasons for communication
  - Clarification of prescriber ID and insurance authorization
  - Possible drug-drug interactions
  - Cross reactivity

Opportunities to Collaborate

- **Devise safety nets** to help patients adhere to long-term oral therapies
  - Ample monitoring and safety checks
    - Pharmacy reporting of premature or delayed prescription refills
- **Communication: efficient process** to share treatment plan and goals among cancer care team, PCP, specialty pharmacy
- **Integrated patient education and support**
  - EMR after visit instructions
    - Med self management
      - Proper use
      - Who to call for what
      - Handle cytotoxic meds
      - Disposal of cytotoxic meds
- **Evaluation of outcomes, including patient experience**

We must place ourselves in our patients’ shoes and try to understand how these medications fit into their daily lives, so we can have the skills and insight to properly care for them.

*It takes a team and many times the team includes outside pharmacists and nurses.*

-Jody Pelusi, PhD, FNP

LaTour K. *Cure.* 2011:43-47.
Supportive Care Requirements and Coordination of Patient-Centered Care

• Identify Current Gaps and Barriers vs. What is Achievable
  – Knowledge causes? Strategy causes? Performance causes?

• What is the Desired Outcome?
  – List the attributes that are needed

• Recommended Solutions
  – Identify practical next steps
Workshop 3 Recommendations

Kelly G Bugos, RN, NP, MS
Program Manager, Cancer Survivorship Program
Stanford Cancer Center
Workshop 3 Recommendations

Supportive Care Requirements and Coordination of Patient-Centered Care

• Current Gaps and Barriers
  – Financial burden
    • Cost to the patient
    • Constraints and gaps with insurance coverage
  – Emotional distress
  – Pain relief
  – No single-best treatment
Workshop 3 Recommendations

Supportive Care Requirements and Coordination of Patient-Centered Care

• Desired Outcome
  – Long-term survival
  – Best achievable quality of life
  – For the patient to feel a sense of purpose / feel valuable
  – Minimize patient and caregiver stress
Supportive Care Requirements and Coordination of Patient-Centered Care

• Practical Next Steps
  – Start behavioral supportive care at the time of diagnosis
  – Educate the patient and caregiver
Work Plan Summary

Jeffrey D. Dunn, PharmD, MBA
Formulary and Contract Manager
SelectHealth, Inc.
Work Plan Keys

• Consider depth of response as a surrogate marker of long-term outcome
• Use treatment guidelines or pathway programs for a balance of clinical, qualitative, and economic features to yield the most cost-effective treatment results
  – Stratify guidelines (eg, NCCN) by costs and survivability rates to define preferred protocols
  – Develop a standardized Plan of Care with reimbursement aligned with each preferred protocol
Work Plan Keys, cont.

• Utilize Patient-Centered Outcomes Research as decision support tool to reduce treatment variability
  – Reduce large variations in the late stages of care, particularly during last-effort salvage therapy

• Devise safety nets with ample monitoring and safety checks to help patients adhere to long term oral therapies
  – Evaluate outcomes, including patient experience
The Evolving Role of Managed Care and Oncology Pharmacy Management: Practical Recommendations for a Changing Environment
# Multiple Myeloma Disease Snapshot

