Comparative Clinical Effectiveness

For adults with multiple myeloma who are not currently on maintenance treatment, are not being considered for stem cell transplant, and whose disease has not responded to, or has relapsed following, at least one line of therapy:

1. Is the evidence adequate to demonstrate that the net health benefit of treatment of each regimen listed below is greater than that of treatment with lenalidomide and dexamethasone?
   a. carfilzomib with lenalidomide and dexamethasone (CFZ+LEN+DEX)
   b. elotuzumab with lenalidomide and dexamethasone (ELO+LEN+DEX)
   c. ixazomib with lenalidomide and dexamethasone (IX+LEN+DEX)

2. Is the evidence adequate to distinguish the net health benefit of treatment between these three regimens?
   - carfilzomib with lenalidomide and dexamethasone (CFZ+LEN+DEX)
   - elotuzumab with lenalidomide and dexamethasone (ELO+LEN+DEX)
   - ixazomib with lenalidomide and dexamethasone (IX+LEN+DEX)

For adults with multiple myeloma who are not currently on maintenance treatment, are not being considered for stem cell transplant, and whose disease has not responded to or has relapsed following two or more lines of therapy:

3. Is the evidence adequate to demonstrate that the net health benefit of treatment with the regimens listed below is greater than that of comparator treatment listed?
   a. carfilzomib with lenalidomide and dexamethasone (CFZ+LEN+DEX) vs. LEN+DEX
   b. elotuzumab with lenalidomide and dexamethasone (ELO+LEN+DEX) vs. LEN+DEX
   c. ixazomib with lenalidomide and dexamethasone (IX+LEN+DEX) vs. LEN+DEX
   d. panobinostat with bortezomib and dexamethasone (PAN+BOR+DEX) vs. BOR+DEX

Voting questions do not include a question regarding pomalidomide due to the difference in populations and the comparator not being widely used in practice.
4. Is the evidence adequate to distinguish the net health benefit of treatment between these regimens:
   - carfilzomib with lenalidomide and dexamethasone (CFZ+LEN+DEX)
   - elotuzumab with lenalidomide and dexamethasone (ELO+LEN+DEX)
   - ixazomib with lenalidomide and dexamethasone (IX+LEN+DEX)

5. For adults with relapsed and/or refractory multiple myeloma who are not currently on maintenance treatment and are not being considered for stem cell transplant, is the evidence adequate to determine the net health benefit of treatment with daratumumab in patients with less than three prior lines of therapy?

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**Comparative Care Value**

For adults with multiple myeloma who are not currently on maintenance treatment, are not being considered for stem cell transplant, and whose disease has not responded to, or has relapsed following, at least one line of therapy:

6. Given the available evidence, what is the care value of treatment with each of the following three regimens listed below versus treatment with lenalidomide and dexamethasone:
   - carfilzomib with lenalidomide and dexamethasone (CFZ+LEN+DEX):
     a. Low  b. Intermediate  c. High
   - elotuzumab with lenalidomide and dexamethasone (ELO+LEN+DEX):
     a. Low  b. Intermediate  c. High
   - ixazomib with lenalidomide and dexamethasone (IX+LEN+DEX):
     a. Low  b. Intermediate  c. High
For adults with multiple myeloma who are not currently on maintenance treatment, are not being considered for stem cell transplant, and whose disease has not responded to or has relapsed following two or more lines of therapy:

7. Given the available evidence, what is the care value of treatment with any of the regimens listed below versus that of comparator treatment (either lenalidomide and dexamethasone OR bortezomib and dexamethasone):

- carfilzomib with lenalidomide and dexamethasone (CFZ+LEN+DEX):
  a. Low  b. Intermediate  c. High

- elotuzumab with lenalidomide and dexamethasone (ELO+LEN+DEX):
  a. Low  b. Intermediate  c. High

- ixazomib with lenalidomide and dexamethasone (IX+LEN+DEX):
  a. Low  b. Intermediate  c. High

- panobinostat with bortezomib and dexamethasone (PAN+BOR+DEX):
  a. Low  b. Intermediate  c. High