<table>
<thead>
<tr>
<th>Feature</th>
<th>Myeloma Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Epidemiology (2011)</strong></td>
<td>Incidence: 20,520</td>
</tr>
<tr>
<td></td>
<td>Deaths: 10,610</td>
</tr>
<tr>
<td></td>
<td>Median age at diagnosis: 62 years</td>
</tr>
<tr>
<td><strong>Etiology</strong></td>
<td>Genetic Mutagens</td>
</tr>
<tr>
<td></td>
<td>Antecedent hematologic disease</td>
</tr>
<tr>
<td></td>
<td>Immune disorders</td>
</tr>
<tr>
<td><strong>Stem Cell Defect</strong></td>
<td>Mature plasma cell</td>
</tr>
<tr>
<td><strong>Chromosomal Findings</strong></td>
<td>High risk cytogenetics: t(4;14), t(14;16), -17p13</td>
</tr>
<tr>
<td></td>
<td>Intermediate-risk cytogenetics: -13q</td>
</tr>
<tr>
<td><strong>Additional Prognostic Factors</strong></td>
<td>Serum albumin &lt; 3 g/dL</td>
</tr>
<tr>
<td></td>
<td>B2 microglobulin (B2M) &gt; 4 mg/L</td>
</tr>
<tr>
<td></td>
<td>Creatinine &gt; 2 mg/dL</td>
</tr>
<tr>
<td></td>
<td>Hypoploidy</td>
</tr>
<tr>
<td></td>
<td>ISS stage III</td>
</tr>
<tr>
<td></td>
<td>Platelet count &lt; 150,000/mm3</td>
</tr>
<tr>
<td></td>
<td>Bone marrow plasma cells (BMPC) &gt; 50%</td>
</tr>
<tr>
<td></td>
<td>Relapse &lt; 12 months from HSCT or first-line therapy</td>
</tr>
<tr>
<td></td>
<td>Plasma cell labeling index (PCLI) &gt; 3%</td>
</tr>
<tr>
<td></td>
<td>ECOG PS 3-4</td>
</tr>
<tr>
<td><strong>Staging</strong></td>
<td>ISS/Durie-Salmon Criteria</td>
</tr>
<tr>
<td><strong>Disease Characteristics (all are incurable)</strong></td>
<td>MGUS: No active therapy required in most cases</td>
</tr>
<tr>
<td></td>
<td>Smoldering: May not require therapy for extended periods</td>
</tr>
<tr>
<td></td>
<td>Symptomatic myeloma: Elevated monoclonal protein and CRAB criteria or organ damage present—requires treatment</td>
</tr>
<tr>
<td></td>
<td>Prognosis is variable based on molecular, genetic, and individual factors</td>
</tr>
<tr>
<td></td>
<td>Risk-adapted treatment selection is recommended</td>
</tr>
<tr>
<td><strong>Clinical Presentation</strong></td>
<td>Anemia (73%)</td>
</tr>
<tr>
<td></td>
<td>Bone pain (58%)</td>
</tr>
<tr>
<td></td>
<td>Renal insufficiency (19%)</td>
</tr>
<tr>
<td></td>
<td>Hypercalcemia (32%)</td>
</tr>
<tr>
<td></td>
<td>Fatigue (32%)</td>
</tr>
<tr>
<td></td>
<td>Infections</td>
</tr>
<tr>
<td></td>
<td>Lytic lesions (66%)</td>
</tr>
<tr>
<td></td>
<td>Peripheral neuropathy (5%)</td>
</tr>
<tr>
<td><strong>Indication to Treat</strong></td>
<td>Symptomatic myeloma: elevated monoclonal protein and CRAB criteria or organ damage present</td>
</tr>
<tr>
<td></td>
<td>C: Calcium &gt; 10.5 mg/dL</td>
</tr>
<tr>
<td></td>
<td>R: Renal insufficiency (SCr &gt; 2 mg/dL)</td>
</tr>
<tr>
<td></td>
<td>A: Anemia Hgb &lt; 10 g/dL</td>
</tr>
<tr>
<td></td>
<td>B: Bone lesions or osteoporosis</td>
</tr>
<tr>
<td></td>
<td>Early treatment for smoldering myeloma is being investigated in clinical trials</td>
</tr>
<tr>
<td><strong>Key Concepts for Effective Treatment</strong></td>
<td>Novel agents have demonstrated significant activity in newly diagnosed relapsed and refractory MM</td>
</tr>
<tr>
<td></td>
<td>Eligibility for autologous PBSCT should be evaluated at the time of diagnosis</td>
</tr>
<tr>
<td></td>
<td>Sequential administration of novel therapies can potentially prolong survival</td>
</tr>
<tr>
<td></td>
<td>Maintenance therapy following Auto-HCT is being investigated in clinical trials</td>
</tr>
<tr>
<td></td>
<td>Chromosomal abnormalities have prognostic value</td>
</tr>
<tr>
<td></td>
<td>Aggressive management of bone disease is central to QOL</td>
</tr>
<tr>
<td></td>
<td>Concurrent management of disease- and treatment-related adverse events is essential to effective therapy</td>
</tr>
<tr>
<td><strong>FDA-Approved Therapies</strong></td>
<td>Bortezomib</td>
</tr>
<tr>
<td></td>
<td>Thalidomide</td>
</tr>
<tr>
<td></td>
<td>Melphalan</td>
</tr>
<tr>
<td></td>
<td>Dexamethasone</td>
</tr>
<tr>
<td></td>
<td>Pegylated liposomal Doxorubicin</td>
</tr>
<tr>
<td></td>
<td>Lenalidomide</td>
</tr>
<tr>
<td><strong>In Clinical Trials</strong></td>
<td>Carfilzomib</td>
</tr>
<tr>
<td></td>
<td>Elotuzumab</td>
</tr>
<tr>
<td></td>
<td>Pomalidomide</td>
</tr>
<tr>
<td><strong>Key Supportive Care Concerns</strong></td>
<td>Myelosuppression</td>
</tr>
<tr>
<td></td>
<td>Renal insufficiency</td>
</tr>
<tr>
<td></td>
<td>Thromboembolism</td>
</tr>
<tr>
<td></td>
<td>Infections</td>
</tr>
<tr>
<td></td>
<td>Neuropathy</td>
</tr>
<tr>
<td></td>
<td>Osteopenia</td>
</tr>
</tbody>
</table>

Multiple Myeloma Treatment: Historical Timeline

1968  Melphalan/prednisone

1980s  Autologous stem cell transplantation

1990s  Intravenous bisphosphonates: reduction skeletal events

1998  First data on thalidomide

2004  FDA approval bortezomib

2006  FDA approval of lenalidomide and thalidomide

2012  2 drugs under FDA review, numerous other agents and combinations being investigated

Survival Improving
## Multiple Myeloma Staging Systems

<table>
<thead>
<tr>
<th>Stage</th>
<th>Durie-Salmon Staging System</th>
<th>International Staging System</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Hemoglobin &gt; 10 g/dL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Calcium normal or ≤ 12 mg/dL</td>
<td>β₂M ≤ 3.5 g/dL and albumin ≥ 3.5 g/dL</td>
</tr>
<tr>
<td></td>
<td>Normal skeletal survey or solitary plasmacytoma</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Low M-protein production</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• IgG &lt; 5 g/dL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• IgA &lt; 3 g/dL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bence-Jones protein &lt; 4 g/24 h</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>Neither stage I nor stage III</td>
<td>Neither stage I nor stage III</td>
</tr>
<tr>
<td>III</td>
<td>One of the following</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Hemoglobin &lt; 8.5 g/dL</td>
<td>β₂M ≥ 5.5 g/dL</td>
</tr>
<tr>
<td></td>
<td>• Calcium &gt; 12 mg/dL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Multiple lytic bone lesions</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• High M-protein component</td>
<td></td>
</tr>
<tr>
<td></td>
<td>o IgG &gt; 7 g/dL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>o IgA &gt; 5 g/dL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>o Bence-Jones protein &gt; 12 g/24 h</td>
<td></td>
</tr>
</tbody>
</table>

Goals of Therapy

• Achieve prompt control of the disease
  – Address pain and disease-related symptoms
  – Control disease activity
  – Preserve performance status and quality of life
• Asymptomatic disease
  – Observe and monitor regularly
• Standard-risk disease
  – Complete response or very good partial response
• Transplant-eligible, high-risk patients
  – Achieving a complete response


Key Principles for Treatment of Multiple Myeloma

<table>
<thead>
<tr>
<th>Key Principle</th>
<th>Clinical Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Criteria for initiation of active therapy</td>
<td>Confirmed diagnosis of multiple myeloma (CRAB)</td>
</tr>
<tr>
<td></td>
<td>Recent trials have evaluated early treatment of smoldering myeloma</td>
</tr>
<tr>
<td>Identify need for immediate intervention</td>
<td>Severe hypercalcemia</td>
</tr>
<tr>
<td></td>
<td>Acute renal failure</td>
</tr>
<tr>
<td></td>
<td>Cord compression</td>
</tr>
<tr>
<td></td>
<td>Severe pain or impending fracture</td>
</tr>
<tr>
<td>Determine transplant eligibility</td>
<td>Performance status (good vs poor)</td>
</tr>
<tr>
<td></td>
<td>Comorbidities</td>
</tr>
<tr>
<td></td>
<td>Age</td>
</tr>
<tr>
<td></td>
<td>Lifestyle and caregiver support</td>
</tr>
<tr>
<td></td>
<td>Insurance</td>
</tr>
<tr>
<td>Individualized treatment selection</td>
<td>Disease characteristics – favorable or poor prognostic findings</td>
</tr>
<tr>
<td></td>
<td>Individual characteristics</td>
</tr>
<tr>
<td></td>
<td>Current treatment options and level of evidence</td>
</tr>
<tr>
<td>Consistent assessment of response</td>
<td>International Myeloma Working Group Response Criteria (IMWG)</td>
</tr>
<tr>
<td></td>
<td>International Myeloma Foundation (IMF) Response Criteria</td>
</tr>
</tbody>
</table>

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**Treatment Response Criteria**

<table>
<thead>
<tr>
<th>Category</th>
<th>EBMT Criteria</th>
<th>IMWG Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete Response (CR)</td>
<td>• No M protein detected in the serum or urine by IFE for ≥ 6 weeks&lt;br&gt;• ≤ 5% BMPC</td>
<td>• Negative serum and urine IFE&lt;br&gt;• Resolution of plasmacytomas&lt;br&gt;• ≤ 5% BMPC</td>
</tr>
<tr>
<td>Stringent CR (sCR)</td>
<td>Not used</td>
<td>• CR plus&lt;br&gt;• Normal FLC ratio&lt;br&gt;• No evidence of clonal BMPC by immunohistochemistry or FISH</td>
</tr>
<tr>
<td>Very Good Partial Response (VGPR)</td>
<td>Not used</td>
<td>• Serum and urine M protein detectable by IFE but not by SPEP&lt;br&gt;Or&lt;br&gt;• ≥ 90% reduction in serum M protein plus urine M protein &lt; 100 mg/24 h</td>
</tr>
<tr>
<td>Partial Response (PR)</td>
<td>• &gt; 50% reduction in serum M protein and/or 90% reduction in urine FLC excretion or reduction to &lt; 200 mg per 24 hours for 6 weeks</td>
<td>• 50% reduction in serum M protein and reduction in 24-hour urine protein by ≥ 90% or to &lt; 200 mg/24 h&lt;br&gt;• If immeasurable M protein:&lt;br&gt;  o ≥ 50% reduction in difference between involved and uninvolved FLC&lt;br&gt;• ≥ 50% reduction in the size of plasmacytoma is present at baseline</td>
</tr>
</tbody>
</table>

EBMT = European Group for Bone Marrow Transplantation  
IMWG = International Myeloma Working Group Response Criteria  
BMPC = bone marrow plasma cells  
IFE = immunofixation electrophoresis  
FLC = free light chains  
FISH = fluorescence in situ hybridization  
SPEP = protein electrophoresis with immunofixation
Sources of Multiple Myeloma Treatment Guidelines

- National Comprehensive Cancer Network (NCCN) guidelines
  - Disease treatment
  - Supportive care

- American Society of Clinical Oncology (ASCO) guidelines
  - Supportive care

Current Multiple Myeloma Treatment Adapted From the NCCN Guidelines

NCCN=National Comprehensive Cancer Network.
Tx=treatment.
TTP=time to progression.
MP=melphalan/prednisone.
VAD=vincristine/doxorubicin/dexamethasone.
DVD=PLD/vincristine/dexamethasone.
Dex=dexamethasone.
PLD=pegylated liposomal doxorubicin.
SCT=stem cell transplantation.

## Agents Approved for Multiple Myeloma (MM)

<table>
<thead>
<tr>
<th>FDA Approval</th>
<th>Drug</th>
<th>Trade Name</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>1962</td>
<td>Melphalan</td>
<td>Alkeran</td>
<td>Palliative treatment of MM</td>
</tr>
<tr>
<td>May 2003</td>
<td>Bortezomib</td>
<td>Velcade</td>
<td>Patients with relapsed MM</td>
</tr>
<tr>
<td>May 2006</td>
<td>Thalidomide</td>
<td>Thalomid</td>
<td>In combination with dexamethasone for the treatment of patients with newly diagnosed MM</td>
</tr>
<tr>
<td>June 2006</td>
<td>Lenalidomide</td>
<td>Revlimid</td>
<td>In combination with dexamethasone for the treatment of MM in patients who have received at least 1 prior therapy</td>
</tr>
<tr>
<td>May 2007</td>
<td>Pegylated liposomal doxorubicin</td>
<td>Doxil</td>
<td>In combination with bortezomib in patients who have not previously received bortezomib and have received at least 1 prior therapy.</td>
</tr>
<tr>
<td>June 2008</td>
<td>Bortezomib</td>
<td>Velcade</td>
<td>Patients with newly diagnosed MM</td>
</tr>
</tbody>
</table>

### Adverse Events and Care Management with Common Agents Used to Treat Multiple Myeloma

#### Bortezomib

<table>
<thead>
<tr>
<th>Drug Profile</th>
<th>Common Adverse Events</th>
<th>Care Management</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Class:</strong> Proteosome Inhibitor&lt;br&gt;<strong>Indication:</strong> newly diagnosed MM&lt;br&gt;<strong>Dosing:</strong> 1.3 mg/m² twice weekly—variable schedules based on protocol</td>
<td>Peripheral neuropathy&lt;br&gt;Overall: 39%&lt;br&gt;Grade ≥ 3: 12%</td>
<td>Patient education/early detection&lt;br&gt;Monitor at each visit&lt;br&gt;Dose adjustment&lt;br&gt;Grade 1 with pain or grade 2: reduce dose to 1.0 mg/m²&lt;br&gt;Grade 2 with pain or grade 3: Hold until toxicity resolves—resume at 0.7 mg/m²&lt;br&gt;Grade 4: discontinue bortezomib&lt;br&gt;Safety evaluation&lt;br&gt;Symptom control with pharmacologic interventions</td>
</tr>
<tr>
<td>Asthenia&lt;br&gt;(fatigue, malaise, weakness)&lt;br&gt;Overall: 64%&lt;br&gt;Grade ≥ 3: 16%</td>
<td>Counsel patient&lt;br&gt;Avoid concurrent meds causing asthenia&lt;br&gt;Balance rest and activity</td>
<td></td>
</tr>
<tr>
<td>Myelosuppression&lt;br&gt;Thrombocytopenia:&lt;br&gt;Overall: 36%&lt;br&gt;Grade ≥ 3: 29%&lt;br&gt;Neutropenia:&lt;br&gt;Overall: 17%&lt;br&gt;Grade ≥ 3: 12%</td>
<td>Cyclical with lowest levels on day 11 of cycle&lt;br&gt;Consistent pattern that is not cumulative&lt;br&gt;Hold if platelets &lt; 25,000/µL; reintroduce at 25% lower dose with recovery</td>
<td></td>
</tr>
<tr>
<td>Diarrhea&lt;br&gt;Overall: 52%&lt;br&gt;Grade ≥ 3: 8%</td>
<td>Adequate hydration&lt;br&gt;Monitor electrolytes&lt;br&gt;Diet modification to avoid aggravating foods/beverages&lt;br&gt;Use of antidiarrheal agents&lt;br&gt;Perineal care if indicated</td>
<td></td>
</tr>
<tr>
<td>Hypotension&lt;br&gt;Overall: 13%&lt;br&gt;Grade ≥ 3: 3%</td>
<td>Baseline evaluation of risk factors&lt;br&gt;May require adjustment of antihypertensive medications&lt;br&gt;Increase oral fluids, additional IV hydration may reduce severity</td>
<td></td>
</tr>
<tr>
<td>Varicella zoster (13%-20% risk)</td>
<td>Prophylactic antiviral therapy is recommended for patients on continued treatment&lt;br&gt;Careful monitoring for any early dermatomal pain, skin rash</td>
<td></td>
</tr>
</tbody>
</table>

## Adverse Events and Care Management with Common Agents Used to Treat Multiple Myeloma

### Dexamethasone/Prednisone

<table>
<thead>
<tr>
<th>Class: Steroid</th>
<th>Indication: all active MM protocols</th>
<th>Dosing: variable based on regimen</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Common Adverse Events</th>
<th>Care Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunosuppression</td>
<td>May require PCP and antiviral prophylaxis</td>
</tr>
<tr>
<td></td>
<td>Careful monitoring for atypical infections</td>
</tr>
<tr>
<td>Constitutional symptoms</td>
<td>Taper schedule may reduce severity of “let down”</td>
</tr>
<tr>
<td>“let down,” flushing, sweating, sleep disturbance</td>
<td>Taking the medication in the morning with food may improve tolerance</td>
</tr>
<tr>
<td>Weight gain, cushingoid appearance</td>
<td>Nutritional consult</td>
</tr>
<tr>
<td></td>
<td>Counseling for the patient—symptoms are reversible once steroids are discontinued but may require several weeks or months</td>
</tr>
<tr>
<td>Personality/mood alterations</td>
<td>Monitor carefully</td>
</tr>
<tr>
<td></td>
<td>Counseling for patient and family as needed</td>
</tr>
<tr>
<td></td>
<td>Discontinue for any signs of suicidal or homicidal ideation</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>Take with food</td>
</tr>
<tr>
<td></td>
<td>Use of H₂ blocker or PPI may reduce symptoms of gastritis</td>
</tr>
<tr>
<td>Myopathy</td>
<td>Baseline and ongoing assessment</td>
</tr>
<tr>
<td></td>
<td>Differentiate lower-extremity weakness due to steroid myopathy vs cord compression</td>
</tr>
<tr>
<td></td>
<td>Physical therapy consultation</td>
</tr>
<tr>
<td></td>
<td>Strengthening exercises</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>Baseline and ongoing evaluation</td>
</tr>
<tr>
<td></td>
<td>Of particular importance in patients who are diabetic or who have a strong family history of diabetes</td>
</tr>
<tr>
<td></td>
<td>May require initiating antidiabetic medication or adjustment of existing regimen</td>
</tr>
<tr>
<td></td>
<td>Nutritional consultation</td>
</tr>
<tr>
<td>Acneiform rash</td>
<td>Antibacterial wash</td>
</tr>
<tr>
<td>Oral candidiasis</td>
<td>Regular oral assessment</td>
</tr>
<tr>
<td></td>
<td>Institute oral care regimen: mucolytic and neutralizing rinses</td>
</tr>
<tr>
<td></td>
<td>May require antifungal agent</td>
</tr>
<tr>
<td>Blurred vision, cataracts</td>
<td>Baseline evaluation</td>
</tr>
<tr>
<td></td>
<td>Regular ophthalmic evaluation</td>
</tr>
</tbody>
</table>

## Adverse Events and Care Management with Common Agents Used to Treat Multiple Myeloma

### Lenalidomide

<table>
<thead>
<tr>
<th>Class:</th>
<th>Immunomodulatory Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Indication:</strong></td>
<td>newly diagnosed patients when combined with dexamethasone</td>
</tr>
<tr>
<td><strong>Dosing:</strong></td>
<td>25 mg PO daily 21/28 days</td>
</tr>
<tr>
<td>Dose modifications for renal impairment</td>
<td>Variable dosing in combination regimens</td>
</tr>
</tbody>
</table>

### Common Adverse Events

<table>
<thead>
<tr>
<th>Event</th>
<th>Care Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myelosuppression Neutropenia 28% (21% grade 3-4) Anemia 24% (8% grade 3-4) Thrombocytopenia 17% (10% grade 3-4)</td>
<td>Monitor CBC, diff, platelet count every 1-2 weeks for the first 12 weeks and monthly thereafter Hold drug or reduce dose based on symptomatic cytopenias Transfusions and growth factors</td>
</tr>
</tbody>
</table>

### Renal Impairment (CrCl)

<table>
<thead>
<tr>
<th>Clearance</th>
<th>Lenalidomide Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate (30 to &lt; 60 mL/min)</td>
<td>10 mg qd</td>
</tr>
<tr>
<td>Severe (&lt; 30 mL/min, not requiring dialysis)</td>
<td>15 mg q 48 h</td>
</tr>
<tr>
<td>ESRD (&lt; 30 mL/min, requiring dialysis)</td>
<td>5 mg qd following dialysis on following day</td>
</tr>
</tbody>
</table>

### Thromboembolic events

<table>
<thead>
<tr>
<th>Event</th>
<th>Care Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>DVT—7% PE—3%</td>
<td>More common in combination with high-dose dexamethasone or doxorubicin Screen patients for risk factors Institute baby ASA vs full anticoagulation based on risk assessment</td>
</tr>
</tbody>
</table>

### Rash (morbilliform)

<table>
<thead>
<tr>
<th>Event</th>
<th>Care Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generally self-limiting Treatment symptomatically with antihistamines Careful evaluation for potential severe drug reactions (rare)</td>
<td></td>
</tr>
</tbody>
</table>

### Gastrointestinal

<table>
<thead>
<tr>
<th>Event</th>
<th>Care Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constipation 30% Diarrhea 20%</td>
<td>Usually mild—less common than with thalidomide Adequate hydration Modification of diet Increased fluids Use of laxatives and stool softeners Usually mild intermittent cramping or diarrhea Modification of diet Use of antidiarrheal agents Rarely requires dose reduction</td>
</tr>
</tbody>
</table>

### Secondary malignancies

<table>
<thead>
<tr>
<th>Event</th>
<th>Care Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lenalidomide maintenance after HCT has been associated with small number of secondary malignancies in patients treated with cyclophosphamide, etoposide, cisplatin—incidence similar to SEER data for patients age 60-85</td>
<td></td>
</tr>
</tbody>
</table>

---

Adverse Events and Care Management with Common Agents Used to Treat Multiple Myeloma

**Pegylated Liposomal Doxorubicin (PLD)**

<table>
<thead>
<tr>
<th>Class: Anthracycline</th>
<th>Common Adverse Events</th>
<th>Care Management</th>
</tr>
</thead>
</table>
| Indication: in combination with bortezomib for MM patients who have not previously received bortezomib and who have had at least 1 previous therapy | Most common adverse events in MM patients (> 20%):  
- Asthenia, fatigue, fever, anorexia, nausea, vomiting, stomatitis, diarrhea, constipation, hand-foot syndrome, rash, neutropenia, thrombocytopenia, and anemia | Monitoring of blood counts with each cycle—more frequently if cytopenias are present  
Premedicate for nausea and vomiting  
Institute oral care regimen  
Baseline evaluation for hand-foot syndrome—  
instruct patient to avoid aggravating factors (friction, hot liquids, tight shoes)  
Stomatitis is generally mild and responds to oral care regimen |
| Dosing: 30 mg/m²—given with bortezomib on day 4 of a 21-day cycle—IV over 1 hour with initial titration of the rate (start at 1 mg/min—then increase after 15 minutes if no reaction) | Black box warning:  
- Myocardial damage, acute infusion-related reactions, myelosuppression, hepatic dysfunction | Careful cardiovascular screening  
Regular monitoring of hepatic enzymes  
Institute oral care regimen  
Avoid friction to reduce severity of hand-foot syndrome |

**Melphalan—Oral**

<table>
<thead>
<tr>
<th>Class: Alkylating Agent</th>
<th>Common Adverse Events</th>
<th>Care Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indication: use in non-transplant-eligible MM patients for initial therapy</td>
<td>Myelosuppression</td>
<td>Myelosuppression may be delayed with prolonged recovery</td>
</tr>
</tbody>
</table>
| Dosing: variable dosing based on regimen | Diarrhea | Usually mild intermittent cramping or diarrhea  
Modification of diet  
Use of antidiarrheal agents  
Rarely requires dose reduction |
Adverse Events and Care Management with Common Agents Used to Treat Multiple Myeloma

<table>
<thead>
<tr>
<th>Common Adverse Events</th>
<th>Care Management</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Peripheral neuropathy</strong></td>
<td>Patient education/early detection</td>
</tr>
<tr>
<td>Mild: 85%</td>
<td>Monitor at each visit</td>
</tr>
<tr>
<td>Severe: 3%-5%</td>
<td>Dose adjustment</td>
</tr>
<tr>
<td><strong>Somnolence</strong></td>
<td>Grade 1: Continue with 50% dose reduction</td>
</tr>
<tr>
<td>Mild: 75%</td>
<td>Grade 2: Hold until PN has resolved, continue with 50% dose reduction</td>
</tr>
<tr>
<td>Severe: 5%-10%</td>
<td>Symptom control with pharmacologic interventions</td>
</tr>
<tr>
<td><strong>Skin rash</strong></td>
<td>PM dosing</td>
</tr>
<tr>
<td>Mild: 45%</td>
<td>Avoid concurrent meds causing drowsiness</td>
</tr>
<tr>
<td><strong>Thromboembolic complications (DVT/PE)</strong></td>
<td>Dose adjustment</td>
</tr>
<tr>
<td>(Monotherapy: 1%-3%</td>
<td>Escalate dose gradually</td>
</tr>
<tr>
<td>With dex: 10%-12%</td>
<td>Anticoagulation recommended</td>
</tr>
<tr>
<td><strong>Myelosuppression (neutropenia)</strong></td>
<td>Monitor coagulation assays</td>
</tr>
<tr>
<td>15%-25%</td>
<td>Do not initiate if ANC &lt; 750/mm^3</td>
</tr>
<tr>
<td><strong>Gastrointestinal (constipation)</strong></td>
<td>If ANC &lt; 500/mm^3, withhold thalidomide until</td>
</tr>
<tr>
<td>Mild: 80%-90%</td>
<td>ANC &gt; 500/mm^3 and restart at 50% lower dose</td>
</tr>
<tr>
<td>Severe: 5%</td>
<td><strong>Bowel regimen (call office if no BM in 3 days)</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Increase fluid and fiber intake</strong></td>
</tr>
</tbody>
</table>

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## Lenalidomide: Suggested Dose Modifications

### Dose Adjustments for Thrombocytopenia in Multiple Myeloma (MM) Patients

<table>
<thead>
<tr>
<th>When Platelets</th>
<th>Recommended Course</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fall to &lt; 30,000/μL</td>
<td>Interrupt lenalidomide treatment, follow CBC weekly</td>
</tr>
<tr>
<td>Return to ≥ 30,000/μL</td>
<td>Restart lenalidomide at 15 mg daily</td>
</tr>
<tr>
<td>For each subsequent drop &lt; 30,000/μL</td>
<td>Interrupt lenalidomide treatment</td>
</tr>
<tr>
<td>Return to ≥ 30,000/μL</td>
<td>Resume lenalidomide at 5 mg less than previous dose. Do not dose below 5 mg daily</td>
</tr>
</tbody>
</table>

### Dose Adjustments for Neutropenia in MM Patients

<table>
<thead>
<tr>
<th>When Neutrophils</th>
<th>Recommended Course</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fall to &lt; 1,000/μL</td>
<td>Interrupt lenalidomide treatment, add G-CSF, follow CBC weekly</td>
</tr>
<tr>
<td>Return to ≥ 1,000/μL and neutropenia is the only toxicity</td>
<td>Resume lenalidomide at 25 mg daily</td>
</tr>
<tr>
<td>Return to ≥ 1,000/μL and if other toxicity</td>
<td>Resume lenalidomide at 15 mg daily</td>
</tr>
<tr>
<td>For each subsequent drop &lt; 1,000/μL</td>
<td>Interrupt lenalidomide treatment</td>
</tr>
<tr>
<td>Return to ≥ 1,000/μL</td>
<td>Resume lenalidomide at 5 mg less than previous dose. Do not dose below 5 mg daily</td>
</tr>
</tbody>
</table>

Please see full prescribing information, including boxed warnings, contraindications, precautions, and adverse reactions.

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# Starting Dose Adjustment for Renal Impairment (Cockcroft-Gault CLcr)

## Multiple Myeloma and Myelodysplastic Syndromes

<table>
<thead>
<tr>
<th>Category</th>
<th>Renal function</th>
<th>Dose: Multiple Myeloma</th>
<th>Dose: MDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate Renal Impairment</td>
<td>&lt; 60 mL/min/ 30 ≤ CLcr</td>
<td>10 mg every 24 hours</td>
<td>5 mg every 24 hours</td>
</tr>
<tr>
<td>Severe Renal Impairment (not requiring dialysis)</td>
<td>CLcr &lt; 30 mL/min</td>
<td>15 mg every 48 hours</td>
<td>5 mg every 48 hours</td>
</tr>
<tr>
<td>End Stage Renal Disease (requiring dialysis)</td>
<td>CLcr &lt; 30 mL/min</td>
<td>5 mg once daily. On dialysis days the dose should be administered following dialysis</td>
<td>5 mg every 24 hours dialysis 3 times a week following dialysis</td>
</tr>
</tbody>
</table>

After initiation of lenalidomide (REVLIMID®) therapy, subsequent lenalidomide (REVLIMID®) dose modification should be based on individual patient treatment tolerance.
Bortezomib: Suggested Dose Modifications

Dose Modification for the Management of Peripheral Neuropathy

<table>
<thead>
<tr>
<th>Severity of Peripheral Neuropathy Signs/Symptoms</th>
<th>Modification of Dose and Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1 (paresthesia, weakness, and/or loss of reflexes without pain or loss of function)</td>
<td>No action</td>
</tr>
<tr>
<td>Grade 1 with pain or grade 2 (interfering with function but not with activities of daily living)</td>
<td>Reduce bortezomib to 1.0 mg/m²</td>
</tr>
<tr>
<td>Grade 2 with pain or grade 3 (interfering with activities of daily living)</td>
<td>Withhold bortezomib therapy until toxicity resolves. When toxicity resolves, reinitiate with a reduced dose of bortezomib at 0.7 mg/m² and change treatment schedule to once per week</td>
</tr>
<tr>
<td>Grade 4 (sensory neuropathy that is disabling, or motor neuropathy that is life-threatening or leads to paralysis)</td>
<td>Discontinue bortezomib</td>
</tr>
</tbody>
</table>

Symptoms may improve or return to baseline in some patients on discontinuation of Bortezomib

Dose Modification Recommendations for Adverse Events, Excluding Peripheral Neuropathy

- At the onset of grade 3 nonhematologic toxicities, therapy with bortezomib should be held
- At the onset of grade 4 hematologic toxicities, therapy with bortezomib should be held
- Once toxicity has resolved, bortezomib may be reinitiated at a 25% reduced dose
  - 1.3 mg/m² per dose reduced to 1.0 mg/m² per dose
  - 1.0 mg/m² per dose reduced to 0.7 mg/m² per dose
- Decreased neuropathy, nausea, and diarrhea seen when dose is decreased

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### Potential Clinical and Economic Outcomes of Selected Scientific Developments for Multiple Myeloma

<table>
<thead>
<tr>
<th>Scientific Development</th>
<th>Key Elements</th>
<th>Potential Economic or Clinical Impact</th>
<th>Implications for Clinicians</th>
</tr>
</thead>
</table>
| Implementation of a continuum approach to treatment selection using a risk-adapted treatment model for MM | • Cytogenetics  
• Molecular analysis  
• ISS staging  
• Serum-free light chain analysis  
• Age and ethnicity  
• Eligibility for stem cell transplant and timing of the transplant(s)  
• Duration of complete remission from treatment initiation | • Patient-specific treatment selection with potential to improve clinical outcomes by utilizing the most beneficial treatment option early in the course of disease  
• Reduction in use of ineffective therapies with associated short-term and cumulative toxicities  
• Preservation of future treatment options  
• Refined utilization of diagnostics and therapeutics | • Requires familiarity and implementation of the most recent clinical trials data and practice guidelines  
• Risk-based criteria for initiation of active therapies  
• Comprehensive diagnostics at the time of diagnosis are essential to effective risk stratification and treatment selection with application of the continuum approach  
• Identification of transplant eligibility at the time of diagnosis allows adapted therapies feasible in the older adult  
• Opportunities for refinement of cost and outcomes analysis of ongoing clinical evaluation, including  
• Development of monitoring guidelines specific to MM based on the continuum approach  
• Frequency of radiology and laboratory monitoring  
• Impact on treatment  
• Inclusion of diagnostic analysis in clinical trials with consideration of postmarketing recommendations for safety monitoring |
| Minimizing treatment related toxicity: Consensus statements on side effect management for novel agents in the treatment of MM from the International Myeloma Foundation Nurse Leadership Board | Management of myelosuppression  
*Micelli et al, 2008*  | • Reduction in treatment delay or discontinuation  
• Reduction in hospitalization due to neutropenic fevers  
• Improved patient satisfaction | • Requires familiarity with the potential severity of treatment related toxicities, dose and schedule modifications, and prevention strategies  
• Appropriate use of colony stimulating factors with consideration of safety  
• Awareness of recent data on the use of erythropoietin-stimulating proteins  
• Effective use of granulocyte colony-stimulating factor may allow continuation of therapy to achieve optimal benefit  
• Implementation of a patient education and treatment plan for monitoring of blood counts, review of reportable signs and symptoms and early intervention to reduce treatment delays or dose modifications |
| Management of thromboembolic events  
*Rome et al, 2008*  | • Decreased incidence of VTE  
• Reduction in treatment discontinuation or delay  
• Reduction in cost of anticoagulation monitoring | • Identification of predisposing risk factors  
• Initiate aspirin therapy for patients on low-dose dexamethasone and lenalidomide with no high-risk factors  
• Full anticoagulation therapy is recommended for patients with increased risk or development of thrombosis while on treatment |
| Management of peripheral neuropathy | Tariman et al, 2008 | • Continuation of effective therapies  
• Improvement in QOL  
• Increased patient productivity  
• Reduction in pain associated with peripheral neuropathy | • Complete baseline assessment of neuropathy is required  
• Assessment of individual lifestyle and the potential impact of neuropathy is necessary to minimize loss of function or decrease in QOL  
• Implications for the use of thalidomide or bortezomib  
• Familiarity with dose modifications or criteria for treatment continuation  
• Continued research for evaluation of strategies for the treatment and prevention of peripheral neuropathy associated with MM therapy  
• Familiarity with toxicities associated with supportive care measures |
| Management of Gastrointestinal side effects | Smith et al, 2008 | • Improvement in QOL  
• Reduction in treatment delays or dose reductions | • Requires familiarity with the potential severity of treatment related toxicities, dose and schedule modifications, and prevention strategies  
• Appropriate use of antiemetic therapies  
• Familiarity with toxicities associated with antiemetic therapies |
| Management of steroid-associated side effects | Faiman et al, 2008 | • Improvement in QOL  
• Reduction in infectious complications  
• Reduction in thromboembolic events | • Requires familiarity with common toxicities associated with chronic steroid use and appropriate monitoring and treatment guidelines  
• Patient education for reportable signs and symptoms  
• Careful assessment for infection, hyperglycemia, proximal muscle weakness, adrenal insufficiency, and psychological toxicities |
| Management of bone disease |  | • Improvement in QOL  
• Reduction in incidence of osteonecrosis or renal impairment | • Requires familiarity with common toxicities associated with administration of bisphosphonates  
• Dental evaluation prior to treatment is recommended  
• Patient and family education for reportable signs and symptoms |
| Improved communication between providers and patients | Electronic medical Records  
Patient and caregiver education | • Reduction of drug-drug interactions, contraindicated interventions, or duplication of services  
• Improved patient satisfaction | • Continued compliance with the Health Information Privacy Protection Act (HIPPA)  
• Documentation must be timely and complete with inclusion of treatment and symptom management recommendations  
• Provider (cross specialties), patient, and family education is essential throughout the treatment continuum |
| Patient satisfaction and quality of life | Incorporation of patient reported outcomes in post-marketing analysis of new therapies | • Evaluation of a population more representative of the general population  
• Opportunity to refine therapies and monitoring strategies beyond the clinical trial design | • Minimize time spent in the health care system vs normal daily activities  
• Requires awareness of out-of-pocket expenses for the patient, including co-pay, prescription costs, gas, housing, time off work for patient and caregiver, cost of or loss of insurance due to treatment schedule or toxicity, intensity of monitoring requirements |

Adapted from Kurtin. Multidisciplinary Cancer Care. 2008.  
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Sample Criteria for Defining Oncology Drug Benefits

- Stratify guidelines (eg, NCCN) by costs and survivability rates to define preferred protocols
- Develop a standardized Plan of Care with reimbursement aligned with each preferred protocol
  - Position cognitive services and clinical outcomes as the primary basis for payment
- Encourage use of preferred protocols and products via a tiered oncology benefit paradigm
- Reduce large variations in the late stages of care, particularly during last-effort salvage therapy
  - Offer incentives to providers to discuss treatment options and costs with the patient and family

Charles BM. *Oncology 2011: today's payer strategies and tomorrow's market innovations*. Specialty Pharmacy Times. Published Online: December 5, 2011.
Categories of Multiple Myeloma Supportive Care

• Bone health and disease
  – Bony manifestations develop in 85% of patients and negatively impact on quality of life and performance status.
• Hypercalcemia
  – Excess bone resorption can lead to increased release of calcium into the blood.
• Renal Dysfunction
  – Both acute and chronic renal dysfunction can develop due to hypercalcemia.
• Pain
  – Bone pain related to multiple lytic lesions is common clinical presentation of MM.
• Peripheral Neuropathy
  – Causes numbness, pain, weakness in the extremities and negatively impacts coordination. It can be severe and sometimes debilitating.
• Infection
  – Infections due to suppressed immune function are the leading cause of death in MM.
• Anemia
  – 70% of MM patients have anemia (median hemoglobin at diagnosis: ~10.5 g/dL).
• Thrombosis
  – MM increases the risk of venous and arterial thrombosis. Treatment with thalidomide or lenalidomide + dexamethasone or multi-agent chemotherapy can increase risk.
• Hyperviscosity
  – Results from increased cellular blood components (typically white or red blood cells) due to myeloproliferative disorders such as MM.

Listing of Patient and Care Manager Resources

American Cancer Society
1-800-ACS-2345 (1-800-227-2345); www.cancer.org

Association of Cancer Online Resources
1-212-226-5525; www.acor.org

*CancerCare, Inc.*
1-800-813-HOPE (1-800-813-4673); www.cancercare.org

Chronic Disease Fund
1-877-968-7233; www.cdfund.org

International Myeloma Foundation
1-800-452-CURE (1-800-452-2873); www.myeloma.org

The Leukemia & Lymphoma Society
1-800-955-4572; www.leukemia-lymphoma.org

Multiple Myeloma Research Foundation
1-203-229-0464; www.multiplemyeloma.org

National Cancer Institute (US National Institutes of Health)
1-800-4-CANCER (1-800-422-6237); www.cancer.gov

The Myelodysplastic Syndromes Foundation
1-800-MDS-0839 (1-800-637-0839); www.mds-foundation.org

National Comprehensive Cancer Network (clinical practice and treatment guidelines)
www.nccn.org

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